Top Line Results of Phase I Intravenous Trial for NPC

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Cyclo Therapeutics, Inc.

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Phase I Intravenous Trial with Trappsol® Cyclo™ Overview

A Phase I Study to Evaluate the Single and Multiple-dose Pharmacokinetics of Intravenous Trappsol® Cyclo™ (HPβCD) in Patients With NPC1 and the Effects of Dosing Upon Biomarkers of NPC Disease (NCT02939547)

- Randomized double blinded, parallel group study with no control to evaluate safety and tolerability of Trappsol® Cyclo™ in 12 subjects aged 18 years and older.
- Two doses studied: 1500 mg/kg and 2500 mg/kg
- Intravenous infusion over 8-9 hours every two weeks for 14 weeks
- All patients were enrolled at UCSF Benioff Children's Hospital Oakland with
  - Dr. Caroline Hastings and Dr. Benny Liu as Co-Principal Investigators

- Study was locked in May 2020
- Top Line results announced in May 2020
- Cyclo Therapeutics working on Clinical Study Report

Phase I Intravenous Trial with Trappsol® Cyclo™ Overview

Demographics of enrolled subjects:

- Age range: 18 years to 69 years
- Gender: 8 male, 5 female
- Ethnicity: 1 Hispanic or Latino, 12 Not Hispanic or Latino
- Race: 11 White, 2 Asian

Safety & Tolerability – Phase I trial

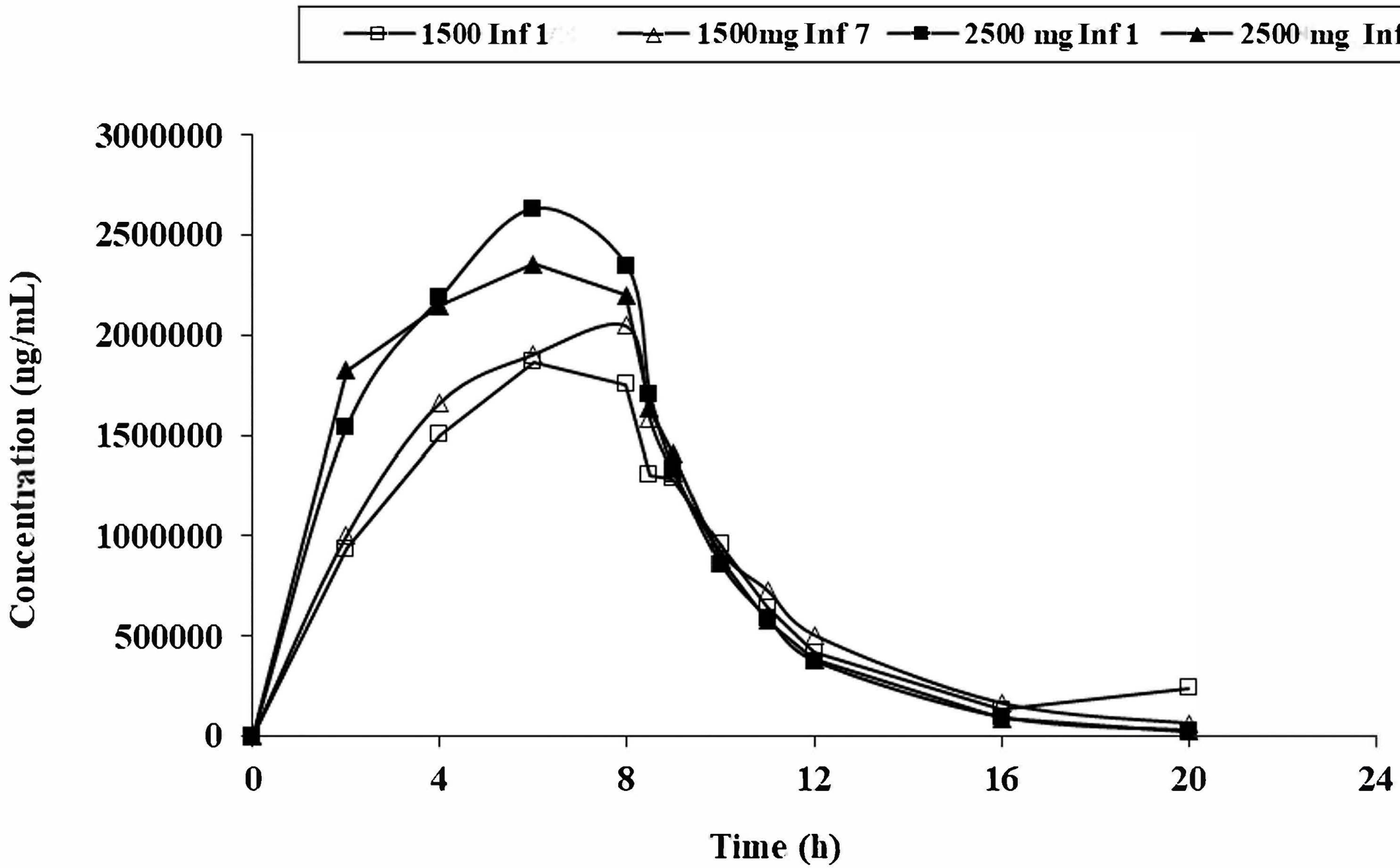
Adverse Event (AE) by Treatment group	Low-dose (1500 mg/kg)	High-dose (2500 mg/kg)
Total Number AE's	13	31
Total Number TEAE's (Treatment-emergent AE's)	13	27
Total Number SAE's (Serious AE's)	0	8
Total Number Treatment-emergent SAE's	0	6

