AR1001 Phase 2 Trial
Plasma Biomarker Analysis
(AR1001-ADP2-US01)

AD/PD™ 2023 (March 28 - April 1, 2023)

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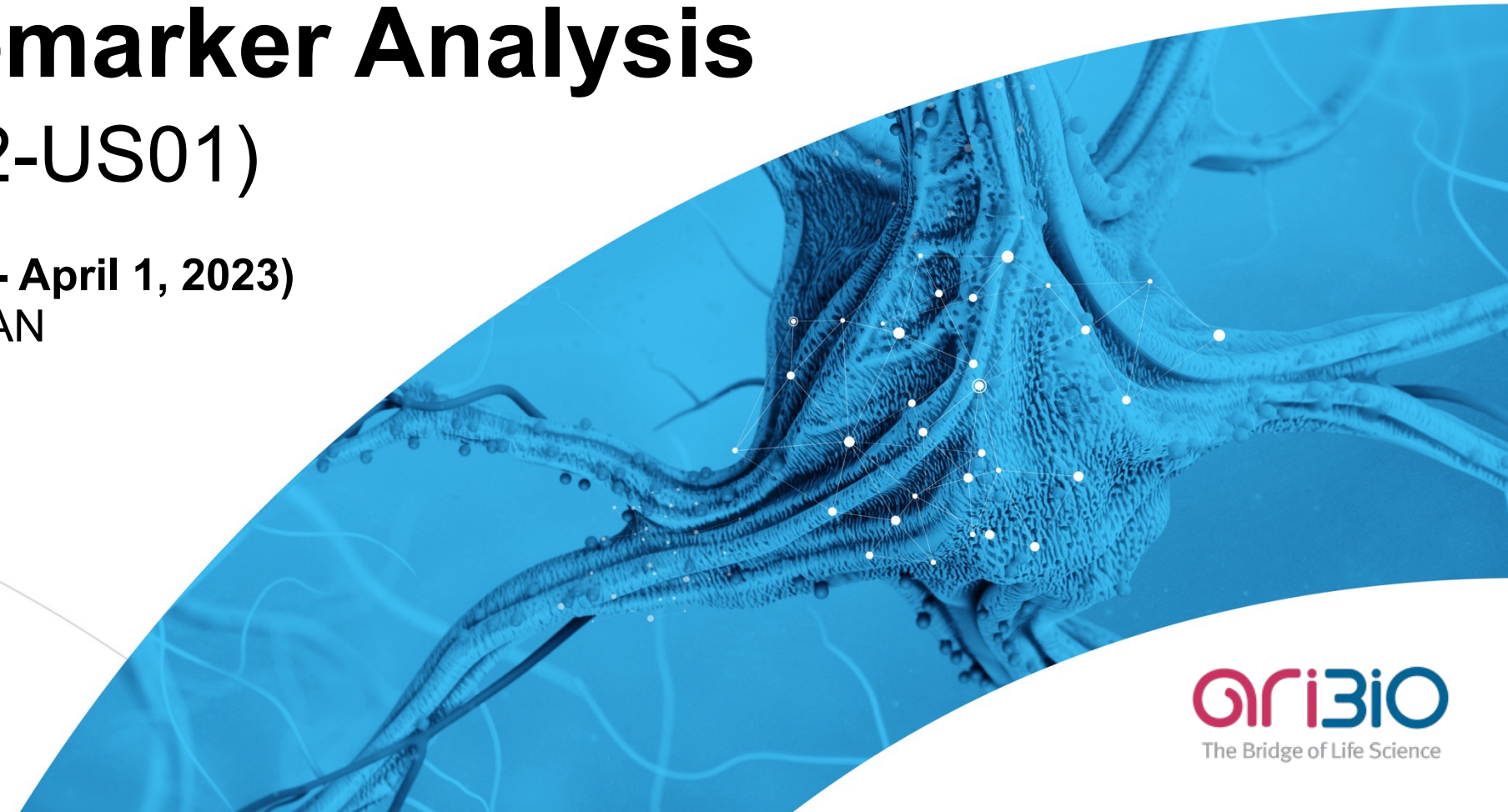

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Disclosure : David R. Greeley is the consulting Chief Medical Officer of AriBio Co., Ltd.

