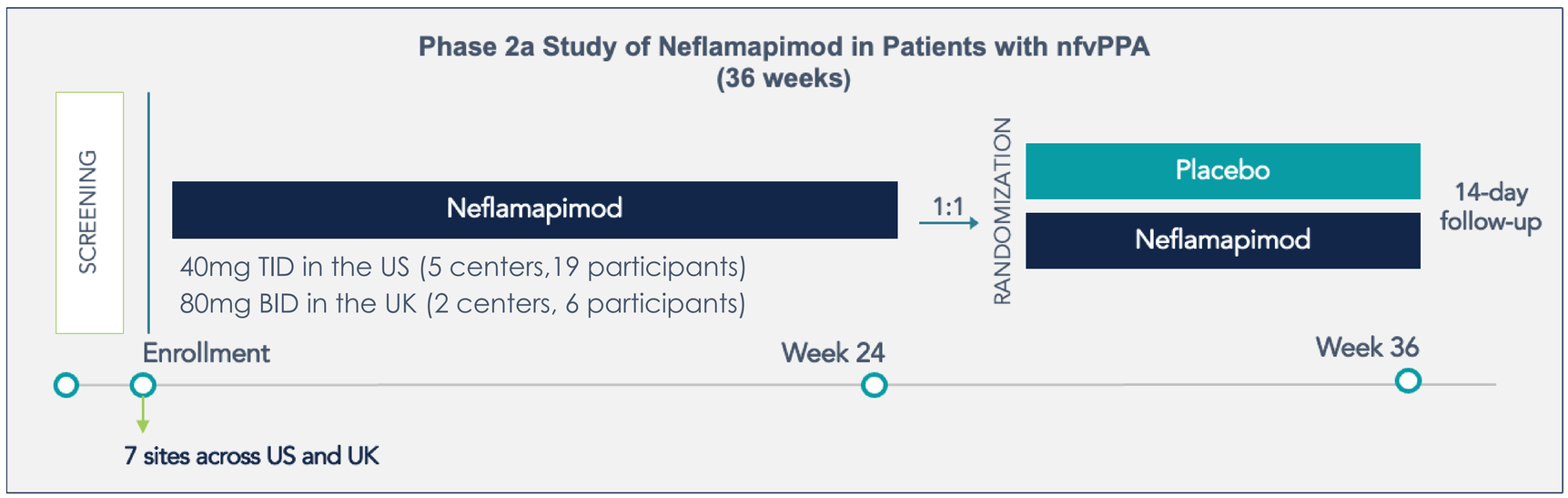
P045 Initial neurodegeneration biomarker results from a Phase 2a clinical trial of neflamapimod in patients with nonfluent variant primary progressive aphasia

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Patients

- 40 to 85 years
- Clinical diagnosis of nfvPPA by consensus criteria[1]
- Global CDR® plus NACC FTLD score of 0.5 or 1
- CDR® plus NACC FTLD language domain score of 0.5, 1 or 2

BASELINE CHARACTERISTICS

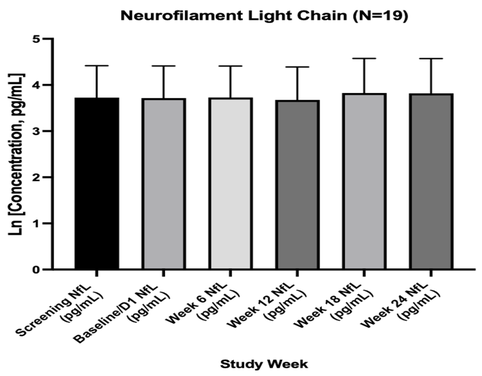
	Neflamapimod (N=25)
Male: Female	14:11
Age (mean, SD)	69.5 (8.1)
CDR + NACC FTLD-SB (Mean, SD)	3.2 (2.0)
CDR + NACC FTLD-SB Language Domain, 0.5/1.0/2.0	8/10/7
CDR-SB (Mean, SD)	2.0 (1.4)
Western Aphasia Battery (WAB) Aphasia Quotient (Mean, SD)	85.5 (9.2)
WAB Language (Mean, SD)	82.2 (12.1)
WAB Cortical Quotient (Mean, SD)	85.5 (9.2)
Progressive Aphasia Severity Scale (PASS) (Mean, SD)	6.6 (2.6)
Category Fluency Test (words correct) (Mean, SD)	10.9 (6.9)
Letter Fluency Test (words correct) (Mean, SD)	16.2 (8.9)