Overall, an excellent Safety and Tolerability profile.

All Serious Adverse Events (SAEs) were in the high-dose group.

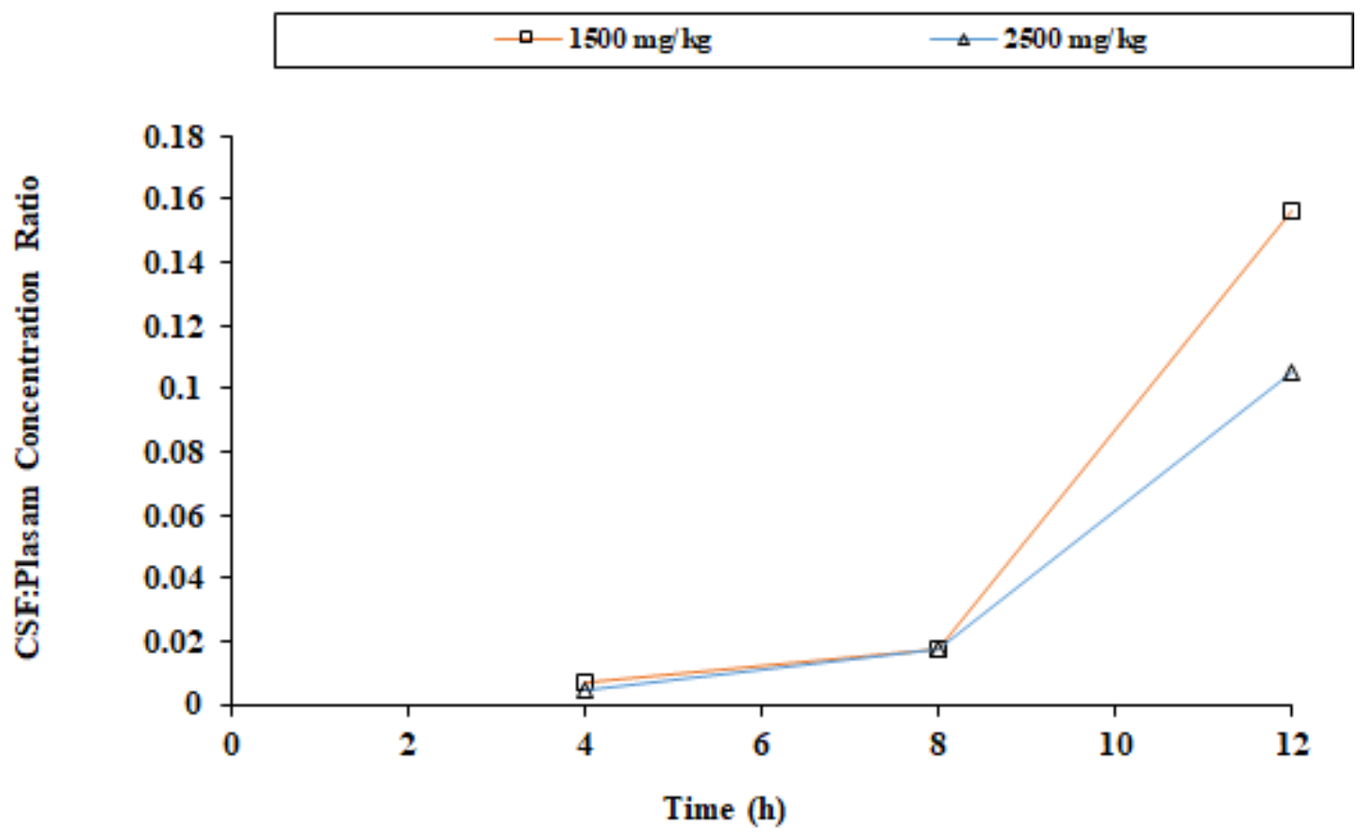
3 SAEs related to hearing - but none were permanent and none were perceived by patients or caregivers.