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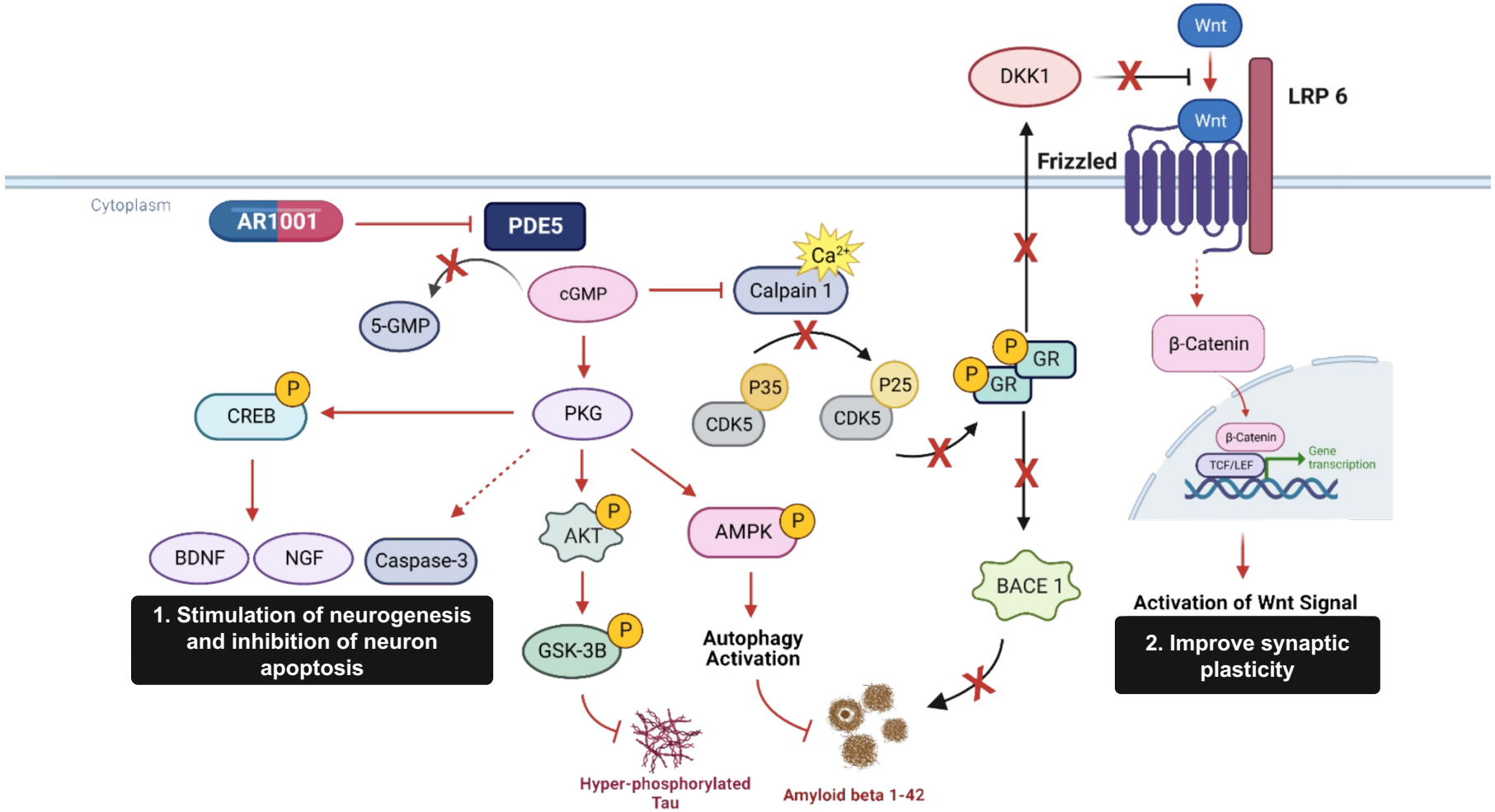
AR1001 Mechanism of Action



AR1001 Phase 2 Trial (AR1001-ADP2-US01)

