Update on the Phase 2b Portion of the ORION Trial in Progressive Supranuclear Palsy (PSP)

Presented as part of:
"Atypical Parkinsonism Revisited: PSP, CBS, MSA and Beyond – Disease Modifying Trials"

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Results from Planned Interim Analysis of Ph. 2b/3 Study of **AMX0035**

ORION was conducted across 43 sites in Germany, Italy, Spain, and the United States.
139 participants randomized 3:2 to AMX0035 or placebo completed 6 months of follow-up:

Table 1. Baseline Characteristics

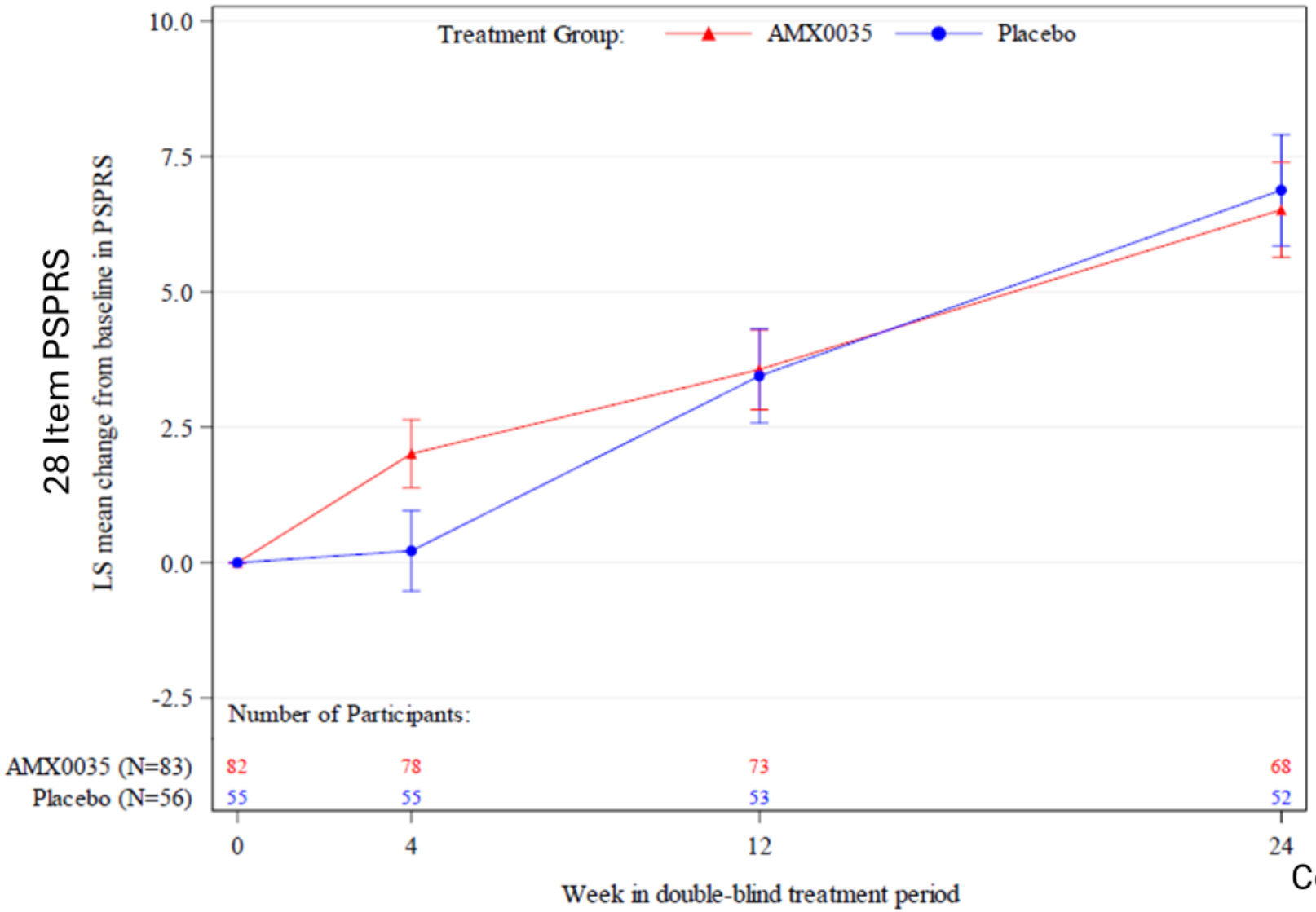
Parameter	AMX0035 (n = 83)	Placebo (n = 56)
Time Since PSP Diagnosis (Month)		
Mean (SD)	16.68 (12.67)	15.04 (12.06)
Protocol-defined PSP Richardson Diagnosis*		
Probable	80 (96.4)	55 (98.2)
Possible	3 (3.6)	1 (1.8)
Baseline use of Parkinson medication		
Yes	52 (62.7)	39 (69.6)
No	31 (37.3)	17 (30.4)
PSPRS (28-item) Total Score		
Mean (SD)	29.7 (6.51)	29.7 (6.77)
PSPRS (10-item) Total Score		
Mean (SD)	8.6 (3.05)	8.3 (3.19)
SE-ADL by Rater		
Mean (SD)	64.5 (18.56)	68.1 (16.33)

Mean values consistent with **less** disease burden than davunetide (PSPRS 40) and/or tilavonemab (36) trials

* Protocol defined PSP-RS based on MDS criteria from Höglinger et al 2017

Courtesy of Amylyx Pharmaceuticals, Inc.

AMX0035 Did Not Show Differences Compared to Placebo At 24 Weeks



At 24 weeks, **no significant difference between AMX0035 and placebo** in the:

- **Primary endpoint** (28-item PSPRS)[a]
- **Secondary endpoints** (10-item PSPRS[a] and MDS-UPDRS Part II Score)
- **Exploratory clinical endpoints**

Safety data consistent with PSP and known safety profile of AMX0035

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