Pharmacokinetics: Plasma



Pharmacokinetics: Plasma and CSF Summary

- Trappsol ® Cyclo ™ acted similarly in the body after 1st infusion and after 7th infusion: No drug accumulation after multiple infusions.
- Rapid clearance: Half-life 2 hrs.
- Time to reach Cmax between 6 hrs and 8 hrs.
- Trappsol® Cyclo™ crosses the blood-brain-barrier: at 8hrs post the start of infusion the CSF:plasma ratio is 2% while the ratio is between 11% and 16% at 12 hrs, suggesting persistence of the drug in the CSF.



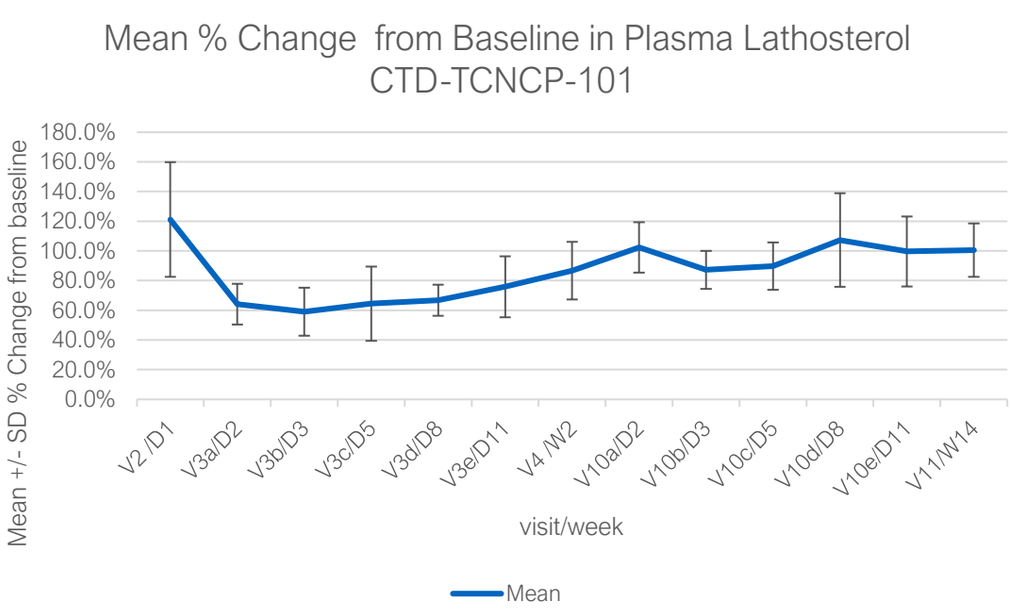
Pharmacodynamics – Target Engagement

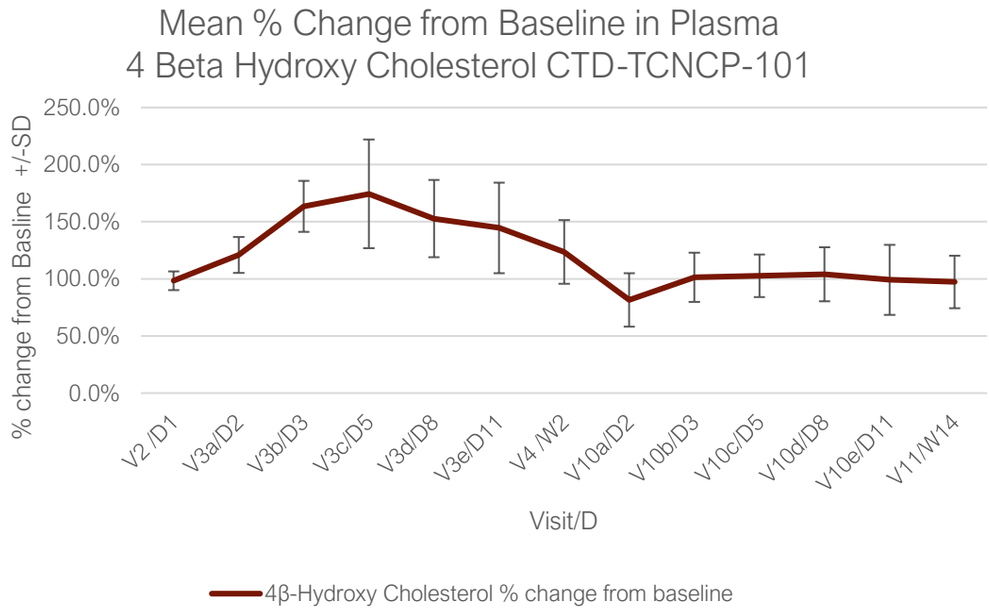
Trappsol® Cyclo™ releases cholesterol from cells as shown by:

Blood markers which indicate shutdown of cholesterol synthesis two days following infusions