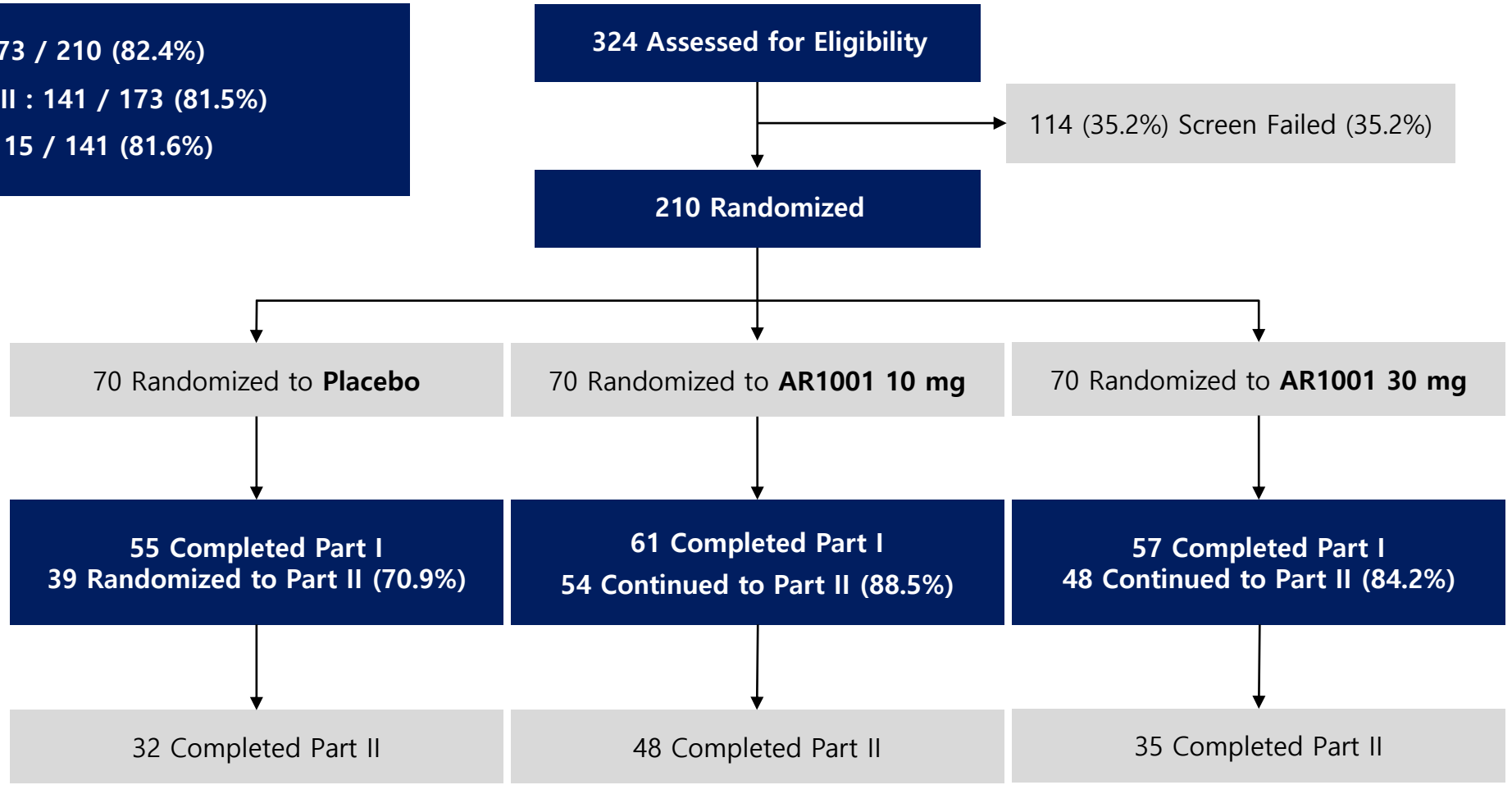
AR1001-ADP3-US01		
Study	52-Week, Randomized, Double-blind, Placebo-controlled, Phase II Study (NCT03625622)	
Objective	Safety and Tolerability	
	Preliminary Efficacy	
Population	55-80 years old (Total of 210 participants)	
	Mild to Moderate Alzheimer's disease : MMSE 16-26, NIA-AA dementia stage 4-5	
Doses	**Part I : Main 26 Week Study**	
	· AR1001 10 mg, AR1001 30 mg, Placebo (1:1:1 randomized)	
	Part II : Optional 26 Week Extension Study	
	· AR1001 10 mg and 30 mg arms continue the same dose · Placebo arm is randomized into 10 mg or 30 mg	
Endpoints	Co-Primary Endpoints	**ADAS-Cog13, ADCS-CGIC**
	Secondary Endpoint	**MMSE, NPI, GDS, QoL-AD**
	Plasma Biomarkers	**pTau-181, GFAP, NfL, Aβ42/40**

