Figure 1.

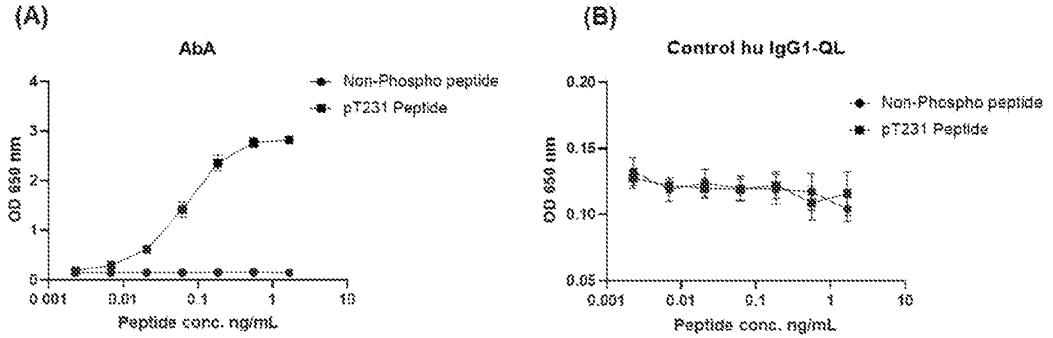

(A)
AbA
Non-Phospho peptide
pT231 Peptide
OD 650 nm
Peptide conc. ng/mL
(B)
Control hu IgG1-QL
Non-Phospho peptide
pT231 Peptide
OD 650 nm
Peptide conc. ng/mL

Figure 2.

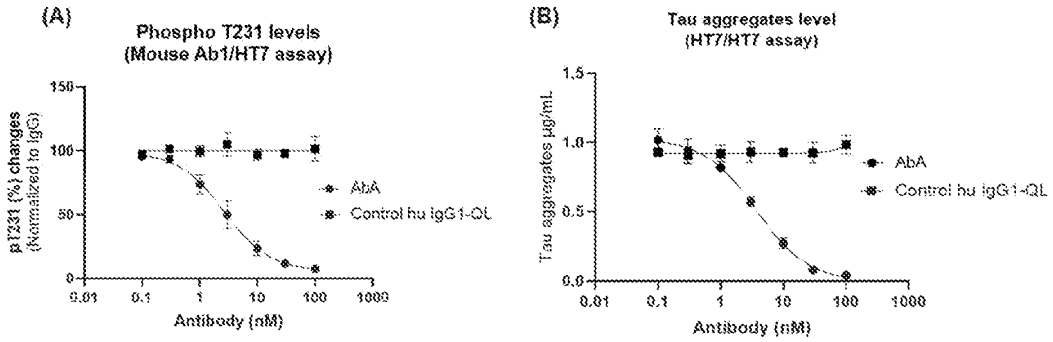

(A)
Phospho T231 levels
(Mouse Ab1/HT7 assay)
pT231 (%) changes
(Normalized to IgG)
150
100
50
0
0.01
0.1
1
10
100
1000
Antibody (nM)
AbA
Control hu IgG1-QL
(B)
Tau aggregates level
(HT7/HT7 assay)
Tau aggregates µg/mL
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
Antibody (nM)
AbA
Control hu IgG1-QL

Figure 3.