Blood markers which indicate increased metabolism of cholesterol, thought to be related to bolus of cholesterol released from lysosomes

Similar level of effect for both low- and high-dose groups





Lathosterol		
Max Change	SD	Dose
-46%	13%	2500mg/kg
-45%	10%	1500mg/kg

4Beta-OH		
Max Change	SD	Dose
80.40%	65%	2500mg/kg
70%	30.60%	1500 mg/kg

Pharmacodynamics – Target Engagement

Liver tissue from patients before and after 7 doses of Trappsol® Cyclo™ shows clearance of cholesterol.

Similar magnitude of effect for low- and high-doses.

1500 mg/kg dose group, n = 6,

Marked reduction in filipin staining at 14 weeks = 2

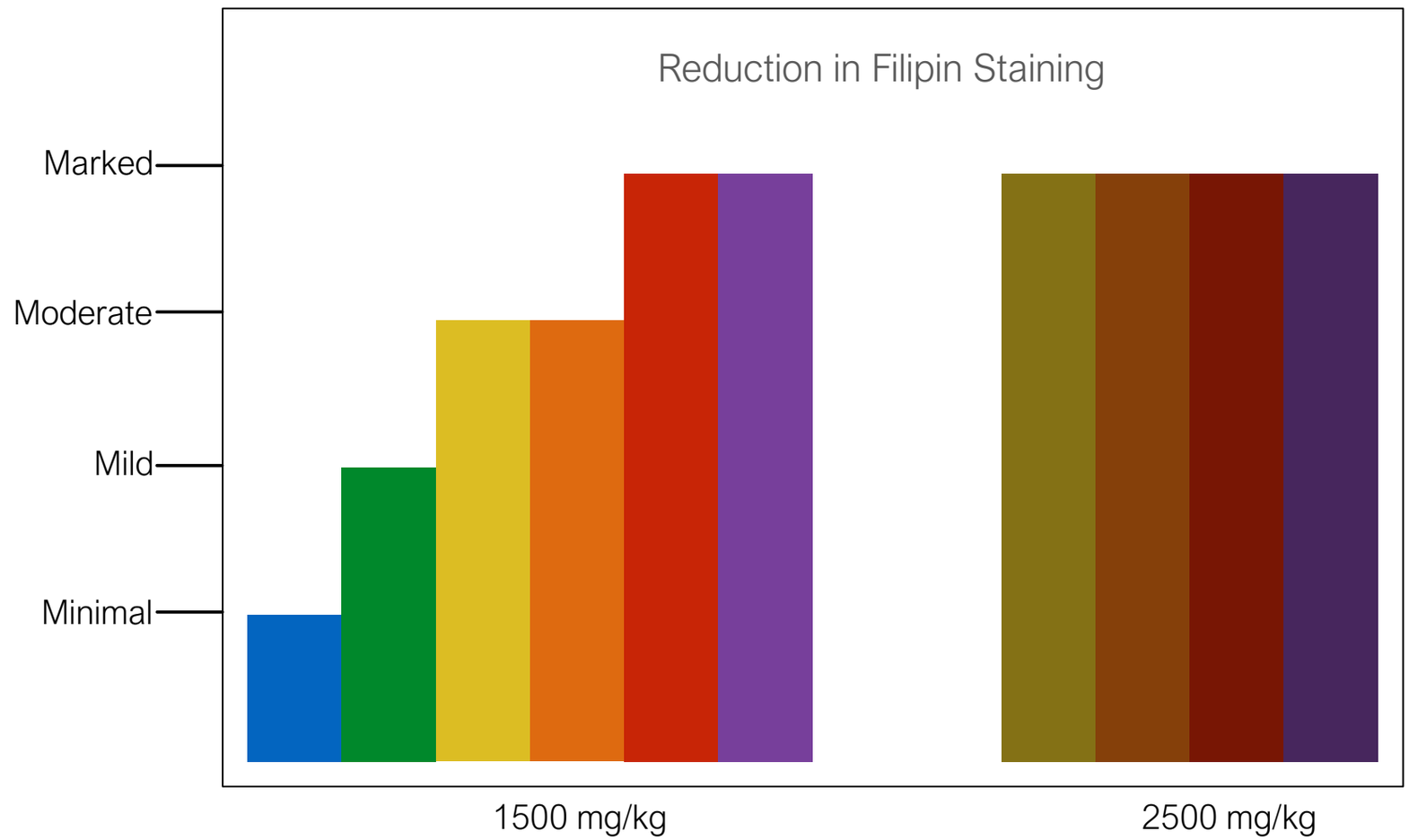
Moderate reduction in filipin staining at 14 weeks = 2

