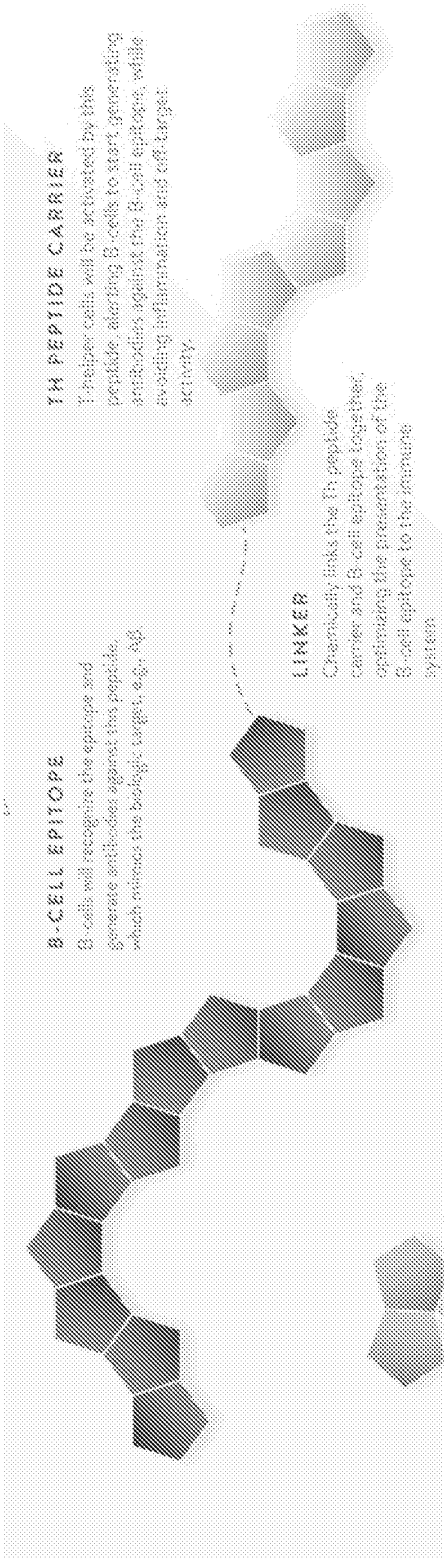
Fig. 1


B-CELL EPITOPE
B cells will recognize the epitope and generate antibodies against this peptide, which mimic the biologic target, e.g. Aβ
TH PEPTIDE CARRIER
T-helper cells will be activated by this peptide, alerting B cells to start generating antibodies against the B-cell epitope, while eliciting inflammation and off-target activity
LINKER
Chemically links the Th peptide carrier and B-cell epitope together, allowing the presentation of the B-cell epitope to the immune system

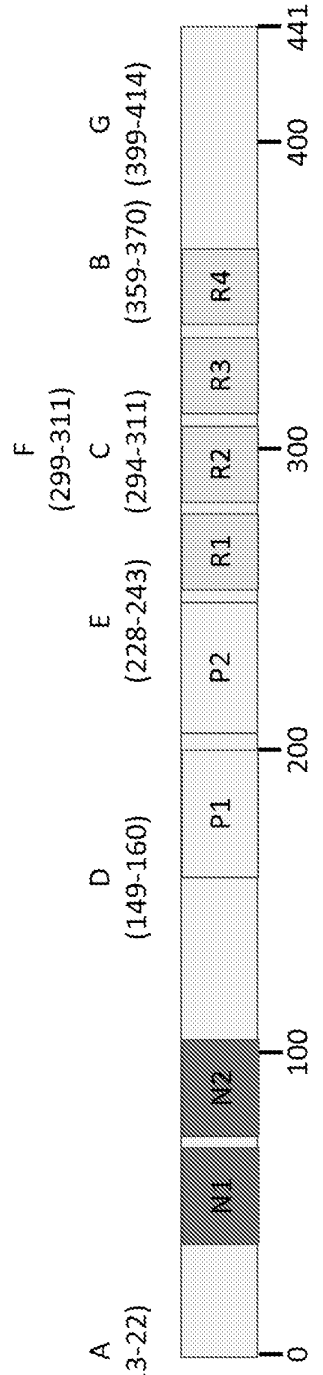
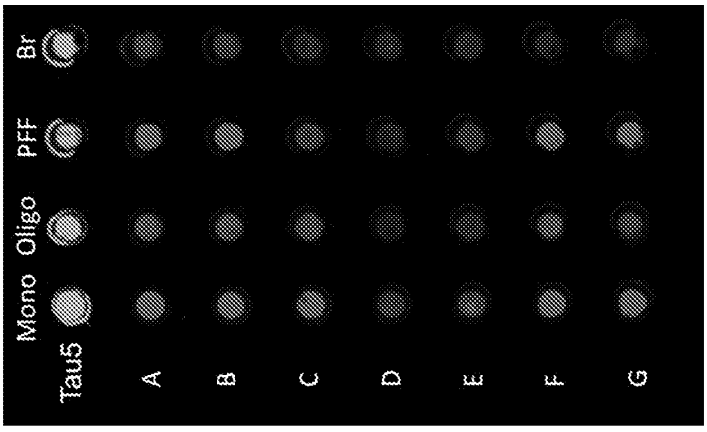
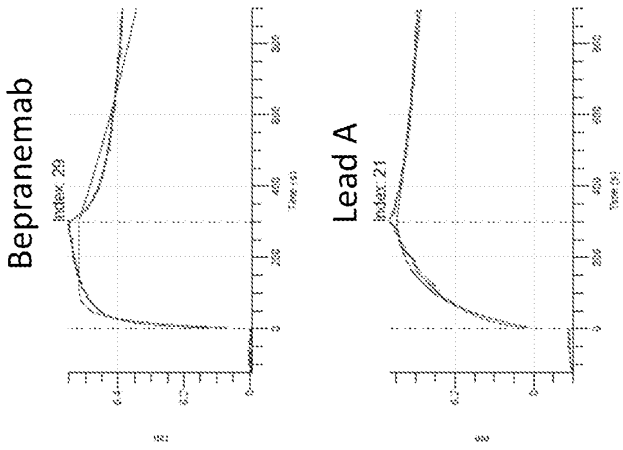