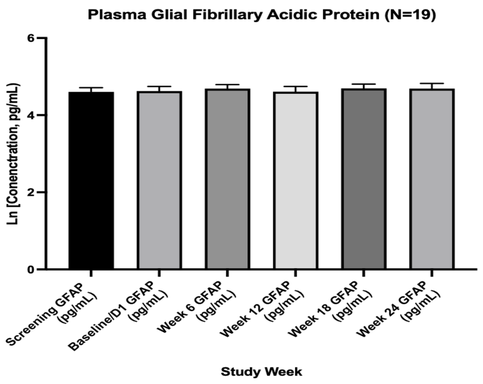
Baseline Levels of Neurofilament Light Chain (NfL) and Glial Fibrillary Acidic Protein (GFAP) in Plasma

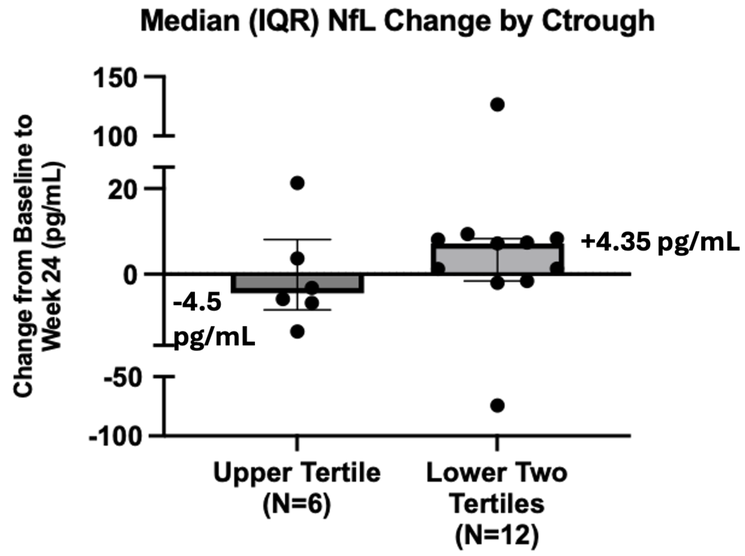
	NfL	Plasma GFAP
Mean (SD)	45.7 (39.6)	103.4 (43.2)
Number (%) > 1 SD above healthy control mean	18 of 25 (72%)	4 of 25 (16%)

BIOMARKER RESULTS

- Biomarker results through to week 24 available in US participants (N=19)
- 24-week biomarker data from UK participants available in Q1



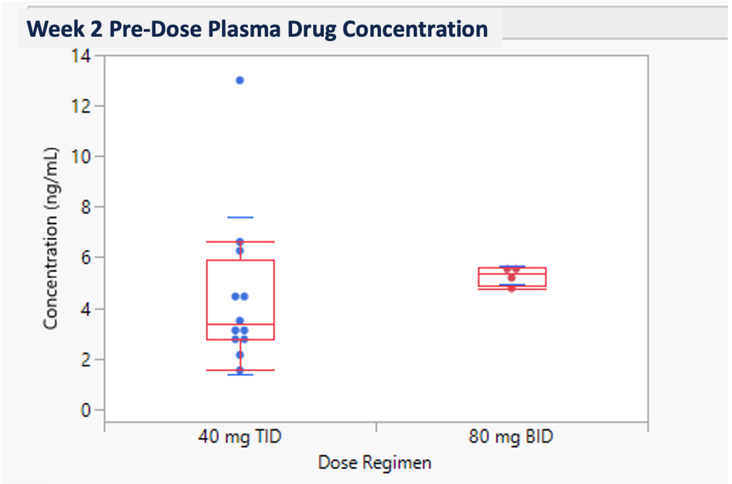




Lowest trough plasma drug concentration (C_{trough}) in upper tertile was 4.3 pg/mL; highest C_{trough} in lower two tertiles was 3.5 pg/mL

In untreated patients, median annual rate of change in nfvPPA is +9 pg/mL (Sheth et al. Molecular Neurodegeneration, 2025)

PHARMACOKINETICS



SAFETY

- Generally well tolerated, with no new safety signals identified and no serious adverse events reported
- Most common treatment emergent adverse events were falls and diarrhea, each reported in 4 (16%) of 25 participants. All events of falls and diarrhea were reported as being mild in severity
- One participant with ALT/AST elevation met protocol-defined criteria for treatment discontinuation. Participant was asymptomatic, with no associated bilirubin elevation, and elevations resolved with treatment discontinuation

CONCLUSIONS

- At 40mg TID, in the overall patient population, NfL levels were stable over 24 weeks
  - C_{trough} levels achieved with 40mg TID were in low range of levels in prior clinical studies
  - In participants were in upper tertile for C_{trough} there was evidence of decline in NfL levels, with a median 4.5 pg/mL reduction; the result is consistent with the C_{trough} threshold for pharmacological activity of 4 ng/mL in prior studies
- Plasma GFAP levels were not elevated at baseline (mean 109 pg/mL vs. health control reference of 104 pg/mL (Doecke, 2025)
- Neflamapimod was well tolerated with no new safety signals identified

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