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ASX ANNOUNCEMENT

Actinogen pivotal Alzheimer's disease trial demonstrates trends toward clinical benefit in older patients and favourable longer term safety profile

Sydney, 19 November 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") today announces topline results from its pivotal, placebo-controlled XanaMIA trial of oral emestedastat (Xanamem®) over 36 weeks of treatment in 247 patients with mild to moderate Alzheimer's disease (AD) and elevated levels of the pTau181 blood biomarker.

Summary:

- In the overall population, Xanamem was numerically, but not statistically, superior to placebo for the primary endpoint of delayed disease progression, measured by the Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB)
- Clinically significant and sustained benefit of 30% disease slowing was observed in older participants, supporting a new patent filing covering Xanamem treatment in older, more advanced AD patients, who are underserved by existing therapies and newer ones in development
- Xanamem was safe and well tolerated over the treatment period of 36 weeks
- In the Open Label Extension (OLE) phase of the trial, disease stabilization over 24 weeks (no mean progression) was observed in the first 29 participants with 24 weeks of active Xanamem therapy and therefore the OLE phase will continue in order to gather additional data
- The next OLE data milestone to be reported when approximately 100 participants have reached at least 24 weeks of treatment (Q1 CY2027)
- The Company is well-funded to CY2028, with $18.9m[1] cash on hand and no debt.

Detailed findings from the topline XanaMIA trial results are:

1. Xanamem was numerically, but not statistically, superior to placebo for the primary endpoint of delayed disease progression, measured by the CDR-SB at Weeks 12, 24 and 36, with a mean Xanamem benefit compared with placebo of 0.10 CDR-SB points at Week 36 (p = 0.65)
2. A statistically and clinically significant benefit on the CDR-SB zero progression rate (40% vs. 22%, p=0.02) for Xanamem was observed in the prespecified analysis of participants above the median age of 75 years, together with a clinically significant benefit of 30% disease slowing (mean CDR-SB superiority of 0.39 points at Week 36, p=0.22) – for context, this rate of disease slowing is similar to that claimed by Eli Lilly and Eisai for their approved anti-amyloid drugs
3. Small trends towards superiority of Xanamem vs. placebo on the key secondary endpoints of cognition and "Activities of Daily Living" were observed
4. The previously established, favourable safety profile for Xanamem 10 mg administered daily for up to 12 weeks was replicated over the longer treatment period of 36 weeks and no serious adverse events were attributed to Xanamem

® Xanamem is a registered trademark of Actinogen Medical Limited

[1] Unless stated otherwise, all financial data is in Australian dollars

5. Unblinding of data used by the Independent Data Monitoring Committee (DMC) in January 2026, for its interim analysis of trial-futility, showed a statistically significant Xanamem treatment benefit of 0.58 points (p=0.03, n=88) on the prespecified, interim analysis Week 24 CDR-SB endpoint, which was not fully sustained in the final analysis of 247 participants.

Available data from the XanaMIA OLE phase of the trial has also been reviewed and shows an encouraging lack of progression in the CDR-SB at 24 weeks in the first 29 participants to reach that timepoint. Continuation of the OLE phase will provide important long-term data on Xanamem treatment and aims to demonstrate durable treatment benefits. The next OLE data milestone will be reported in Q1CY2027 when approximately 100 participants have reached at least 24 weeks.

The Company intends to explore the XanaMIA results with potential co-development partners interested in novel AD therapies, with a focus on the encouraging data observed for older participants, who represent more than 70% of patients with Alzheimer's disease. Given its established safety profile in more than 500 participants and lack of drug-drug interaction potential, Xanamem is particularly well suited as a treatment for the older, more complex AD population, most of whom are on multiple medications including older AD treatments like donepezil.

Immediate steps have been taken to conserve cash by focusing expenditure on the OLE trial, suspending future phase 3 expenditure, expanding the intellectual property portfolio to include the new XanaMIA trial finding on older age, business development outreach, strategic portfolio planning, and finalizing XanaMIA analyses.

As of the date of this announcement, the Company had a cash balance of $18.9 million, and a significant accrued R&D tax incentive given the substantial amount of eligible R&D spend undertaken in the first half of FY2027. As the XanaMIA trial is closed out and with other cost saving initiatives being undertaken, the Company's cash commitments will drop substantially from early CY2027. The Company has no debt. This strong balance sheet provides a cash runway into CY2028 and enables the Company to complete evaluation of the XanaMIA data to determine the optimal strategy for the future development of Xanamem.