A (13-22)
D (149-160)
E (228-243)
F (299-311)
C (294-311)
B (359-370)
G (399-414)
N1
N2
P1
P2
R1
R2
R3
R4
0
100
200
300
400
441

Fig. 2

A

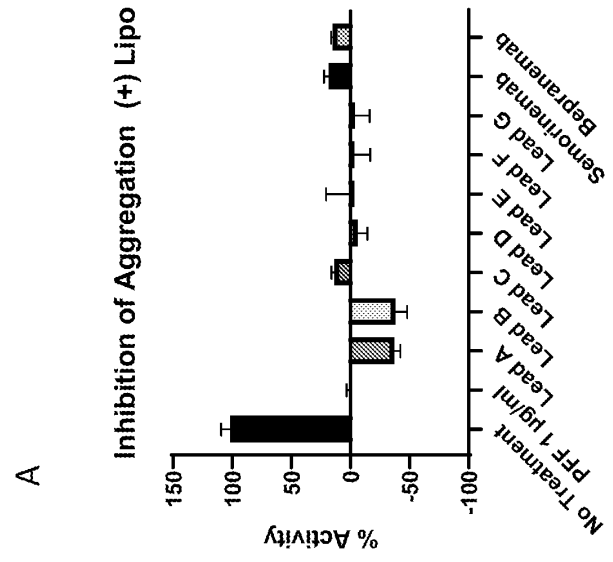


B



PFF					
Rank	Ab	KD (M)	Ab	Koff (1/s)
1	Bep	1.32E-09	A	3.22E-04
2	A	8.03E-09	B	5.25E-04
3	E	1.09E-08	G	5.53E-04
4	F	1.31E-08	Bep	6.88E-04
5	B	1.32E-08	F	7.02E-04
6	G	1.34E-08	E	7.26E-04
7	C	1.50E-08	C	8.47E-04
8	D	2.81E-08	G	1.19E-03

Fig. 3


A
Inhibition of Aggregation (+) Lipo
% Activity
150
100
50
0
-50
-100
No Treatment
PFF 1 µg/ml
Lead A
Lead B
Lead C
Lead D
Lead E
Lead F
Lead G
Semorinemab
Bepranemab

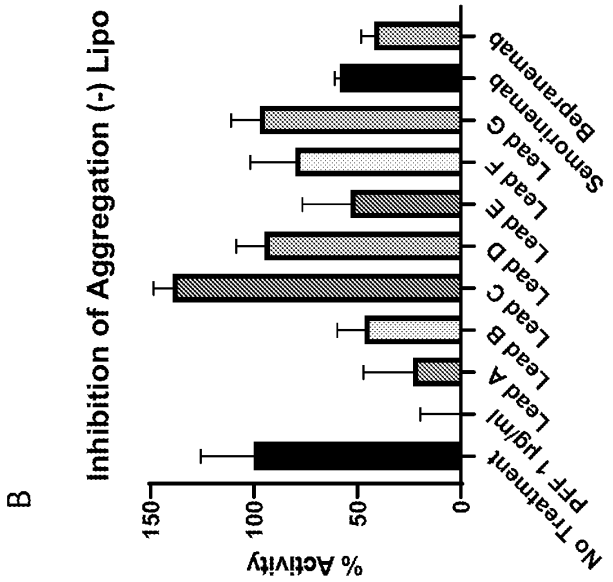
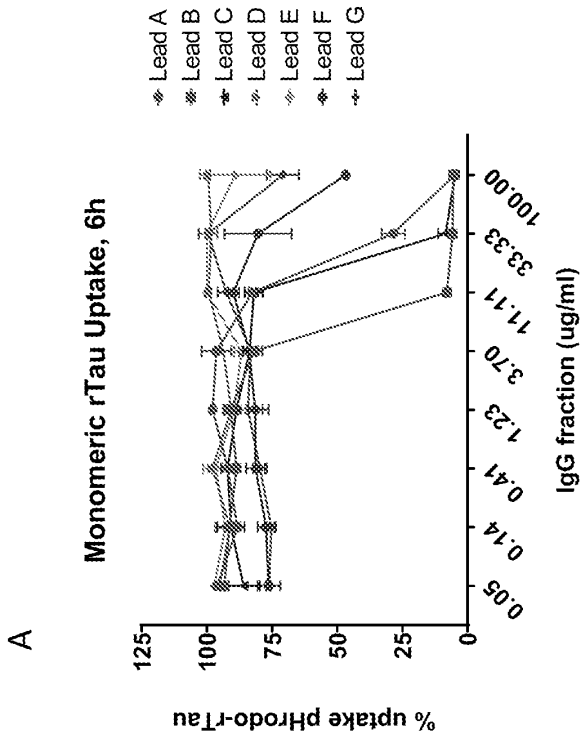