Mild reduction in filipin staining at 14 weeks = 1

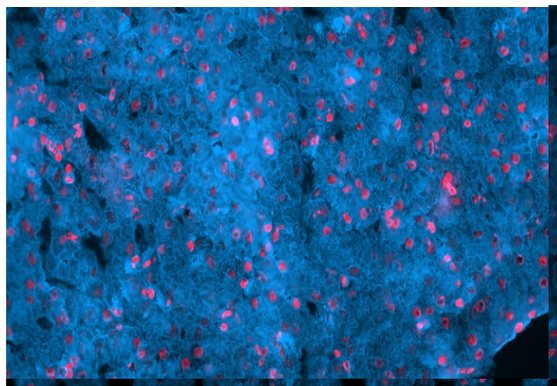
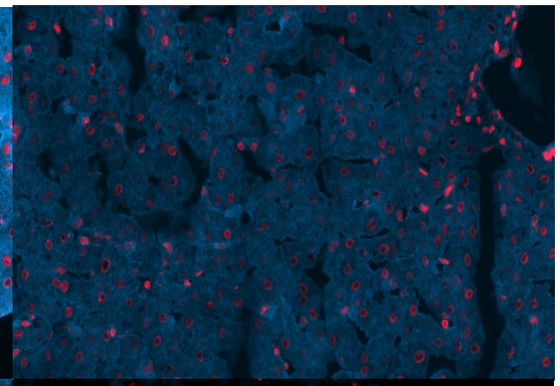
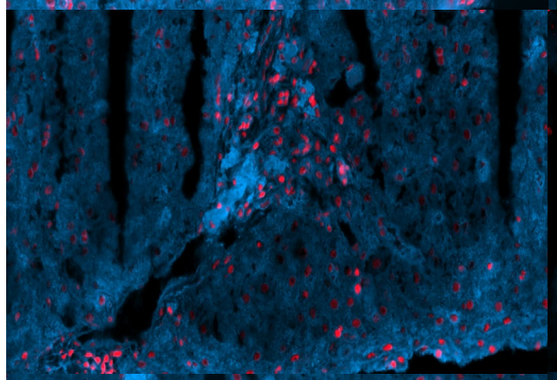
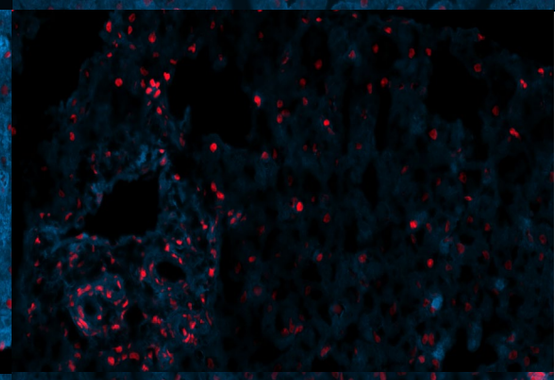
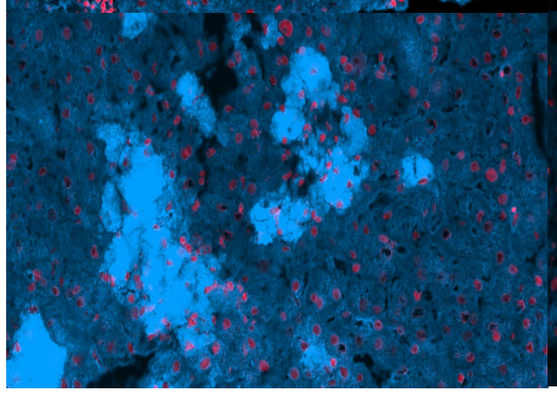
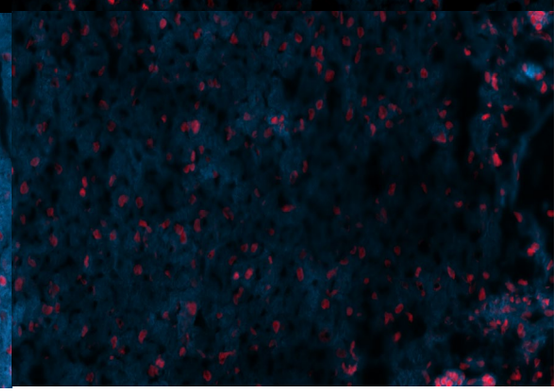
Minimal reduction = 1