Demographics

Variable 3	Placebo (n = 70) N (%)	Low Dose 10 mg (n = 70) N (%)	High Dose 30 mg (n=70) N (%)
Age (years), mean (SD)	70.4 (5.5)	70.9 (6.5)	70.4 (6.8)
Gender, n (%) · Male · Female	 22 (31.4) 48 (68.6)	 27 (38.6) 43 (61.4)	 23 (32.9) 47 (67.1)
Race, n (%) · Black or African American · White · Multiple Races Reported · Unknown	 12 (17.1) 58 (82.9) 0 0	 8 (11.4) 60 (85.7) 1 (1.4) 1 (1.4)	 8 (11.4) 62 (88.6) 0 0
Ethnicity, n (%) · Hispanic or Latino · Not Hispanic or Latino · Not Reported · Unknown	 13 (18.6) 56 (80.0) 0 1 (1.4)	 13 (18.6) 57 (81.4) 0 0	 16 (22.9) 52 (74.3) 1 (1.4) 1 (1.4)
AD medication used, n (%)	36 (51.4)	40 (57.1)	46 (65.7)
Clinical Stage, n (%) · Mild (MMSE 21-26) · Moderate (MMSE 16-20)	 52 (74.3) 18 (25.7)	 52 (74.3) 18 (25.7)	 47 (67.1) 23 (32.9)

Enrollment and Metrics

- **Completed Part I : 173 / 210 (82.4%)**
- **Randomized to Part II : 141 / 173 (81.5%)**
- **Completed Part II : 115 / 141 (81.6%)**



Analysis Method

Analysis was performed at Quanterix (Billerica, MA, USA)

N4PE

[NfL, GFAP, Aβ1-40, Aβ1-42, Simoa® Neuro 4-Plex E Advantage kit (Product # 103670)]

The assays were performed on the Simoa HD-X analyzer using Single Molecule Array (Simoa) technology. Plasma samples were diluted 4x and ran in duplicate. Results were included in the analysis if the coefficient of variation across replicates was < 25%.

pTau-181

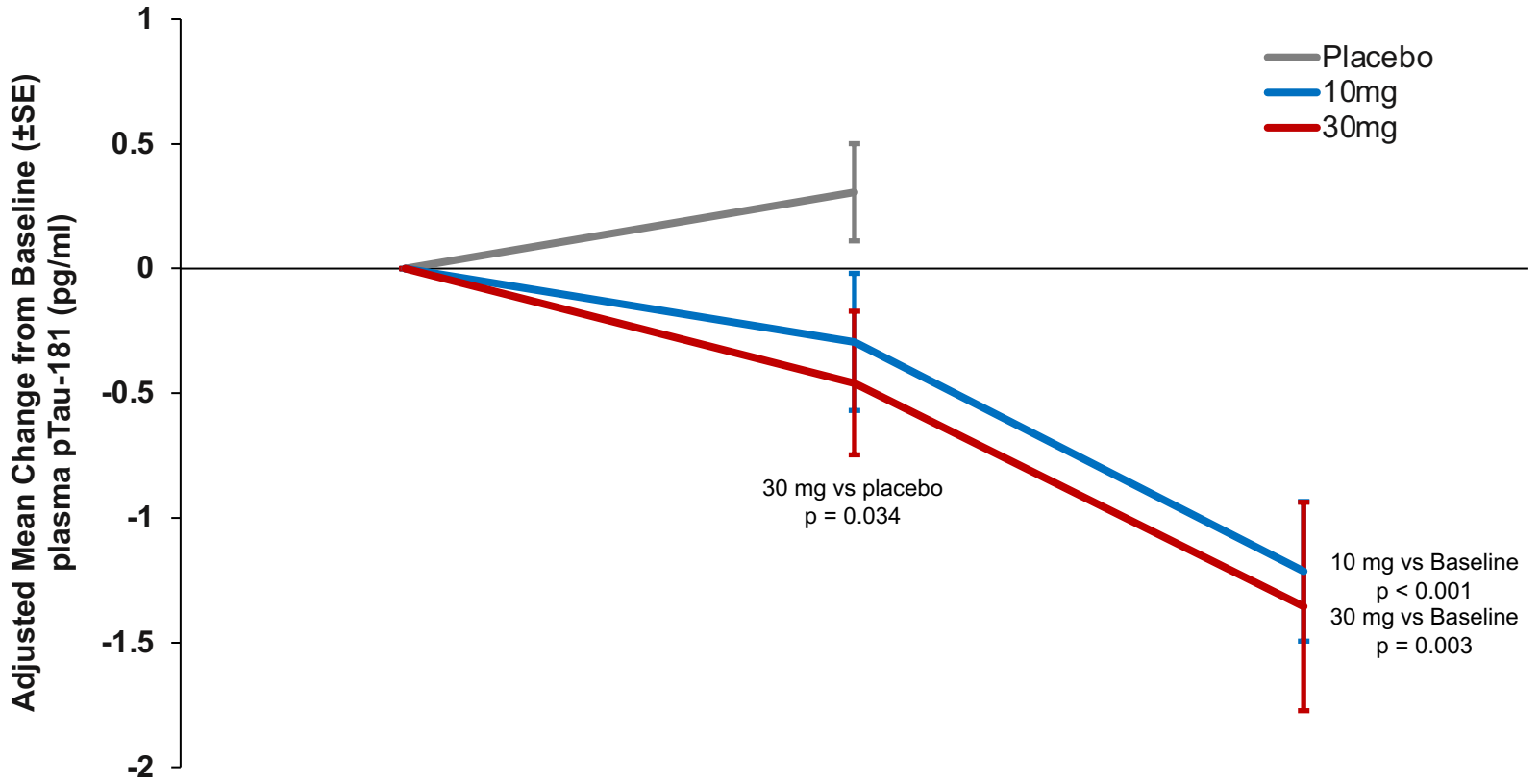
[Simoa® Human pTau-181 Advantage V2 assay kit (Product # 103714)]