B
Inhibition of Aggregation (-) Lipo
% Activity
150
100
50
0
No Treatment
PFF 1 µg/ml
Lead A
Lead B
Lead C
Lead D
Lead E
Lead F
Lead G
Semorinemab
Bepranemab

Fig. 4


A
Monomeric rTau Uptake, 6h
% uptake pHrodo-rTau
125
100
75
50
25
0
0.05
0.14
0.41
1.23
3.70
11.11
33.33
100.00
IgG fraction (ug/ml)
Lead A
Lead B
Lead C
Lead D
Lead E
Lead F
Lead G

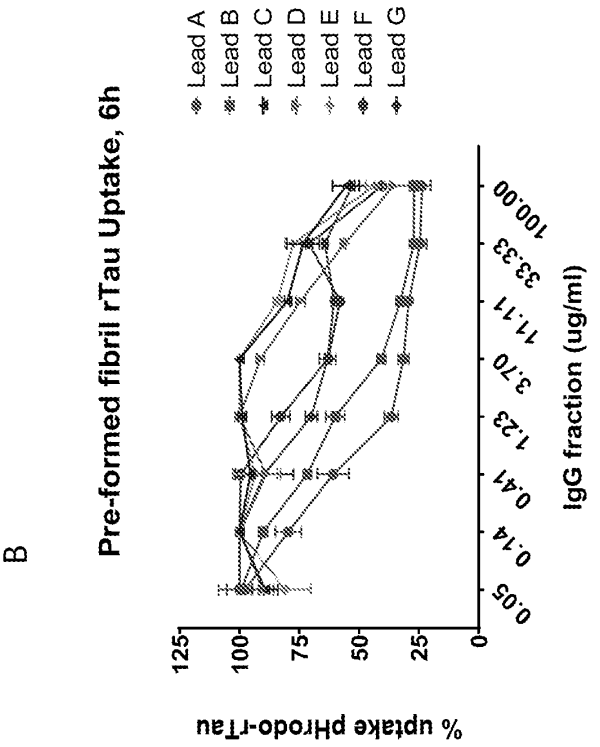

B
Pre-formed fibril rTau Uptake, 6h
% uptake pHrodo-rTau
125
100
75
50
25
0
0.05
0.14
0.41
1.23
3.70
11.11
33.33
100.00
IgG fraction (ug/ml)
Lead A
Lead B
Lead C
Lead D
Lead E
Lead F
Lead G