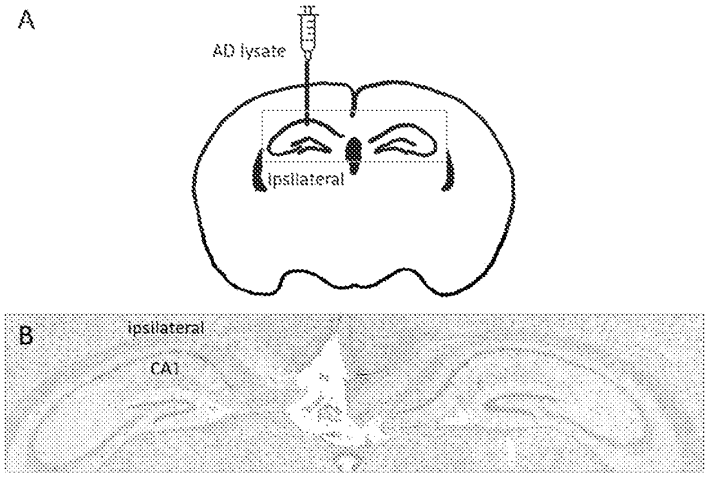
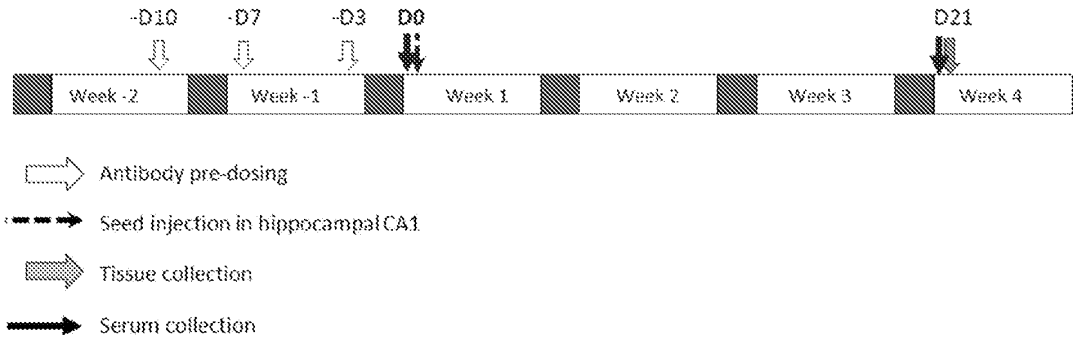


Figure 4.


-D10
-D7
-D3
D0
D21
Week -2
Week -1
Week 1
Week 2
Week 3
Week 4
Antibody pre-dosing
Seed injection in hippocampal CA1
Tissue collection
Serum collection

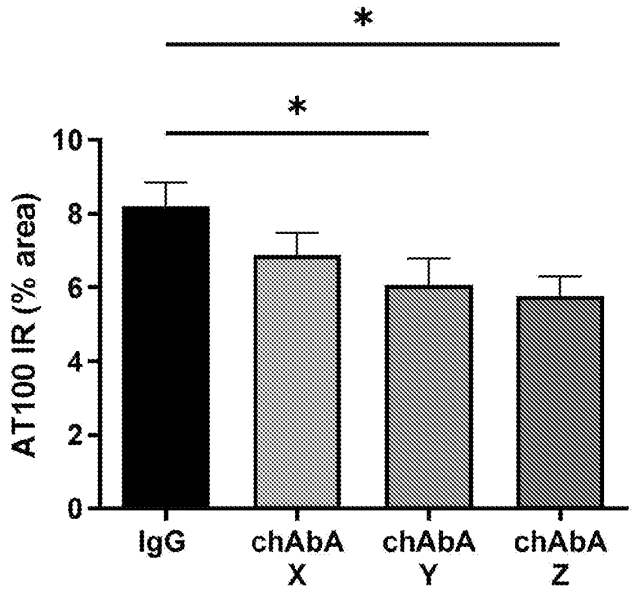

*
*
AT100 IR (% area)
10
8
6
4
2
0
IgG
chAbA X
chAbA Y
chAbA Z

Figure 5A.

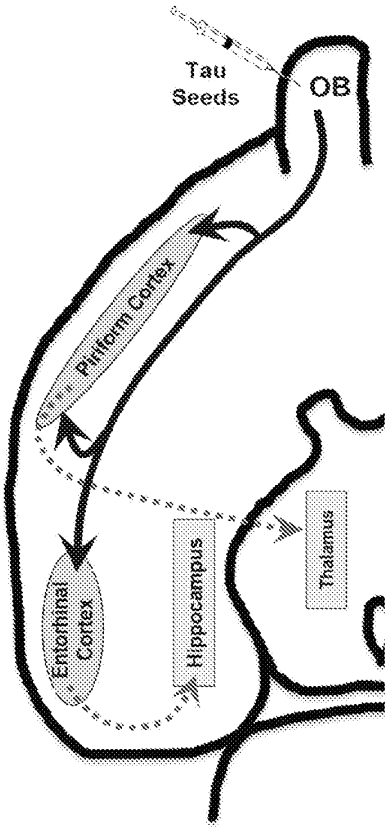

Tau
Seeds
OB
Piriform Cortex
Thalamus
Hippocampus
Entorhinal
Cortex

Figure 5B.