The assays were performed on the Simoa HD-X analyzer using Single Molecule Array (Simoa) technology. Plasma samples were diluted 4x and ran in duplicate. Results were included in the analysis if the coefficient of variation across replicates was < 25%.

Baseline Characteristics

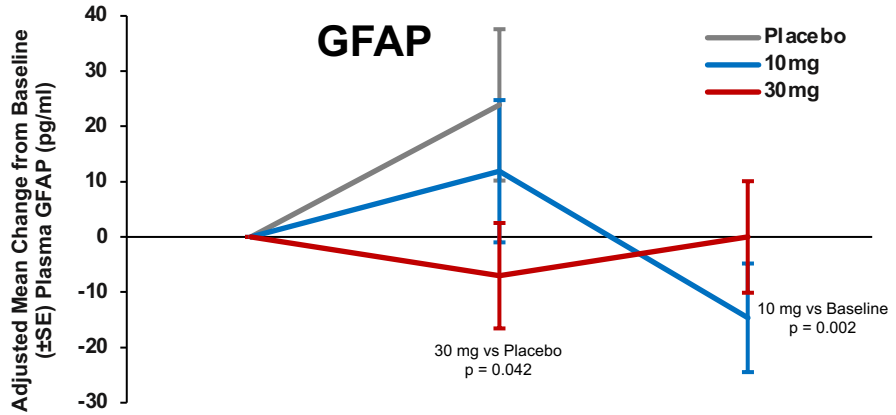
Variable	10 mg dose (N = 70)	30 mg dose (N = 70)	Placebo (N = 70)
Endpoints, mean (SD)			
- ADAS-Cog13	25.2 (9.6)	26.3 (11.0)	24.6 (10.0)
- MMSE-2	21.8 (3.8)	20.7 (3.9)	22.4 (3.8)
Biomarkers, mean (SD)			
- Aβ42/Aβ40 ratio	0.061 (0.019)	0.065 (0.015)	0.064 (0.027)
- pTau-181 (pg/mL)	4.65 (2.43)	4.65 (2.66)	4.24 (2.16)
- NfL (pg/mL)	28.0 (14.6)	33.2 (38.8)	29.4 (16.5)
- GFAP (pg/mL)	259 (119)	257 (114)	256 (108)

Plasma pTau-181



	Week 0 (N=184)	Week 26 (N=137)	Week 52 (N=71)
(N) Placebo	61	41	
(N) 10 mg	62	51	41
(N) 30 mg	61	45	30