Fig. 5

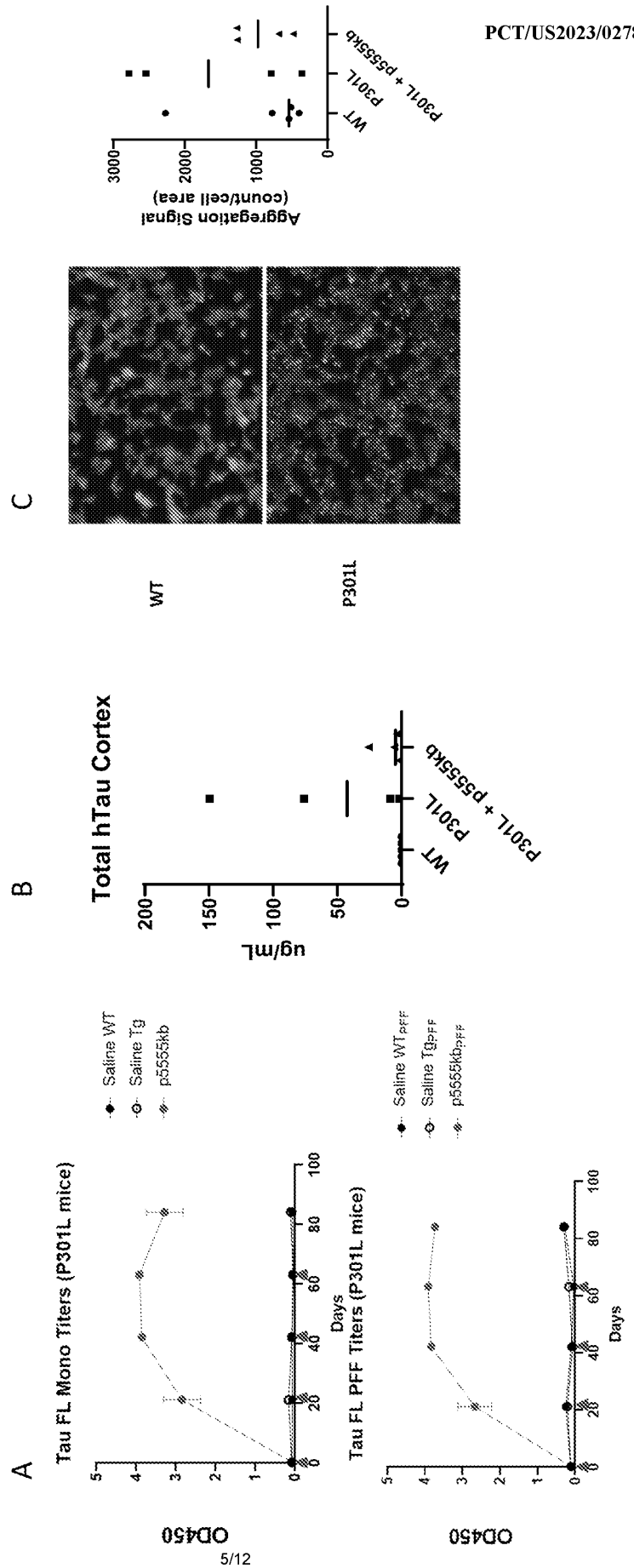
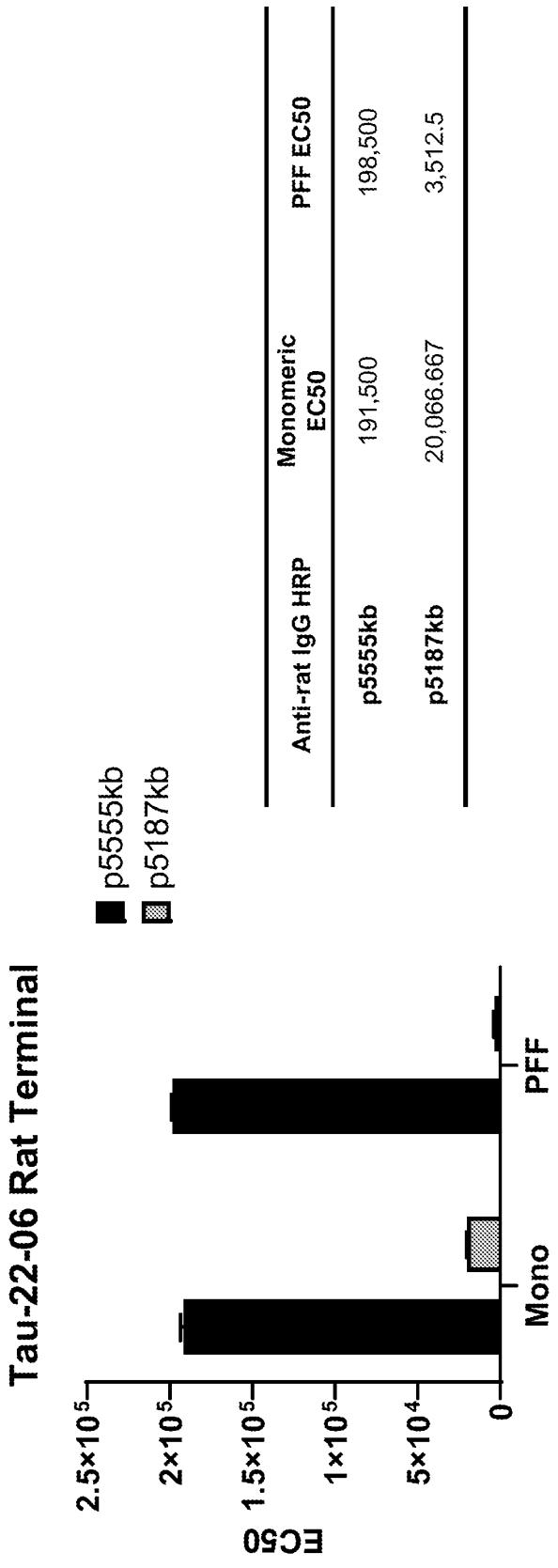

A
Tau FL Mono Titers (P301L mice)
Saline WT
Saline Tg
p5555kb
OD450
Days
Tau FL PFF Titers (P301L mice)
Saline WT PFF
Saline Tg PFF
p5555kb PFF
OD450
Days
B
Total hTau Cortex
ug/mL
WT
P301L
P301L + P5555kb
C
WT
P301L
Aggregation Signal
(count/cell area)
WT
P301L
P301L + P5555kb

Fig. 6



Anti-rat IgG HRP	Monomeric EC50	PFF EC50
p5555kb	191,500	198,500
p5187kb	20,066.667	3,512.5