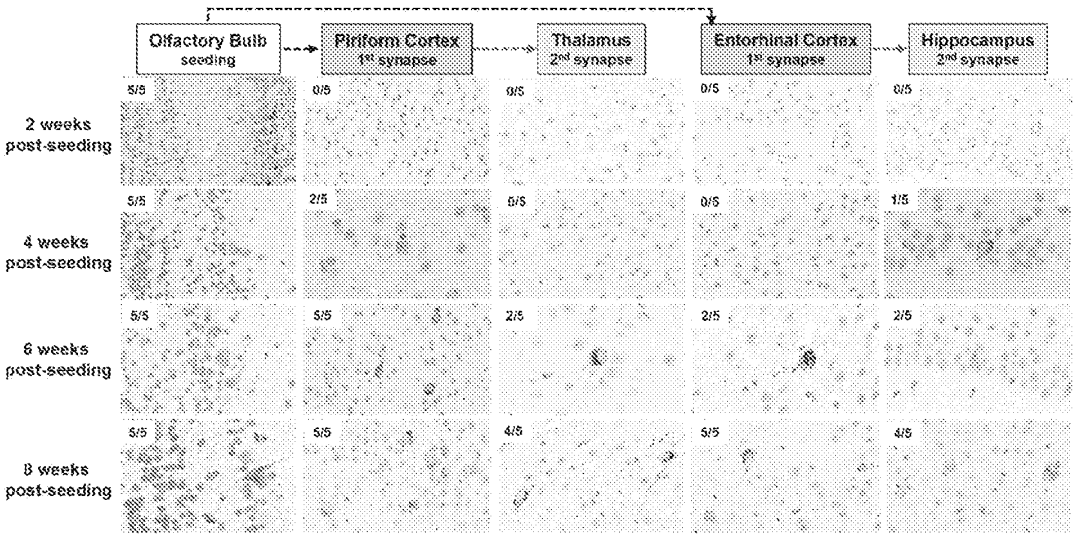

Olfactory Bulb
seeding
Piriform Cortex
1st synapse
Thalamus
2nd synapse
Entorhinal Cortex
1st synapse
Hippocampus
2nd synapse
2 weeks post-seeding
4 weeks post-seeding
6 weeks post-seeding
8 weeks post-seeding
5/5
0/5
0/5
0/5
0/5
5/5
2/5
5/5
0/5
1/5
5/5
5/5
2/5
2/5
2/5
5/5
5/5
4/5
5/5
4/5

Figure 6A.