Other Biomarkers



	Week 0 (N=182)	Week 26 (N=136)	Week 52 (N=71)
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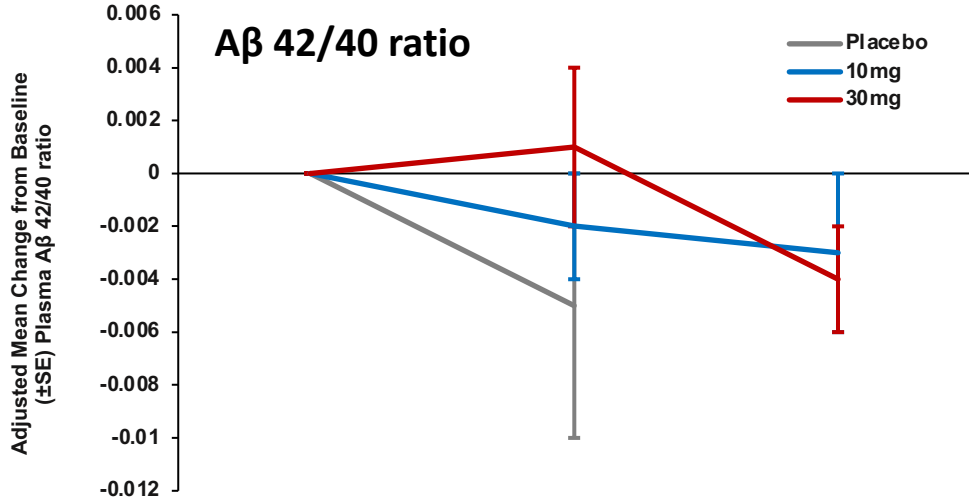
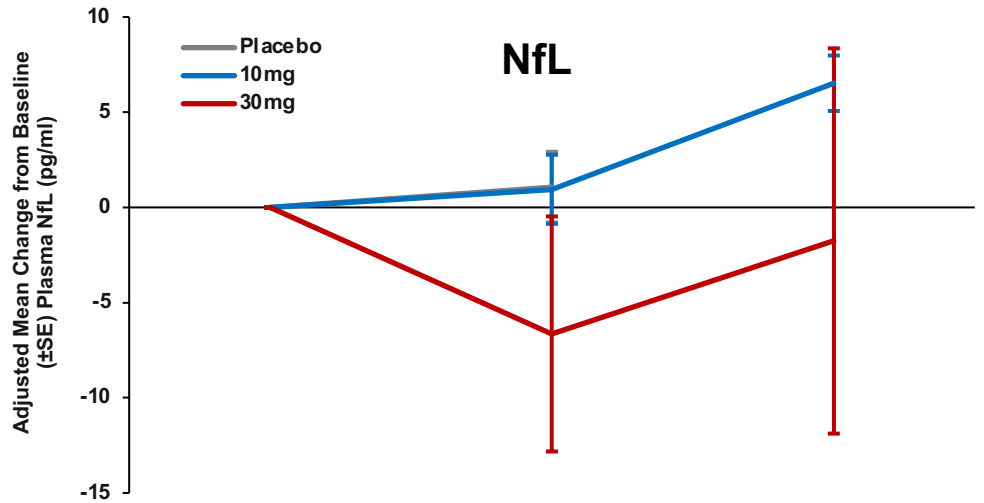
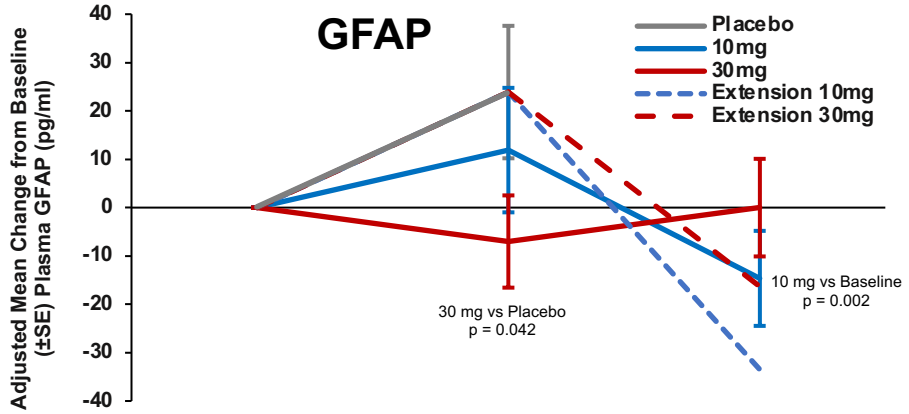


	Week 0 (N=182)	Week 26 (N=136)	Week 52 (N=70)
(N) Placebo	61	41	
(N) 10 mg	61	50	40
(N) 30 mg	60	45	30