Fig. 7

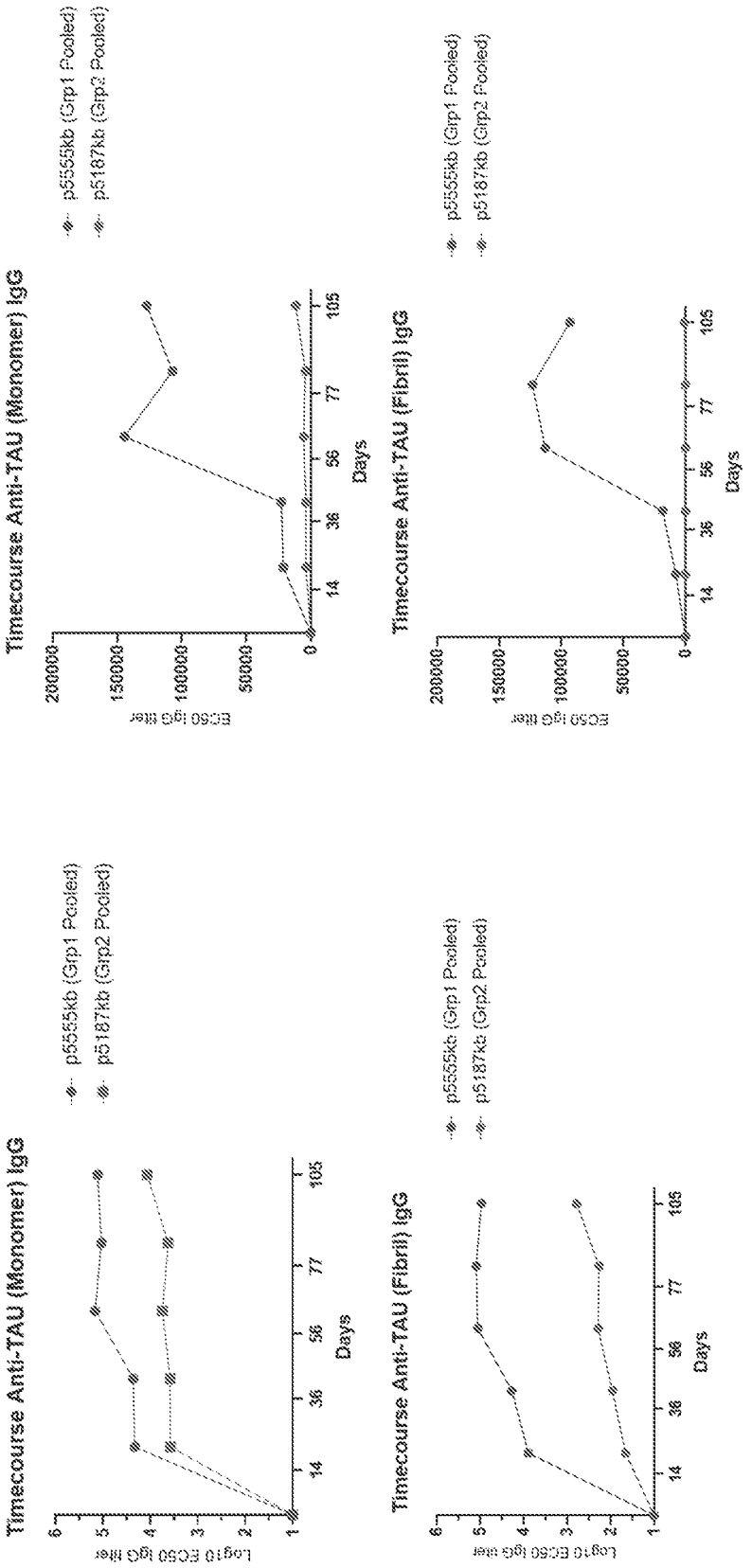

Timecourse Anti-TAU (Monomer) IgG
p5555kb (Grp1 Pooled)
p5187kb (Grp2 Pooled)
Log10 EC50 IgG titer
Days
Timecourse Anti-TAU (Fibril) IgG
p5555kb (Grp1 Pooled)
p5187kb (Grp2 Pooled)
Log10 EC50 IgG titer
Days
Timecourse Anti-TAU (Monomer) IgG
p5555kb (Grp1 Pooled)
p5187kb (Grp2 Pooled)
EC50 IgG titer
Days
Timecourse Anti-TAU (Fibril) IgG
p5555kb (Grp1 Pooled)
p5187kb (Grp2 Pooled)
EC50 IgG titer
Days

Fig. 8

- Additional Data:
  - Grp1-3 day 0, 21, 42, 63, 84, & 105 Anti-TAU (Monomer)
  - Dotted line equates to double the 1:100 pre-bleed O.D450nm value.