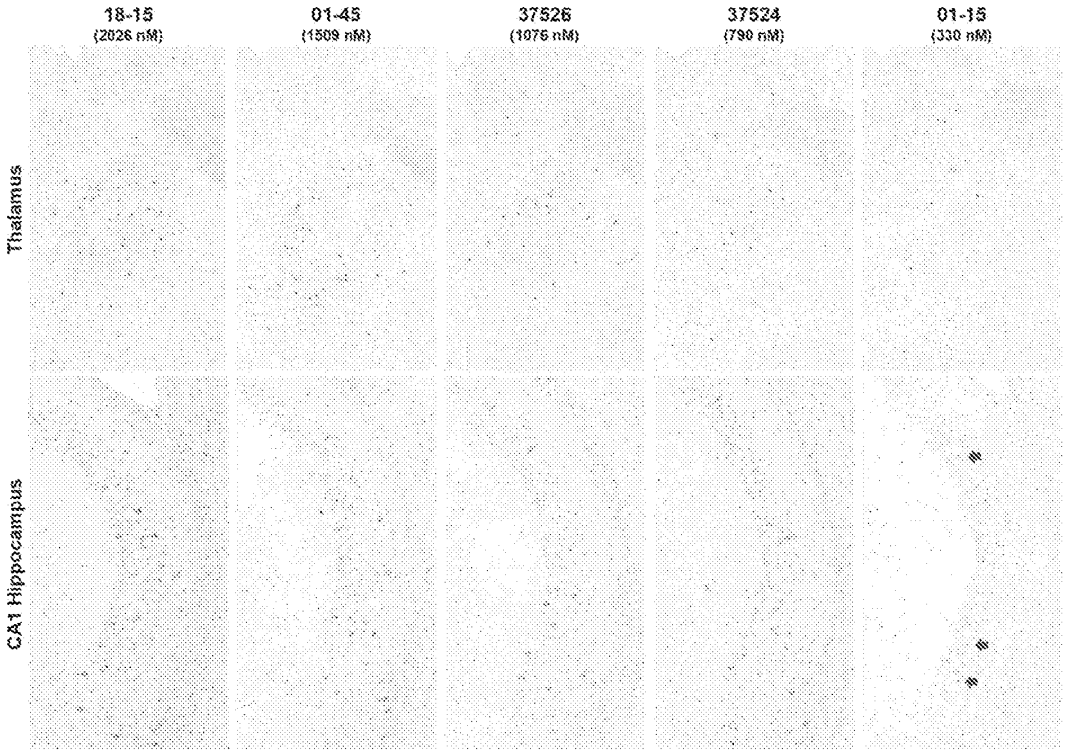

18-15
(2026 nM)
01-45
(1509 nM)
37526
(1076 nM)
37524
(790 nM)
01-15
(330 nM)
Thalamus
CA1 Hippocampus

Figure 6B.

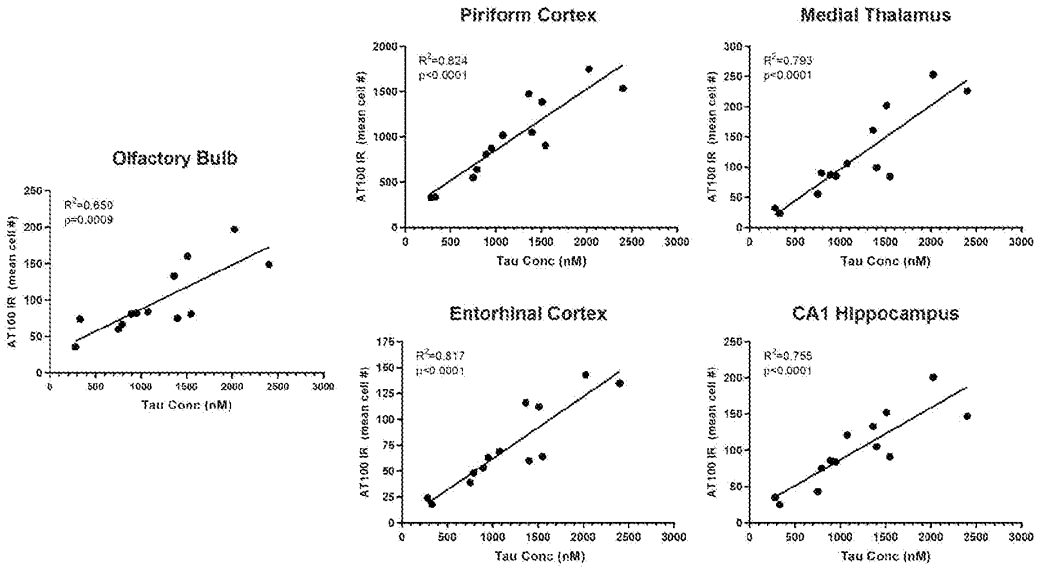
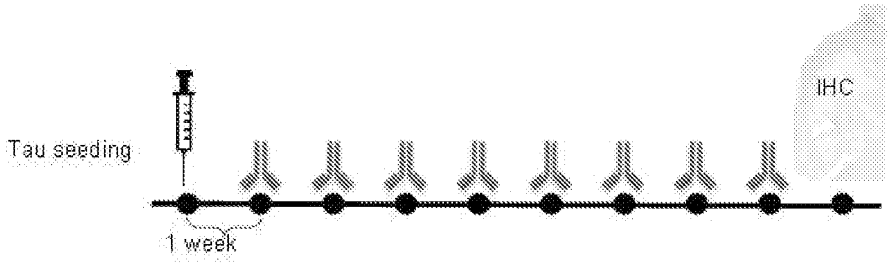

Olfactory Bulb
R²=0.650
p=0.0009
AT100 IR (mean cell #)
Tau Conc (nM)
Piriform Cortex
R²=0.824
p<0.0001
AT100 IR (mean cell #)
Tau Conc (nM)
Medial Thalamus
R²=0.793
p<0.0001
AT100 IR (mean cell #)
Tau Conc (nM)
Entorhinal Cortex
R²=0.817
p<0.0001
AT100 IR (mean cell #)
Tau Conc (nM)
CA1 Hippocampus
R²=0.755
p<0.0001
AT100 IR (mean cell #)
Tau Conc (nM)

Figure 7A.




chAbA: Dose W, X, Y, and Z, i.p.

