ASX ANNOUNCEMENT

Actinogen CEO Steve Gourlay leads $11.1 million capital raising with $1 million investment designed to accelerate XanaMIA Alzheimer's trial[1]

Sydney, 18 September 2024. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the successful completion of an $8.1 million share placement to existing shareholders and new institutional investors, along with the launch of a $3.0 million share purchase plan (SPP) offer to existing shareholders on the same financial terms as the placement.

The funds will be used to accelerate the full enrolment of 220 patients with biomarker-positive Alzheimer's disease (AD) in the 36-week placebo-controlled XanaMIA Phase 2b/3 trial being conducted in Australia and the US. The funds will also allow the trial to be administered according to statistical and quality standards required to achieve "pivotal" status as one of two potential trials required for marketing approval in the US and globally for the treatment of AD.

Combined with other available funding sources, this capital raising will provide a cash runway to at least mid-2026.

Key Highlights:

- **CEO, Dr Steven Gourlay, subscribed for $1 million in the placement, while other directors subscribed for a total of $130,000, subject to shareholder approval at an Extraordinary General Meeting (EGM) to be advised**
- **The $8.1 million placement to institutional and professional investors was at an issue price of $0.03 (3 cents) per share, with three options granted for every four shares subscribed for (new options). The options have an exercise price of $0.05 (five cents) and an expiry date of 30 September 2027. The new options are intended to be listed on the ASX**
- **Approximately 270 million new fully paid shares and 203 million new options will be issued in total under the placement**
- **The SPP offers a maximum of 100 million shares and 75 million new options on the same terms as the placement. SPP shares and attached options are also subject to shareholder approval at the upcoming EGM**
- **The funds raised will be used to accelerate enrolment of the full 220 participants in the XanaMIA phase 2b/3 Alzheimer's disease trial at Australian and new US clinical sites, with interim data from the first 100 participants anticipated in mid 2025 and final results in mid 2026.**

[1] All financial data is quoted in Australian dollars, unless stated otherwise

Webinar today

ACW management will conduct a webinar at 11am this morning to discuss the details of the capital raising and the Company's clinical trial program. Pre-register or join at 11am AEST today by clicking on the following link or pasting the address into your browser:
https://actinogenmedical.zoom.us/webinar/register/WN_P1oto5nyQuKwMvNPeEQoNg

The webinar presentation is attached to this announcement.

At the conclusion of the presentation, there will be an opportunity for questions from webinar attendees. A recording of the webinar will be made available as soon as possible after the conclusion of the event on the Company's YouTube channel, with links provided on the Company's website (https://actinogen.com.au/) and social media platforms.

Dr Steven Gourlay, Actinogen CEO and MD, said:

"Following the validation of Xanamem's 10 mg dose and clinical activity in the recent depression trial, I am pleased to invest a further $1 million into the Company with the goal of establishing Xanamem as a novel and important therapy for depression and Alzheimer's disease.

"As we accelerate the XanaMIA phase 2b/3 trial towards full recruitment the new funding ensures we can continuously enrol patients at an expanded number of clinical sites in Australia and the US to meet our timelines.

"The new funding strengthens our balance sheet position as we enter a period of negotiation with potential co-development and regional commercial partners for depression and Alzheimer's disease.

"We are pleased to offer eligible retail shareholders the opportunity to participate in a share purchase plan (SPP) on the same terms as the placement to a maximum of $30,000 per shareholder."

Capital Raising

The $11.1m million capital raising comprises a $7.0 million institutional placement, a further $1.1 million from CEO Steven Gourlay and the Actinogen Board, and a $3.0 million share purchase plan. The offer price for the capital raising is $0.03 per new share, representing an 18.2% discount to the 5-day VWAP of $0.0375 per share to 16 September 2024.

For every four new shares acquired under the capital raising, three new options will be attached at an exercise price of $0.05 per option expiring 30 September 2027. The Company intends to list the options on the ASX as soon as practicable following the close of the SPP.

CEO Dr Steven Gourlay has invested $1.0 million into the placement (subject to shareholder approval), while non-executive directors will subscribe for a further $130,000 combined in the placement, also subject to shareholder approval.

Placement

The placement to institutional, sophisticated and professional investors will raise $7.0 million, before transaction-related costs and has attracted strong demand from existing shareholders and new investors. Subscriptions for shares under the placement were more than double the availability, resulting in scale-backs.

Excluding the shares and options subscribed for by the CEO and non-executive directors, the placement will result in the issue of approximately 233 million new, ordinary fully paid Actinogen shares at $0.03 per share and approximately 174 million options with an exercise price of $0.05 expiring 30 September 2027. Bell Potter Securities Limited and Moelis Australia Advisory Pty Ltd acted as Joint Lead Managers.