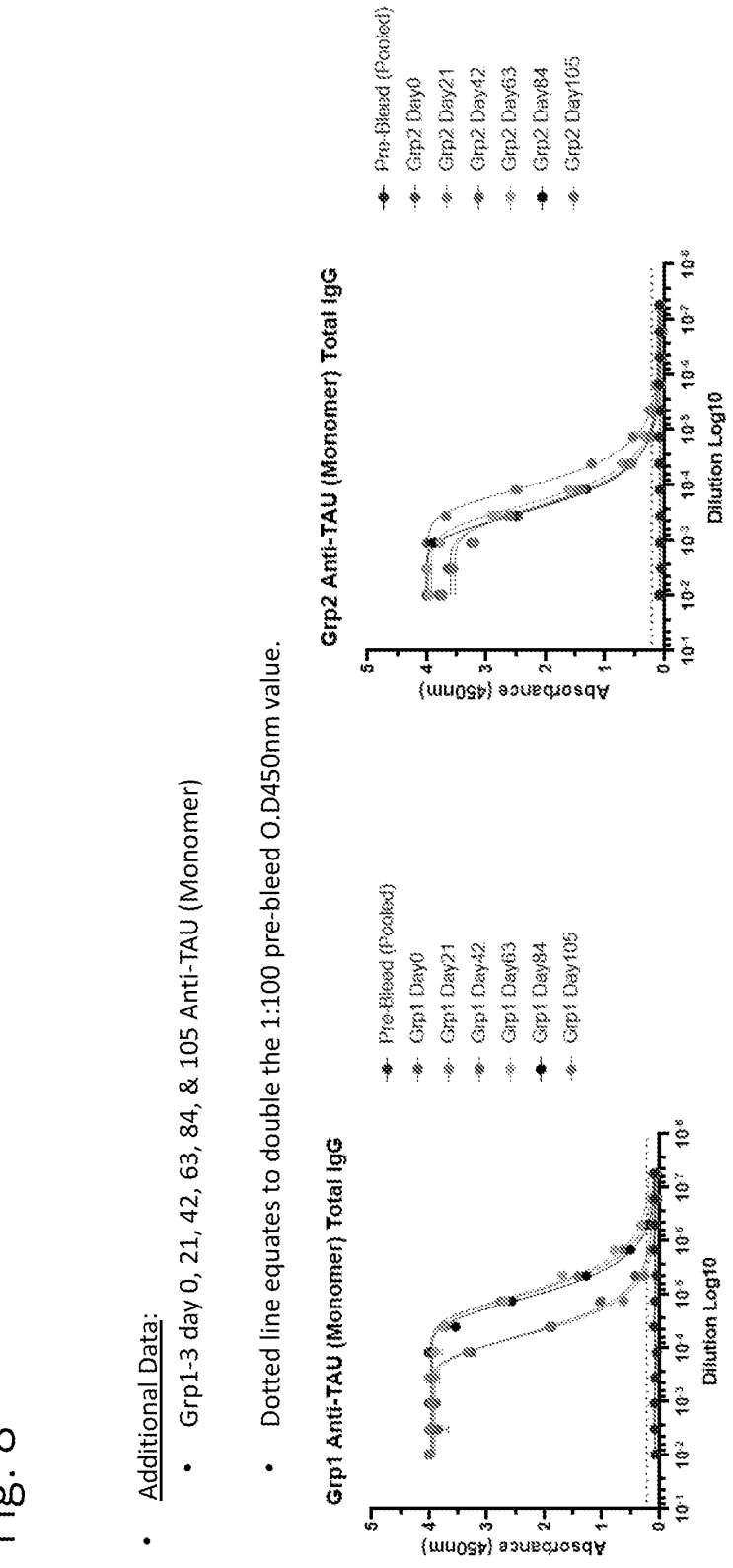
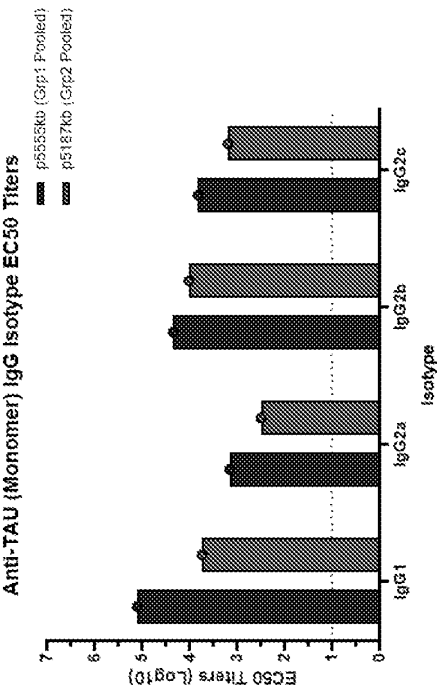


Fig. 9


Anti-TAU (Monomer) IgG Isotype EC50 Titers
p5555kb (Grp1 Pooled)
p5187kb (Grp2 Pooled)
EC50 Titers (Log10)
0
1
2
3
4
5
6
7
IgG1
IgG2a
IgG2b
IgG2c
Isotype