Actinogen's CEO, Dr Steven Gourlay, commented:

"Following our topline analysis of the XanaMIA trial we remain confident in the risk-benefit profile of Xanamem in mild to moderate Alzheimer's disease, with notable findings of clinically significant disease slowing in older participants, who represent a poorly served and large segment of the market. Our strong balance sheet provides optionality to fully explore the trial data with potential partners over the coming months and determine the optimal development path for Xanamem. We sincerely thank everyone for their ongoing support of Xanamem development including patients and their families living with Alzheimer's disease, as well our shareholders."

The Company will be holding a webinar at 11.00am (AEDT) this morning to discuss the trial results. **Register for the webinar** at any time through to the 11.00am start at: **https://tinyurl.com/mr3js44b**

A recording of the webinar will be available on the Company's InvestorHub site and YouTube channel as soon as possible following the event.

A copy of the webinar presentation is attached to this announcement.

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/Pmodbe

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Announcement authorised by the Board of Actinogen Medical Limited

About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company in the late clinical stages of development for Xanamem® (emestedastat), its novel oral therapy for Alzheimer's disease. Xanamem also has other applications in diseases driven by elevated tissue cortisol including depression. The Company is based in Sydney, Australia with operations and clinical trials in Australia and the US. Xanamem has been studied in eight clinical trials with more than 500 people treated to date and has a promising safety and efficacy profile with treatment up to 36 weeks.

About the phase 2b/3 XanaMIA pivotal trial and Open Label Extension (OLE) phase

The XanaMIA trial was a randomized (1:1), double-blind, placebo-controlled phase 2b/3 trial evaluating Xanamem 10 mg versus placebo over 36 weeks in 247 participants across Australia and the United States. On 19 November 2026 Actinogen reported the initial results from the trial, showing trends towards overall slowing of disease progression and clinically significant slowing in older participants. Further analyses are on-going. The OLE phase of the trial is on-going following closure of enrolment of 168 participants in November 2026.

About Xanamem (emestedastat)

Xanamem's novel mechanism of action is to control the level of cortisol in brain, liver and adipose tissue (fat) through the inhibition of the tissue cortisol synthesis enzyme, 11β-HSD1, without blocking normal production of cortisol by the adrenal glands. Xanamem is a first-in-class, once-a-day pill designed to deliver high levels of tissue cortisol control in regions where 11β-HSD1 is highly expressed such as the hippocampus and grey matter in the brain, as well as in liver and adipose tissue. Chronically elevated cortisol is associated with progression in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Elevated cortisol is also associated with more severe forms of depression. Xanamem has demonstrated excellent target enzyme engagement and in human trials has shown potential benefit in older people with Alzheimer's disease and anti-depressive benefits in patients with moderately severe depression. To view Xanamem's two-minute Mechanism of Action animation, click here.

Xanamem is an investigational product and is not approved for use outside of a clinical trial by the FDA or by any global regulatory authority. Xanamem® is a trademark of Actinogen Medical.

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XanaMIA Alzheimer's disease trial demonstrates clinically significant trend toward benefit in participants over 75 years but not in overall trial population

Xanamem demonstrates good long-term safety and tolerability with a promising rate of disease slowing in older Alzheimer's patients

Topline Results Webinar 19 November 2026

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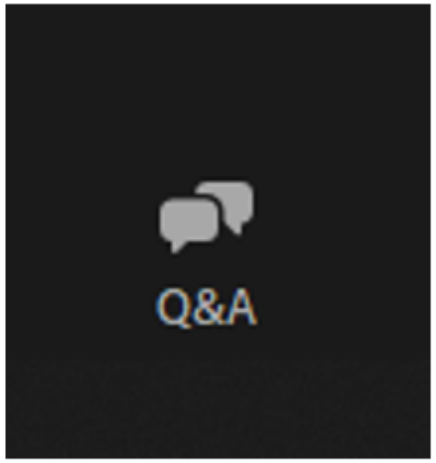

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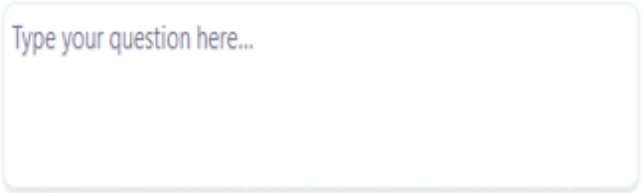

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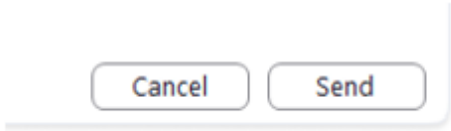