2500 mg/kg dose group, n = 4

Marked reduction = 4

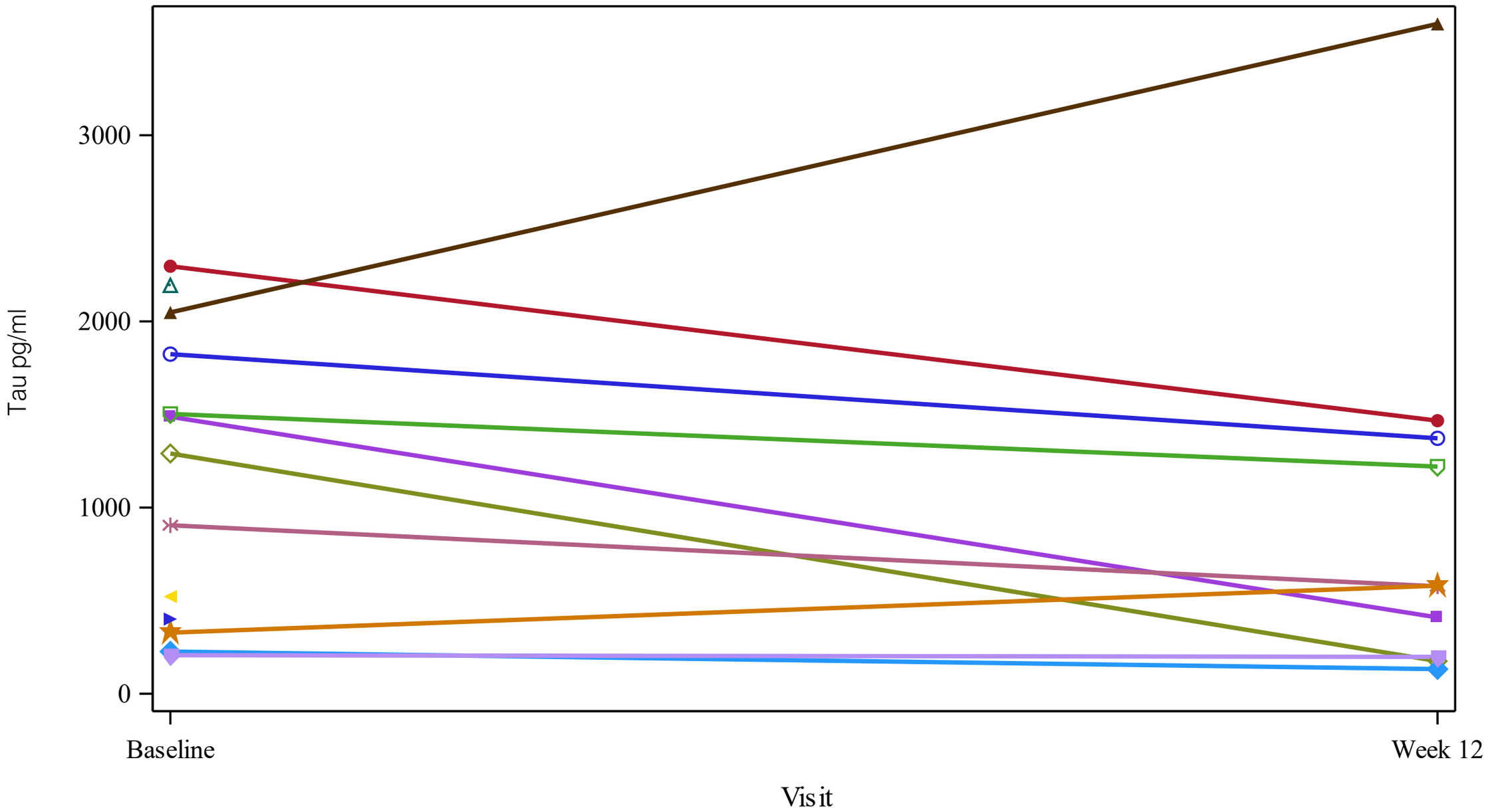


Cholesterol as measured by filipin staining at baseline and after 7 doses over 14 weeks

	Baseline	14 Weeks	
1500 mg/kg			Mild
2500 mg/kg			Marked
2500 mg/kg			Marked

Pharmacodynamics – Target Engagement

Biomarkers of NPC in CSF Following the 7th Dose by Subject and Time



NPC Severity Score outcomes

Parameter Visit Statistics	1500 mg/kg (N=6) Actual Value	 CFB	2500 mg/kg (N=7) Actual Value	 CFB	Total (N=13) Actual Value	 CFB
NCSS Total Score						
Screening						
n	6		7		13	
Mean (SD)	14.5 (3.89)		17.6 (7.32)		16.2 (5.97)	
Median	13.0		15.0		14.0	
Min, Max	11, 22		8, 26		8, 26	
Baseline						
n	6		7		13	
Mean (SD)	15.2 (4.49)		17.7 (7.36)		16.5 (6.10)	
Median	13.0		16.0		15.0	
Min, Max	11, 23		8, 26		8, 26	
Week 14 / End of Study						
n	6	6	6	6	12	12
Mean (SD)	14.8 (4.83)	-0.3 (1.21)	19.8 (6.34)	0.8 (1.47)	17.3 (5.97)	0.3 (1.42)
Median	13.0	-0.5	20.5	0.5	16.0	0.0
Min, Max	11, 24	-2, 1	10, 26	-1, 3	10, 26	-2, 3

Patient Reports and Clinical Observations

Individual patients reported feeling:

--More focused

--More engaged in social interactions

--More likely to initiate conversations or activities

--Word finding ability reaching back into the past

--Improvements in ability to swallow without coughing

--Improvements in stance and gait

Families and caregivers reported similar observations.

Continuing on the Drug after the Trial

Every patient who completed the study wished to remain on the study drug.

8 **US-based patients** were eligible for the extension protocol, and all enrolled.

-- Home-based infusions with periodic assessments at clinic.

--One patient discontinued after several months, not for safety or tolerability reasons.

-- With some disruptions due to COVID-19, patients continue to be dosed and assessed.

After 3 or 6 months in the Extension protocol, the safety parameters continue to be favorable and Efficacy measures continue to show Stability or Improvement.

4 **foreign-based patients** continued on the study drug on an expanded access basis, or are in the process of applying for approval. The safety profile for those on the drug through expanded access to date continues to be favorable.

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Thank You!