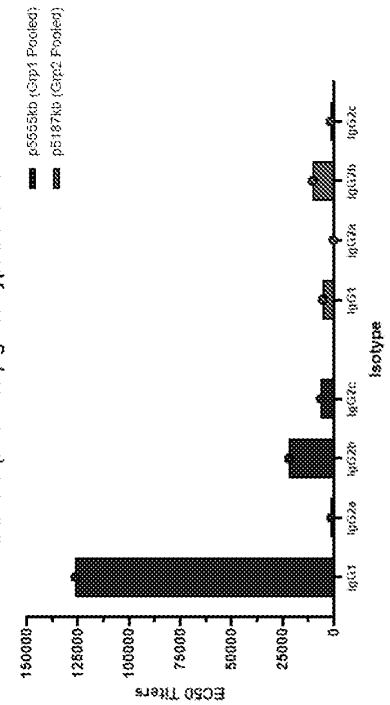
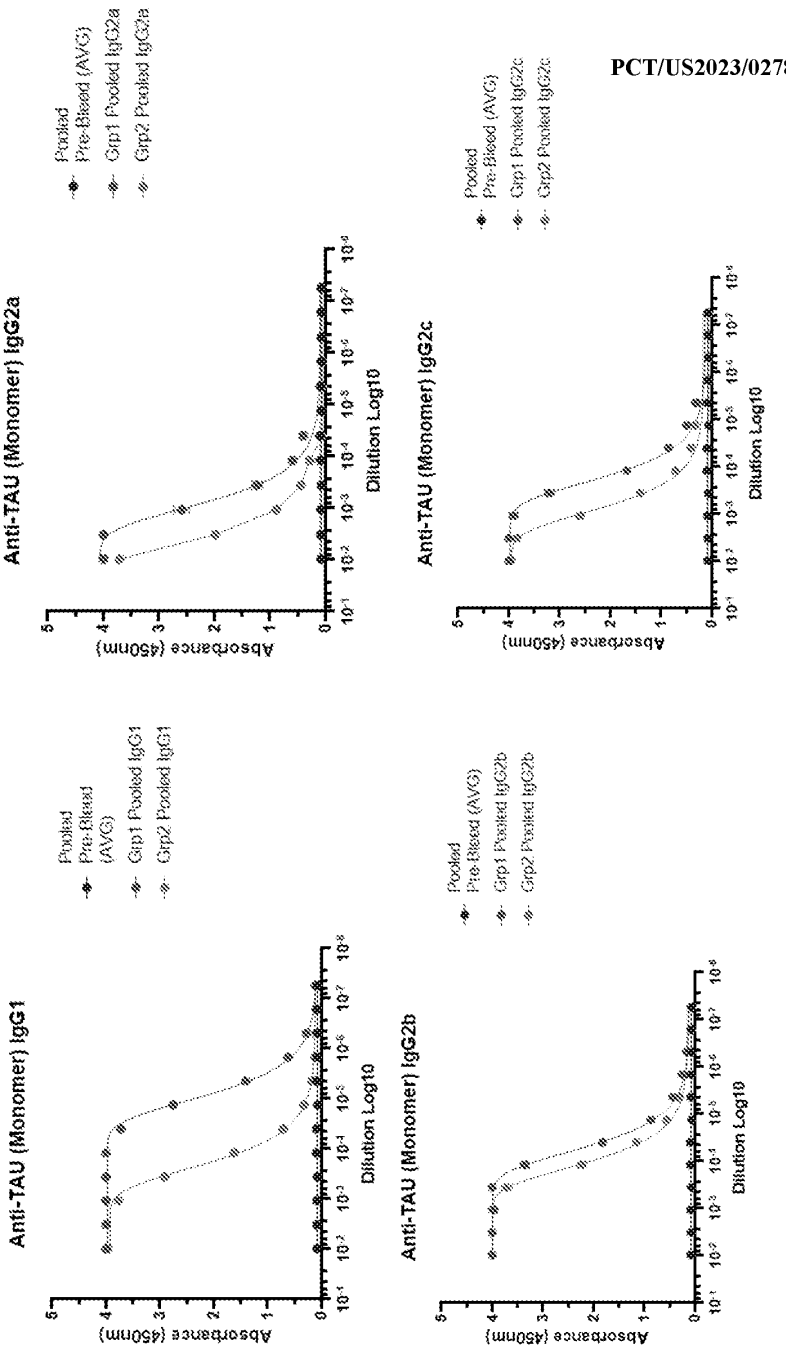
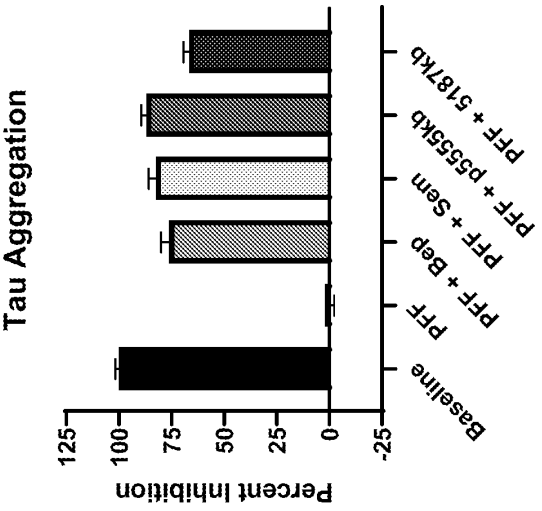

Anti-TAU (Monomer) IgG Isotype EC50 Titers
p5555kb (Grp1 Pooled)
p5187kb (Grp2 Pooled)
EC50 Titers
0
25000
50000
75000
100000
125000
150000
Isotype

Fig. 10



- Additional Data:
  - Grp1-3 day105 Anti-TAU (Monomer) IgG Isotypes IgG1, 2a, 2b, &2c
  - Dotted line equates to double the 1:100 pre-bleed O.D450nm value.