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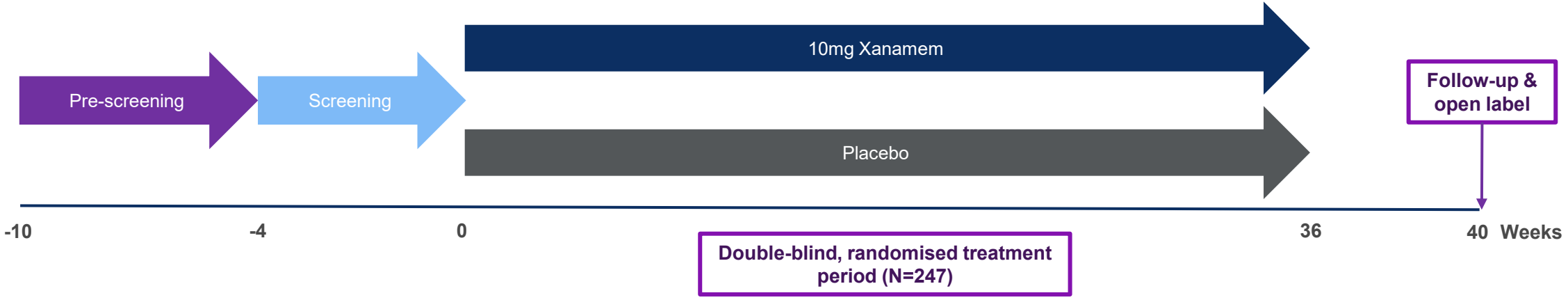
XanaMIA trial design and methods

A double-blind, randomized, 36-week, 2-arm clinical trial to assess safety, tolerability, and efficacy of Xanamem 10 mg daily in patients with mild to moderate AD (MMSE 18-26)



Primary Endpoint	Key Secondary Endpoints
CDR-SB change from baseline to 36 weeks	Change from Baseline to Week 36 in: • Global Cognitive Test Battery (CTB) • Amsterdam Instrumental Activities of Daily Living Questionnaire – short version (A-IADL-Q-SV)

Key baseline characteristics for overall population

Generally well-balanced between groups

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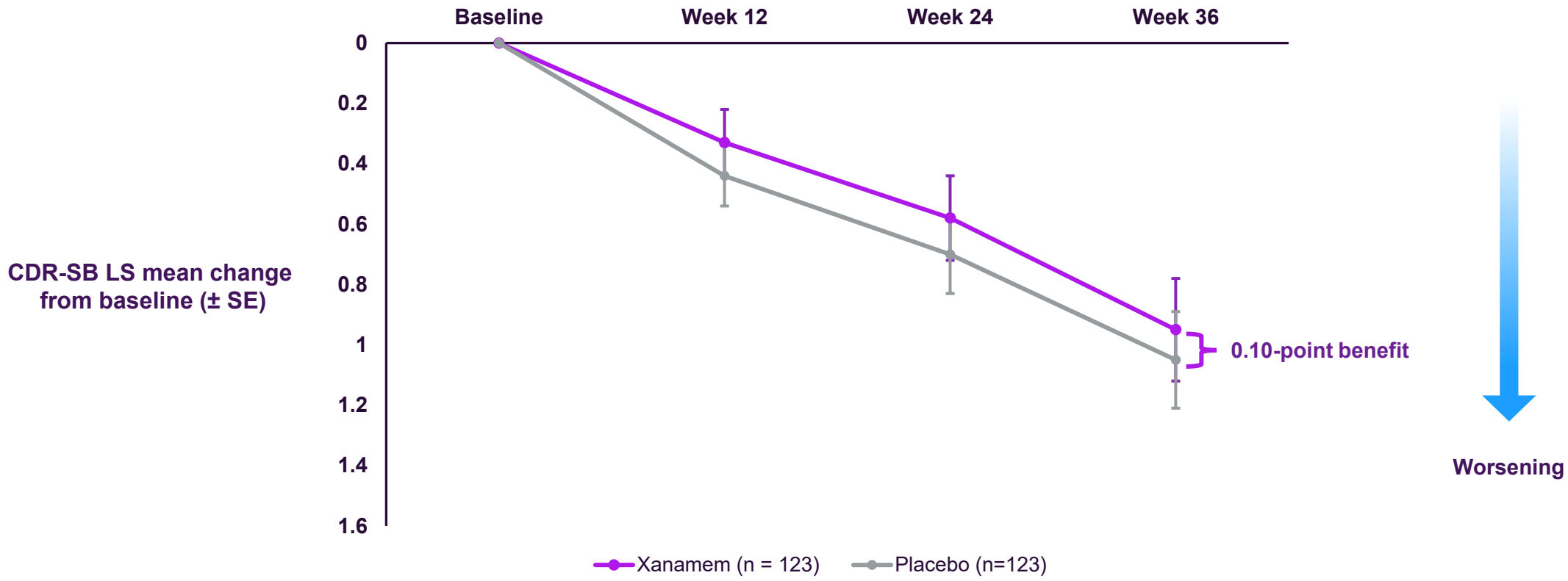
	Xanamem	Placebo
Age (mean, SD)	75.4 (7.5)	73.4 (8.6)
Sex, female (N, %)	63 (51.2)	57 (46.3)
Concomitant AD medications, yes (N, %)	74 (60.2)	75 (61)
ApoE4 carriers (N, %)	93 (75.6)	77 (62.6)
MMSE Total Score (mean, SD)	21.8 (3.4)	21.8 (3.1)
CDR-SB Score (mean, SD)	4.27 (1.84)	4.29 (2.09)
pTau-181 level (pg/ml) (mean, SD)	3.02 (2.13)	2.75 (1.22)
pTau-217 level (pg/ml) (mean, SD)	0.98 (1.32)	0.81 (0.48)