The placement will be conducted using the Company's existing capacity under ASX Listing Rule 7.1. No shareholder approval is required other than for the proposed subscription by Dr. Steven Gourlay and the board for $1.13 million under the placement, and for the SPP as described below. New shares subscribed for under the placement are expected to settle on Monday 23 September 2024 and commence trading on the ASX on Wednesday 25 September 2024.

Share purchase plan (SPP)

In addition to the placement, the Company will offer an SPP to eligible shareholders with a target raise of $3.0 million. Eligible shareholders as of the record date of 7:00pm (AEST) on Tuesday, 17 September 2024 with a registered address in Australia and New Zealand and (under limited circumstances and by invitation only) the United States will be invited to participate in the SPP at the offer price of $0.03 per share (the same issue price as the placement).

The Company reserves the right to place any shortfall under the SPP (at the same issue price) utilising its remaining capacity under ASX Listing Rule 7.1. Shareholder approval is required for the SPP and further information in relation to the proposed EGM will be contained in a Notice of Meeting to be issued to shareholders shortly.

The SPP will open on Tuesday, 24 September 2024 and close at 5:00pm (AEDT) on Tuesday, 8 October 2024. The proposed SPP is subject to shareholder approval, and allotment under the SPP (where approved by shareholders) will take place after that shareholder approval. The EGM notice will be lodged with the ASX and despatched as soon as reasonably practical, The SPP offer is not underwritten.

Based on the Company's capital structure as of the record date, should the targeted $3.0 million (before offer-related costs) be raised, approximately 100 million new shares will be issued under the SPP. An application for the quotation of the SPP Shares will be made immediately following their issuance.

An offer document containing the terms and conditions of the SPP will be lodged with ASX and sent to eligible shareholders on 24 September 2024. It will include a link to a personalised application form, and shareholders should read the offer document in full before submitting an application under the SPP.

Key dates for the SPP Offer

Record date	7pm (AEST), Tuesday 17 September 2024
Announcement date	Wednesday 18 September 2024
Despatch of Prospectus for the SPP, SPP Options and Placement Options **SPP Opening date**	Tuesday 24 September 2024
Expected issue date of placement shares and options	Tuesday 24 September 2024
Closing date	5pm (AEDT), Tuesday 8 October 2024
Announcement of SPP results, (issue subject to shareholder approval)	Thursday 10 October 2024

This timetable is indicative only and subject to change. The Company reserves the right to amend the dates at its discretion and without notice, subject to ASX Listing Rules and the *Corporations Act 2001* (Cth).

ENDS

Dr. Steven Gourlay
CEO & Managing Director
P: +61 2 8964 7401
E. steven.gourlay@actinogen.com.au

Investors

Michael Roberts
Investor Relations
M: +61 423 866 231
E. michael.roberts@actinogen.com.au

Media

George Hazim
Media & Public Affairs Australia
M: +61 417 516 262
E: georgehazim@mediaaffairs.com.au

Announcement authorised by the Board of Directors of Actinogen Medical

About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company developing a novel therapy for neurological and neuropsychiatric diseases associated with dysregulated brain cortisol. There is a strong association between cortisol and detrimental changes in the brain, affecting cognitive function, harm to brain cells and long-term cognitive health.

Cognitive function means how a person understands, remembers and thinks clearly. Cognitive functions include memory, attention, reasoning, awareness and decision-making.

Actinogen is currently developing its lead compound, Xanamem, as a promising new therapy for Alzheimer's Disease and Depression and hopes to study Fragile X Syndrome and other neurological and psychiatric diseases in the future. Reducing cortisol inside brain cells could have a positive impact in these and many other diseases. The cognitive dysfunction, behavioural abnormalities, and neuropsychological burden associated with these conditions is debilitating for patients, and there is a substantial unmet medical need for new and improved treatments.

Current Clinical Trials

The **XanaCIDD Phase 2a depression trial** was a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 167 patients with moderate depression and a degree of baseline cognitive impairment. Participants were evenly randomized to receive Xanamem 10 mg once daily or placebo, in most cases in addition to their existing antidepressant therapy, and effects on cognition and depression were assessed. Positive topline results on depression were announced 12 August CY2024 and updated 26 August CY2024.

The **XanaMIA Phase 2b Alzheimer's disease trial** is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 220 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of the pTau181 protein biomarker in blood. Patients receive Xanamem 10 mg or placebo, once daily, and its ability to slow progression of Alzheimer's disease is assessed with a variety of endpoints. The primary endpoint of the trial is the internationally-recognized CDR-SB (Clinical Dementia Rating scale – Sum of Boxes). Initial results from an interim analysis of the first 100 participants are anticipated in mid 2025 and final results mid 2026.