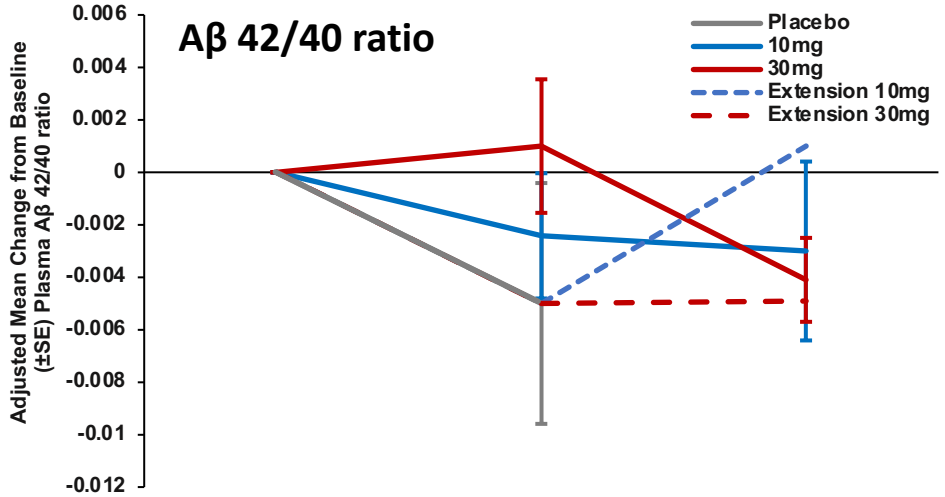


	Week 0 (N=182)	Week 26 (N=136)	Week 52 (N=71)
(N) Placebo	61	41	
(N) 10 mg	61	50	41
(N) 30 mg	60	45	30

Other Biomarkers (including placebo group through week 52)



	Week 0 (N=182)	Week 26 (N=136)	Week 52 (N=92)
(N) Placebo	61	41	10 (10 mg) / 11 (30 mg)
(N) 10 mg	61	50	41
(N) 30 mg	60	45	30