Primary endpoint: small overall CDR-SB benefit

Effect size 0.10 points at end of treatment, not statistically significant (p = 0.65 Week 36)



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Major Xanamem trend in prespecified age > 75 years

CDR-SB effect size 0.39 points, p = 0.22 at Week 36

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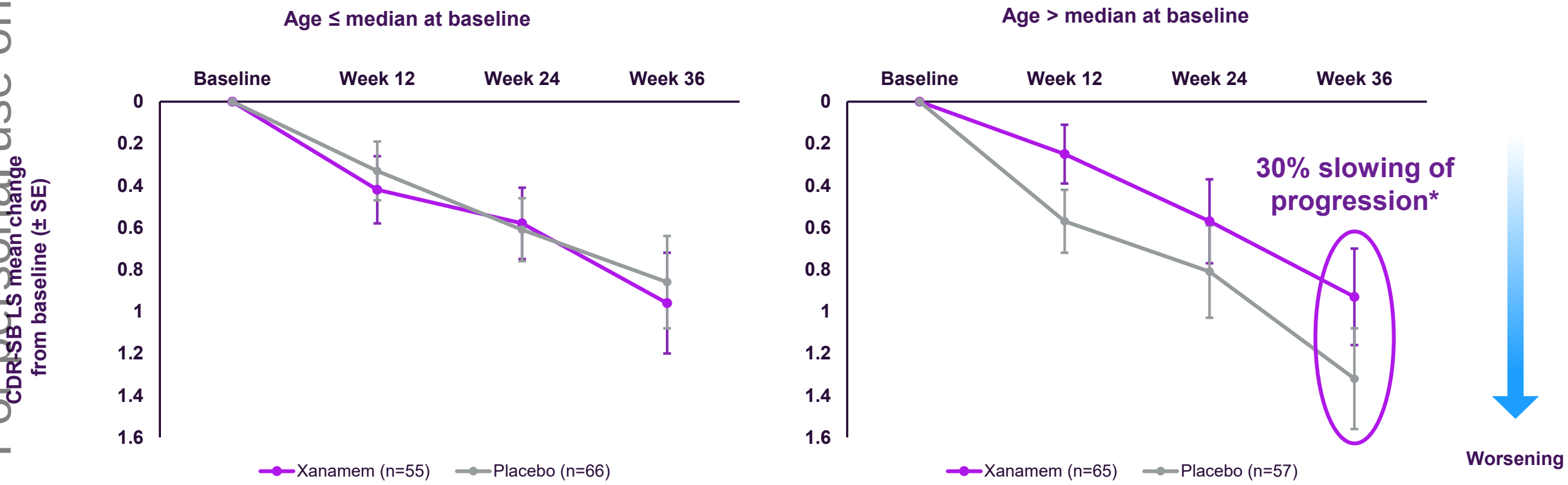

* 30% slowing similar to approved antibody therapies; older people have higher 11β-HSD1