About Xanamem

Xanamem's novel mechanism of action is to control the level of cortisol in the brain through the inhibition of the cortisol synthesis enzyme, 11β-HSD1, without affecting production of cortisol by the adrenal glands. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with progression in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has

shown some promise in prior clinical trials. The recent XanaCIDD trial demonstrated clinically and sometimes statistically significant benefits on depressive symptoms.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 380 volunteers and patients in eight clinical trials. Xanamem has a promising safety profile and has demonstrated clinical activity in patients with depression, patients with biomarker-positive Alzheimer's disease and cognitively normal volunteers. High levels of target engagement in the brain with doses as low as 5 mg daily have been demonstrated in a human PET imaging study.

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.

Disclaimer

This announcement and attachments may contain certain "forward-looking statements" that are not historical facts; are based on subjective estimates, assumptions and qualifications; and relate to circumstances and events that have not taken place and may not take place. Such forward looking statements should be considered "at-risk statements" - not to be relied upon as they are subject to known and unknown risks, uncertainties and other factors (such as significant business, economic and competitive uncertainties / contingencies and regulatory and clinical development risks, future outcomes and uncertainties) that may lead to actual results being materially different from any forward looking statement or the performance expressed or implied by such forward looking statements. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Actinogen Medical does not undertake any obligation to revise such statements to reflect events or any change in circumstances arising after the date hereof, or to reflect the occurrence of or non-occurrence of any future events. Past performance is not a reliable indicator of future performance. Actinogen Medical does not make any guarantee, representation or warranty as to the likelihood of achievement or reasonableness of any forward-looking statements and there can be no assurance or guarantee that any forward-looking statements will be realised.

ACTINOGEN MEDICAL ENCOURAGES ALL CURRENT INVESTORS TO GO PAPERLESS BY REGISTERING THEIR DETAILS WITH THE DESIGNATED REGISTRY SERVICE PROVIDER, AUTOMIC GROUP.

Actinogen

Oral Xanamem®

Controlling brain cortisol to treat depression and slow progression in Alzheimer's disease - a novel therapeutic mechanism in late phase trials

Capital Raising – $11.1 million to accelerate Alzheimer's phase 2b/3 trial

18 September 2024

Disclaimer

- This presentation has been prepared by Actinogen Medical Limited. (“Actinogen” or the “Company”) based on information available to it as at the date of this presentation. The information in this presentation is provided in summary form and does not contain all information necessary to make an investment decision.
- This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in Actinogen, nor does it constitute financial product advice or take into account any individual’s investment objectives, taxation situation, financial situation or needs. An investor must not act on the basis of any matter contained in this presentation but must make its own assessment of Actinogen and conduct its own investigations. Before making an investment decision, investors should consider the appropriateness of the information having regard to their own objectives, financial situation and needs, and seek legal, taxation and financial advice appropriate to their jurisdiction and circumstances. Actinogen is not licensed to provide financial product advice in respect of its securities or any other financial products. Cooling off rights do not apply to the acquisition of Actinogen securities.
- Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of Actinogen its officers, directors, employees and agents, nor any other person, accepts any responsibility and liability for the content of this presentation including, without limitation, any liability arising from fault or negligence, for any loss arising from the use of or reliance on any of the information contained in this presentation or otherwise arising in connection with it.
- The information presented in this presentation is subject to change without notice and Actinogen does not have any responsibility or obligation to inform you of any matter arising or coming to their notice, after the date of this presentation, which may affect any matter referred to in this presentation.
- This presentation is not for general distribution or third party reliance or use.
- This presentation contains certain budget information, forecasts and forward looking statements that are based on the Company’s management’s beliefs, assumptions and expectations and on information currently available to management in respect of which there is NO guarantee of future performance. Such budget information, forecasts and forward looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results or performance of Actinogen to be materially different from the results or performance expressed or implied by such forward looking statements. These risks and uncertainties include, but are not limited to the performance of Actinogen in its clinical trials including whether it's technology proves to be a safe and effective treatment, market penetration, competition from any other similar products, intellectual property risks (including securing rights in technology and patents) and global economic conditions. Furthermore, Actinogen's research, product development, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. There is no guarantee that Actinogen will obtain the required approvals, licences and registrations from the relevant authorities in jurisdictions in which it operates. Actinogen or others could identify product and efficacy issues relating to the safety of our technology. Accordingly, all forward looking statements are based on numerous assumptions regarding the Company’s present and future business strategies and the political and economic environment in which Actinogen will operate in the future, which are subject to change without notice. Past performance is not necessarily a guide to future performance and no representation or warranty is made as to the likelihood of achievement or reasonableness of any forward looking statements or other forecast. There is no guarantee that Actinogen will achieve its stated objectives/milestones, that any of its forecasts will be met or that forward looking statements will be realised. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.
- Neither Actinogen nor any other entity or person in or associated with Actinogen guarantee any return (whether capital or income) or generally the performance of Actinogen or the price at which its securities may trade. Any investment in Actinogen is subject to investment risks including the possibility of loss of capital invested and no return of income or payment of any dividends.
- To the maximum extent permitted at law, Actinogen and all of its representatives, directors, officers, partners, employees or professional advisers (Parties) exclude all direct and indirect liability arising out of or in connection with any use or reliance of the information contained or described within this presentation. Other than to the extent required by law (and only to that extent), the Parties do not make any representation or give any assurance, guarantee or warranty (express or implied) as to, nor assume any responsibility or liability for, the authenticity, origin, validity, accuracy, suitability or completeness of, or any errors in or omissions from, any information, statement or opinion contained in this presentation or any accompanying, previous or subsequent material or presentation.