Figure 7B.

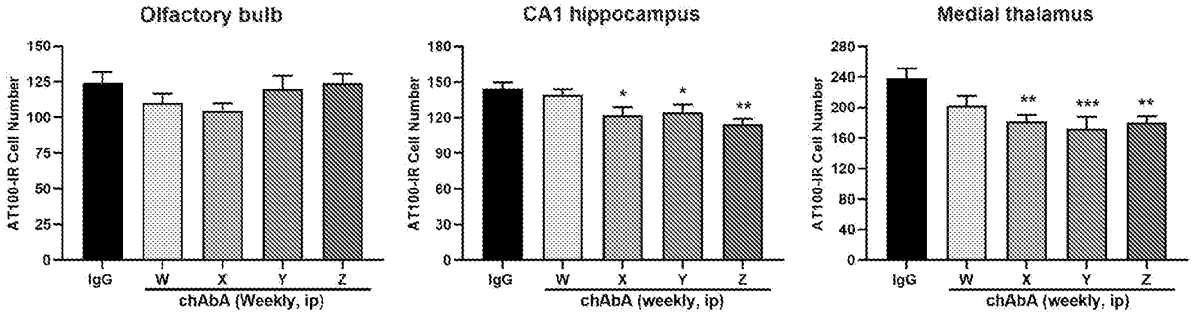

Olfactory bulb
AT100-IR Cell Number
150
125
100
75
50
25
0
IgG
W
X
Y
Z
chAbA (Weekly, ip)
CA1 hippocampus
AT100-IR Cell Number
180
150
120
90
60
30
0
*
*
**
IgG
W
X
Y
Z
chAbA (weekly, ip)
Medial thalamus
AT100-IR Cell Number
280
240
200
160
120
80
40
0
**
***
**
IgG
W
X
Y
Z
chAbA (weekly, ip)

Figure 8

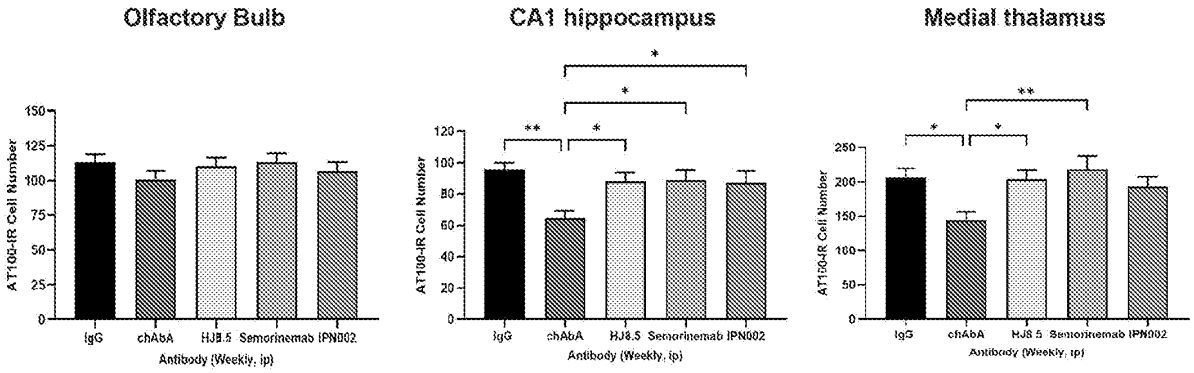

Olfactory Bulb
AT100-IR Cell Number
150
125
100
75
50
25
0
IgG
chAbA
HJ8.5
Semorinemab
IPN002
Antibody (Weekly, ip)
CA1 hippocampus
AT100-IR Cell Number
120
100
80
60
40
20
0
**
*
*
*
IgG
chAbA
HJ8.5
Semorinemab
IPN002
Antibody (Weekly, ip)
Medial thalamus
AT100-IR Cell Number
250
200
150
100
50
0
**
*
*
IgG
chAbA
HJ8.5
Semorinemab
IPN002
Antibody (Weekly, ip)