Clear benefits in response rates in older participants

40% Xanamem stable (no progression) vs. 22% Placebo for age > 75 years*

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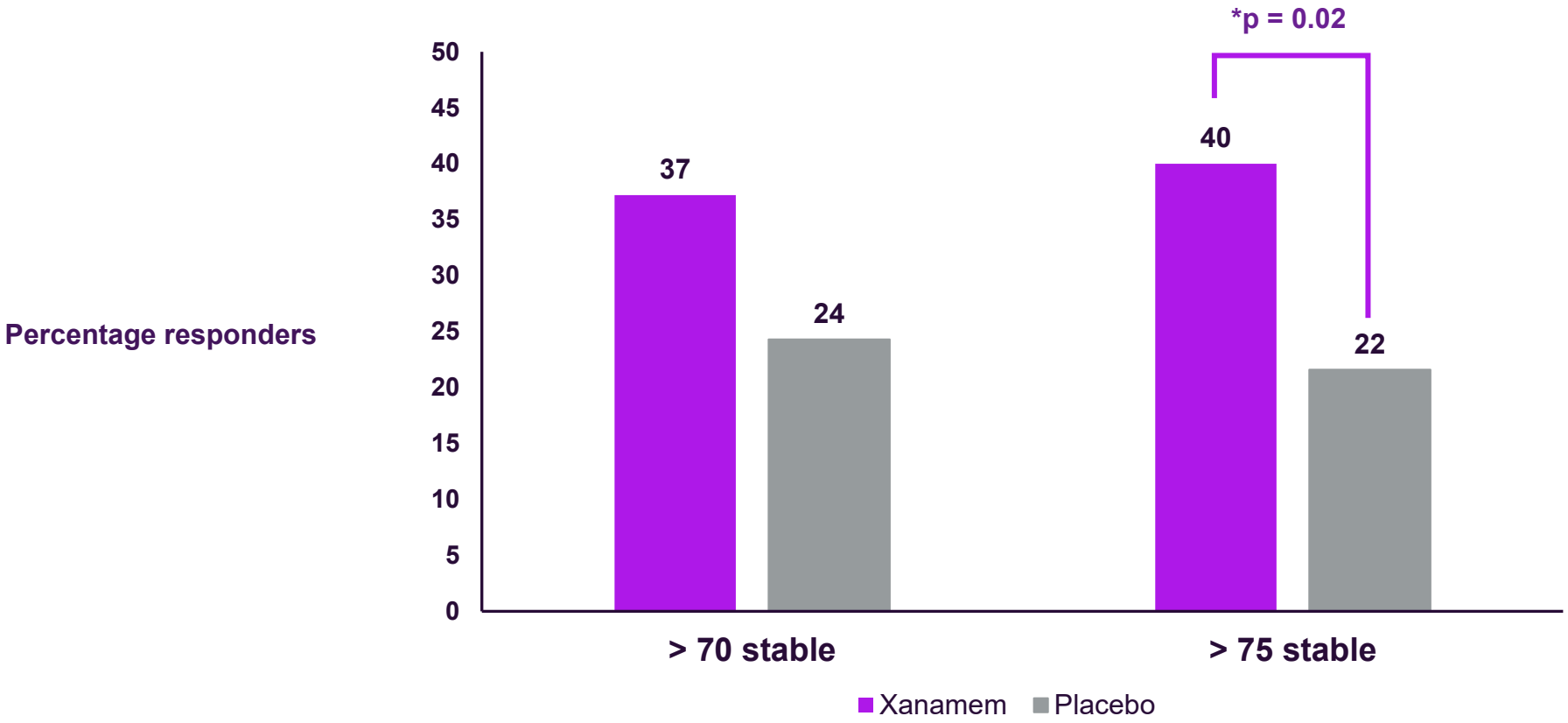

For context, stable disease claim in donanemab trials is similar at 47% vs. 29% at one year

* Statistically significant: rate of stable or improved score of CDR-SB at end of treatment; donanemab data Sims et al. 2023

Major unmet need in Alzheimer's care for adults older than 75

Alzheimer's patients older than 75 represent more than two thirds of the market

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- 5.5 million Americans age 75+ live with Alzheimer's, accounting for 74% of U.S. cases among adults 65 and older. [1]
- ~80% of Alzheimer's cases among adults ages 75–84 were mild or moderate. [2]
- Recently approved Alzheimer's drugs are for earlier stage disease called "Mild Cognitive Impairment" as well as "Mild Alzheimer's disease" – e.g. early intravenous lecanemab uptake was about 80% lower at age 75+ than at ages 66–74. [3, 4]
- An estimated 32 million people had Alzheimer's disease worldwide in 2020. By 2050, the global population age 80+ is projected to triple to 426 million. [5, 6]

[1] Alzheimer's Association, 2026 Facts and Figures, Fig. 4. [2] Yuan et al., J Alzheimers Dis, 2021. [3] U.S. prescribing information for Leqembi and Kisunla, §1. [4] Zhou et al., JAMA Network Open, 2025. [5] Gustavsson et al., Alzheimer's & Dementia, 2023, Table 3. [6] WHO, Ageing and health, 2025.