Tau Aggregation
Percent Inhibition
125
100
75
50
25
0
-25
Baseline
PFF
PFF + Bep
PFF + Sem
PFF + p5555kb
PFF + 5187kb

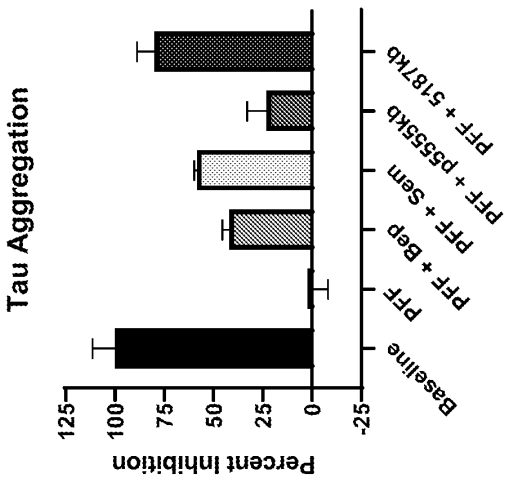
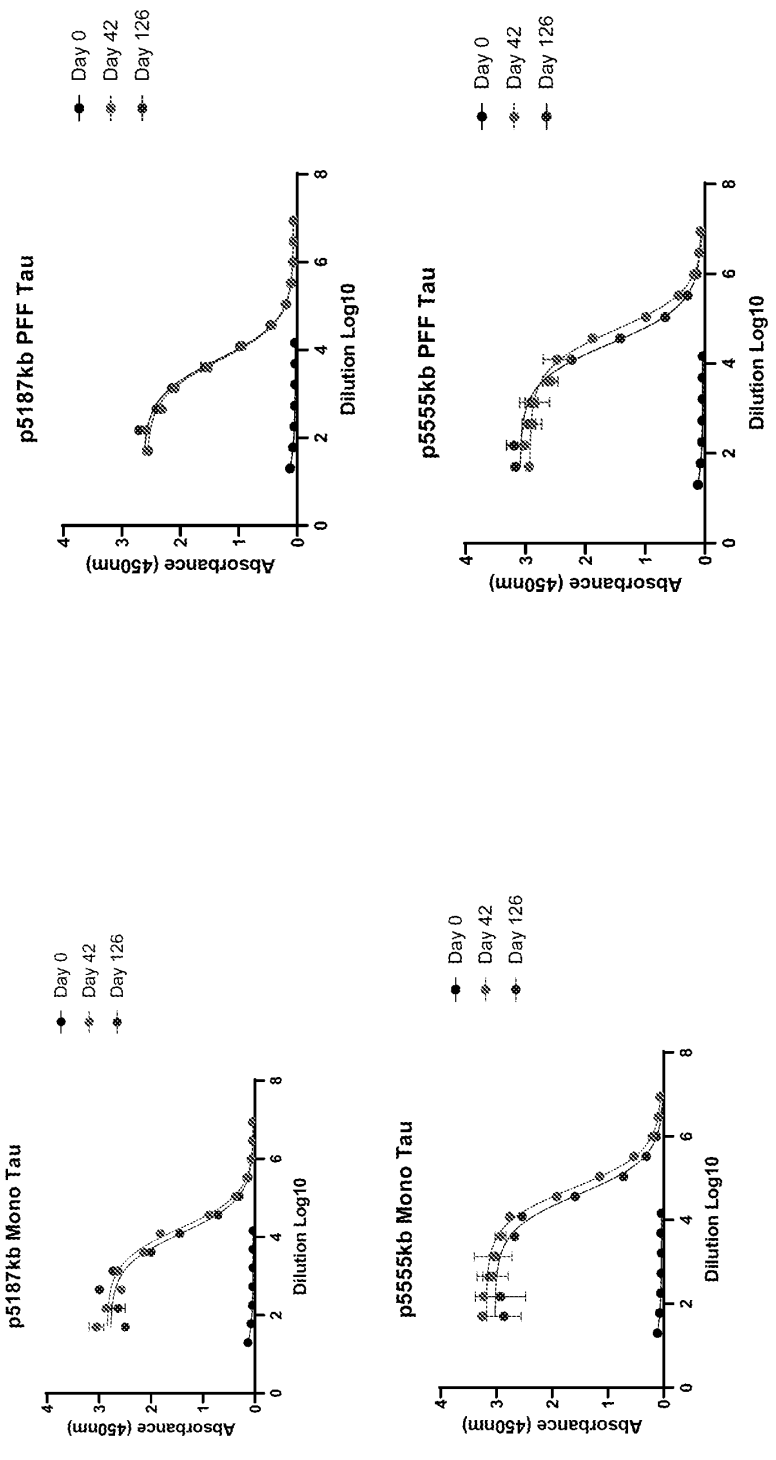

Tau Aggregation
Percent Inhibition
125
100
75
50
25
0
-25
Baseline
PFF
PFF + Bep
PFF + Sem
PFF + p5555kb
PFF + 5187kb

Fig. 11

Fig. 12


p5187kb PFF Tau
Day 0
Day 42
Day 126
Absorbance (450nm)
Dilution Log10
p5555kb PFF Tau
Day 0
Day 42
Day 126
Absorbance (450nm)
Dilution Log10
p5187kb Mono Tau
Day 0
Day 42
Day 126
Absorbance (450nm)
Dilution Log10
p5555kb Mono Tau
Day 0
Day 42
Day 126
Absorbance (450nm)
Dilution Log10