Figure 9A

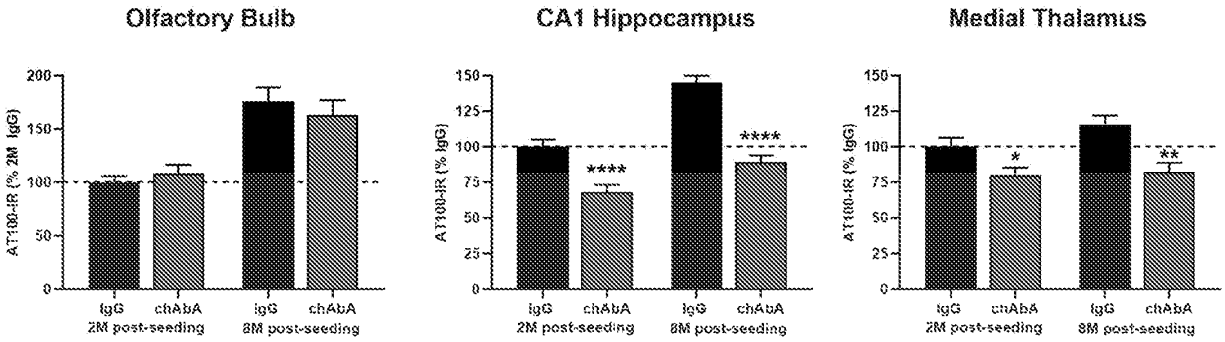
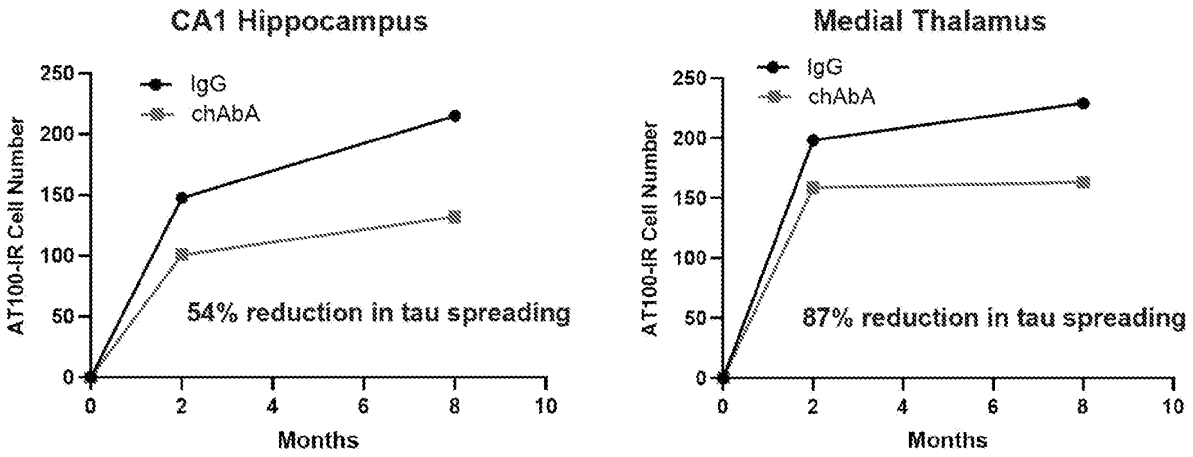

Olfactory Bulb
CA1 Hippocampus
Medial Thalamus
AT100-IR (% 2M IgG)
AT100-IR (% IgG)
IgG
chAbA
2M post-seeding
8M post-seeding
****
*
**

Figure 9B


CA1 Hippocampus
IgG
chAbA
AT100-IR Cell Number
250
200
150
100
50
0
0
2
4
6
8
10
Months
54% reduction in tau spreading
Medial Thalamus
IgG
chAbA
AT100-IR Cell Number
250
200
150
100
50
0
0
2
4
6
8
10
Months
87% reduction in tau spreading