Slight benefit of Xanamem on cognition

Cognitive performance measured by computerized testing, p = 0.59

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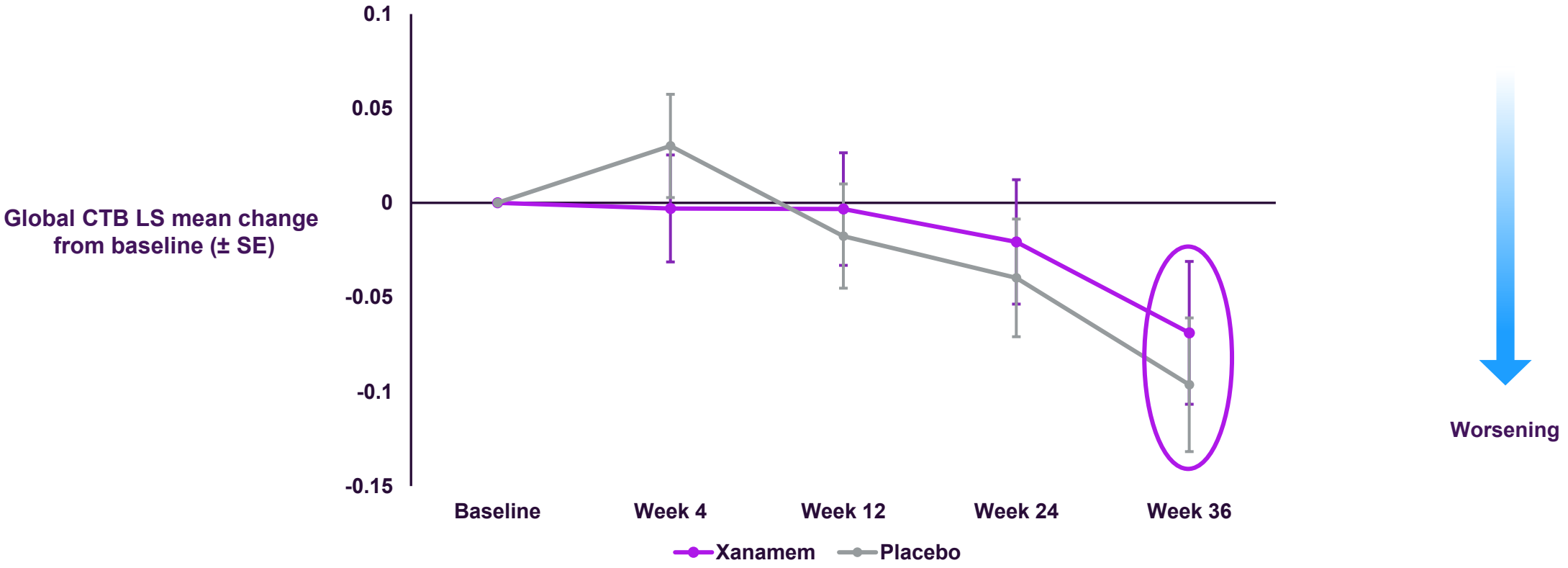