	Week 0 (N=182)	Week 26 (N=136)	Week 52 (N=92)
(N) Placebo	61	41	10 (10 mg) / 11 (30 mg)
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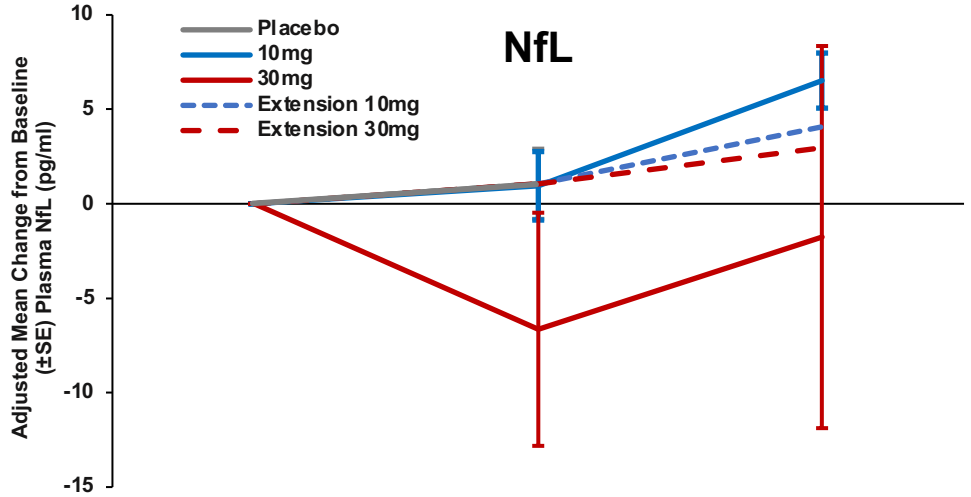
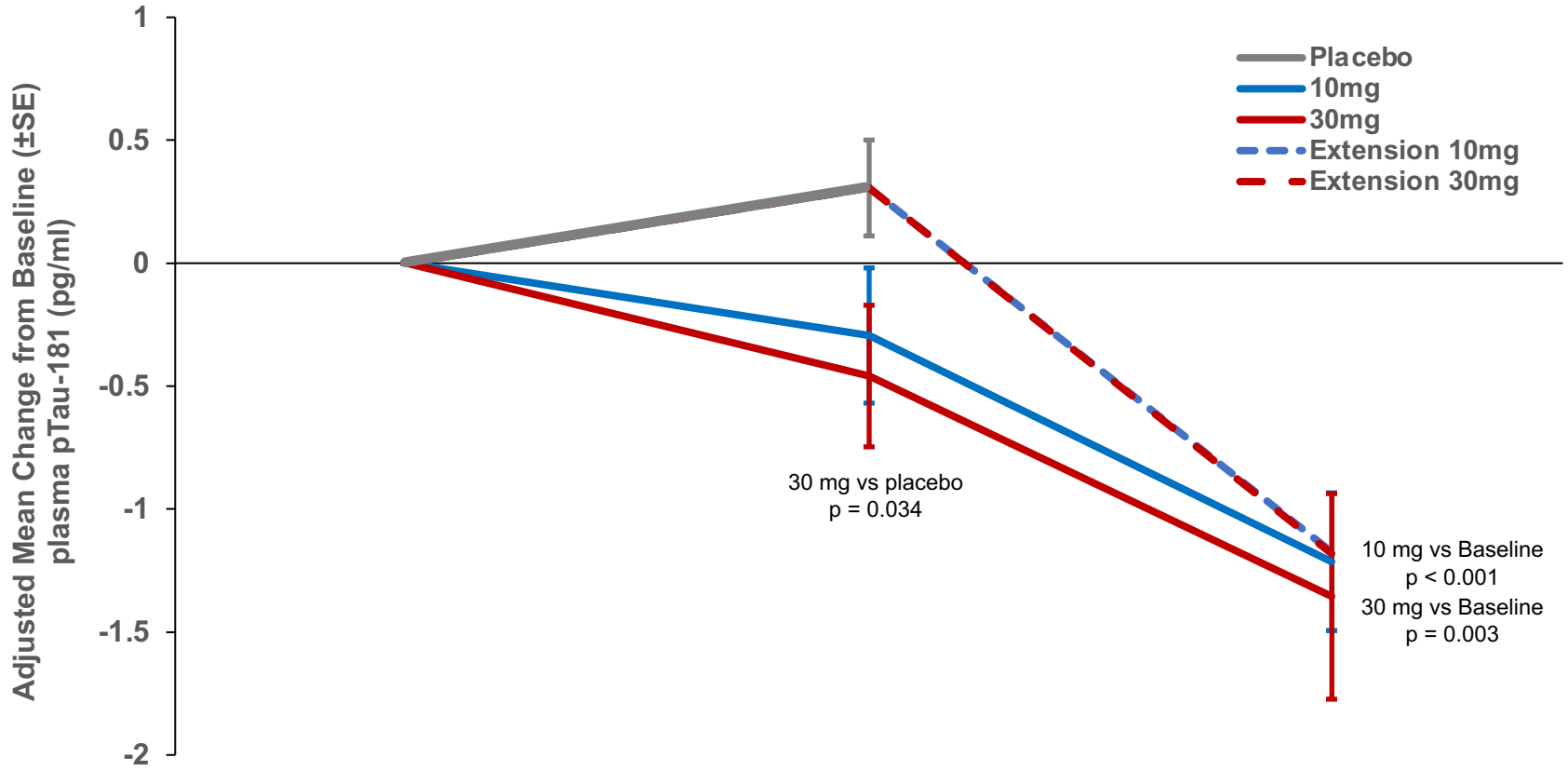


	Week 0 (N=182)	Week 26 (N=136)	Week 52 (N=92)
(N) Placebo	61	41	10 (10 mg) / 11 (30 mg)
(N) 10 mg	61	50	41
(N) 30 mg	60	45	30

Plasma pTau-181 (including placebo group through week 52)



	Week 0 (N=184)	Week 26 (N=137)	Week 52 (N=92)
(N) Placebo	61	41	10 (10 mg) / 11 (30 mg)
(N) 10 mg	62	51	41
(N) 30 mg	61	45	30

Conclusion

1. **AR1001 is a novel PDE5 inhibitor with multiple mechanisms of action**
2. **Plasma pTau-181 and GFAP in 30 mg group showed statistically significant difference at week 26 compared to placebo group**
3. **Plasma pTau-181 dropped more than >1 pg/ml over one year**
4. **Phase III trial (Polaris-AD) is on-going**
   - Early AD : MCI and Mild dementia
     (NIA-AA Stage 3-4, MMSE >20 and CDR-global of 0.5-1.0)
   - Daily oral dose (AR1001 30 mg vs placebo)
   - Topline expected in 2026

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