Slight benefit on daily functioning overall

A-IADL-Q-SV “Amsterdam” activities of daily living questionnaire

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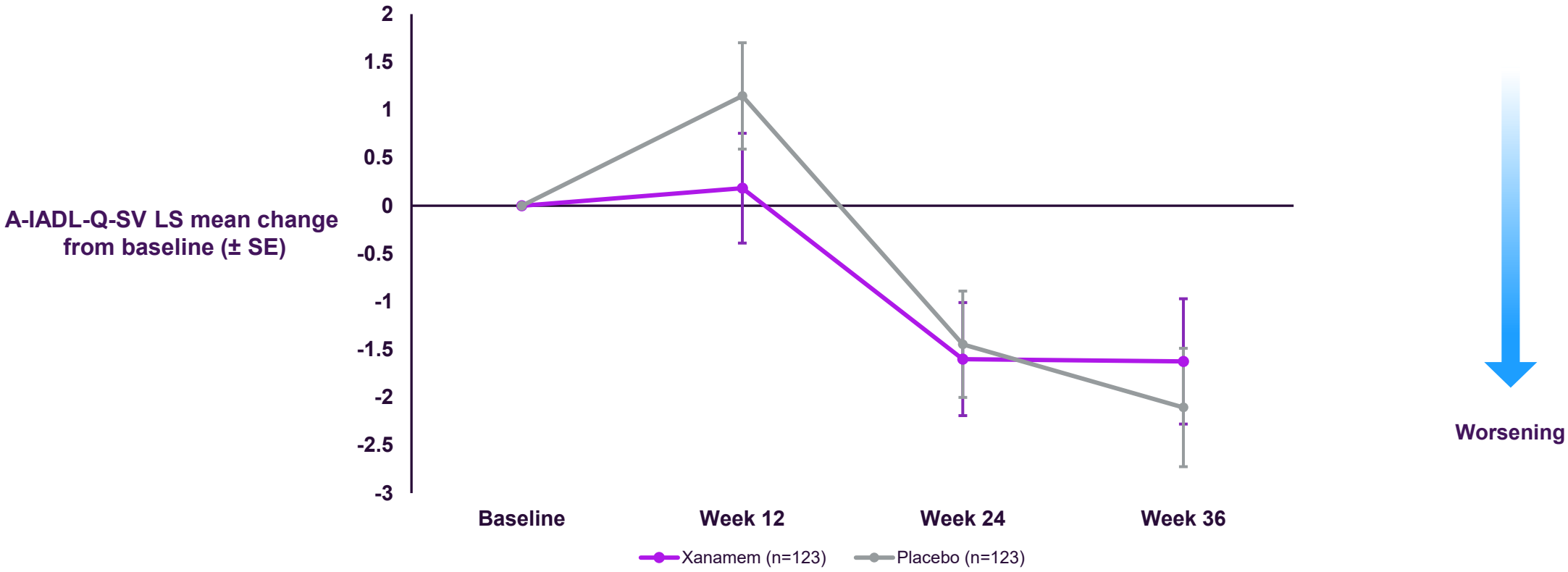

Other preliminary findings

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- Available data from the XanaMIA OLE phase indicates disease stabilization in the mean CDR-SB in the first 29 participants who have reached 24 weeks on active Xanamem
- Trends towards reduction in neuroinflammation markers GFAP, neurofilament light
- No trends towards reduction in Alzheimer's disease biomarkers such as pTau
- Excellent safety profile consistent with prior trials
- No serious adverse events attributed to Xanamem

The XanaMIA interim analysis was strongly positive

Effect sizes 0.58 at Week 24, p = 0.03; 0.38 at Week 36, p = 0.39

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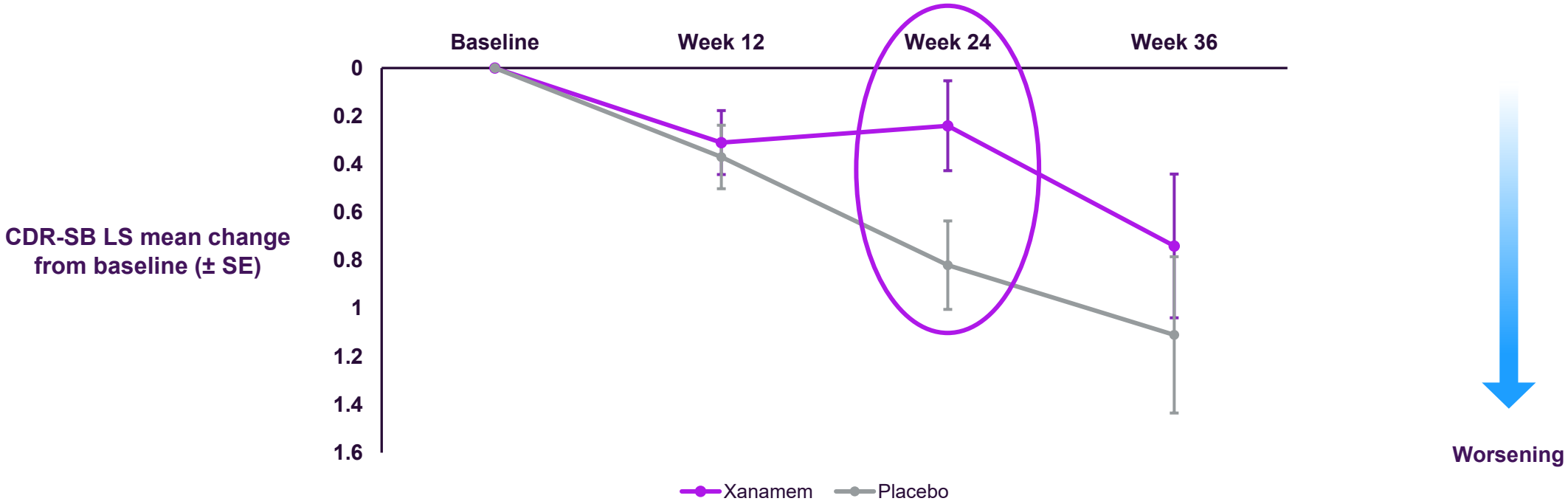

	Week 12	Week 24	Week 36
n (Xanamem)	70	43	29
n (Placebo)	72	45	23

Conclusion

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- The Company sincerely thanks everyone who has supported Xanamem development up to this point including patients and their families living with Alzheimer's disease, as well our shareholders
- The risk-benefit profile of Xanamem is highly suited to treatment in mild to moderate Alzheimer's disease, with notable findings of activity in older participants, who represent a poorly served and large segment of the market
- In patients over 75 a statistically significant disease stabilization rate was observed together with disease slowing of 30% (for comparison, Eli Lilly claim 22% for donanemab, Eisai 27% for lecanemab)
- The Open Label Extension (OLE) phase disease shows stabilization over 24 weeks (no mean progression) in the first 29 participants on Xanamem - OLE phase to continue
- Next OLE milestone when approximately 100 participants reach ≥24 weeks of treatment (Q1 CY2027)
- Balance sheet (cash balance $18.9 million and no debt) provides optionality to fully explore the trial data with potential partners over the coming months and determine the optimal development path for Xanamem

Online Q&A

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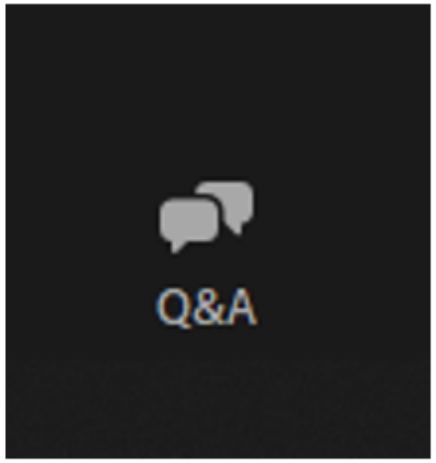

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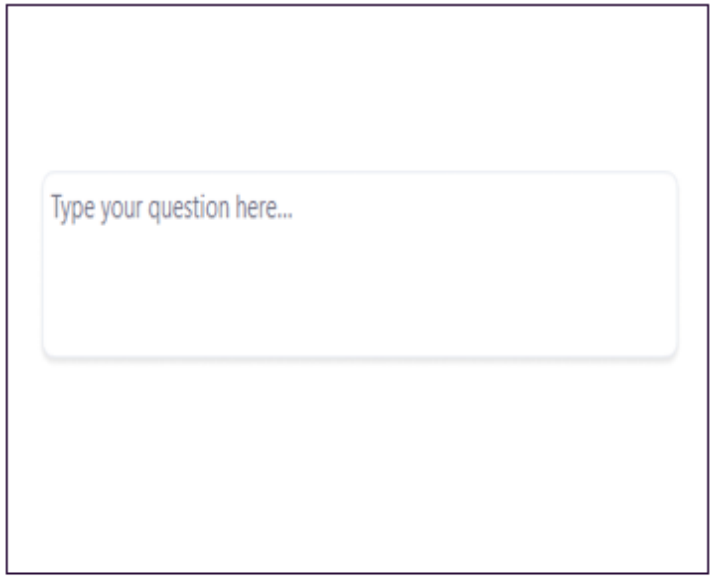

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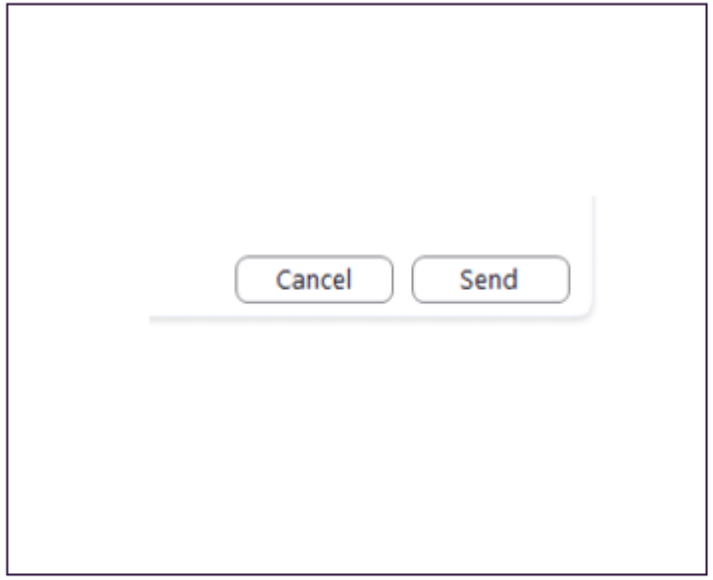

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