Overview

Novel mechanism and attractive oral profile

- Xanamem is a unique brain-penetrant tissue cortisol synthesis inhibitor (11β-HSD1 enzyme)
- Once-daily oral therapy with potential efficacy, safety and ease of use greater than competitors
- More than 380 people treated with promising safety profile and low drug interaction risk

Large and growing market opportunities with significant unmet need

- Significant benefits in major depressive disorder (MDD) in phase 2a trial, phase 2b/3 in planning
- Disease-modifying activity to slow Alzheimer's disease (AD) in phase 2a data, phase 2b/3 on-going
- Trials potentially read through to bipolar disease, other dementias including Parkinson's

Patent protection

- Composition of matter protection to 2031 – to 2036 with extensions in major markets
- Additional recent patents protect further against future competition

Capital Raising of $11.1m led by $1 million investment from CEO, clinical milestones funded

- Undertaking a capital raising of $11.1m via a $8.1m Placement and $3m SPP at $0.03 per share. Placement and SPP shares will receive an attaching three for four option with an exercise price of $0.05 and expiry date of 30 September 2027
- CEO, Dr Steven Gourlay, will be subscribing for $1m in the Placement (subject to shareholder approval)
- Funds raised will be used for XanaMIA phase 2b/3 trial
- Post capital raising the company will have a cash runway through mid 2026
- Phase 2b/3 XanaMIA Alzheimer's Disease interim data mid 2025, final data mid 2026

Experienced board and management team

Dr. Geoff Brooke
Chairman
MBBS; MBA

Dr. Steven Gourlay*
CEO & MD
MBBS; FRACP; PhD; MBA

Mr. Malcolm McComas
Non-Executive Director
BEc, LLB; FAICD; SF Fin

Dr. George Morstyn
Non-Executive Director
MBBS; PhD; FRACP CD

Dr. Nicki Vasquez
Non-Executive Director
PhD

Management Team

Dr. Steven Gourlay
CEO & MD

Dana Hilt
Chief Medical Officer
MD

Will Souter
Chief Financial Officer
BComm, LLB

Cheryl Townsend
VP Clinical Operations
RN, M Health Law

Fujun Li
Head of Manufacturing
PhD

Michael Roberts
Head of IR & Comms
B.Ec (Hons), CPA, FFIN

* Invested ~$2m post raise on personal account

Alzheimer's disease phase 2b/3

Recent developments increase confidence in XanaMIA

XanaMIA Alzheimer's disease trial moving to full enrolment and full phase 2b/3 design

- Recently released data showing clinically and statistically significant improvement in depression symptoms validate Xanamem's mechanism of action and 10 mg dose to control brain cortisol
- Lack of superiority over placebo for cognitive enhancement in depressed patients prioritizes modification and functional endpoints as the primary evaluation tool in XanaMIA
- XanaMIA is established as one of two potential "pivotal" trials by:
  - Continuous enrolment of the full 220 participants in Australia and US to speed enrolment
  - CDR-SB as the primary endpoint (used for Eisai's Leqembi's FDA approval)
  - Independent Data Monitoring Committee to conduct interim analysis similar to market precedents
  - "Phase 3-standard" statistical methods
    - Full statistical power for primary endpoint ($p < 0.05$)
    - Sequential examination of secondary endpoints after primary ($p < 0.05$)
  - Additional quality oversight and auditing of trial sites, vendors and procedures
  - Use of commercial tablet formulation

Alzheimer's disease

Strong scientific rationale to address huge unmet medical need

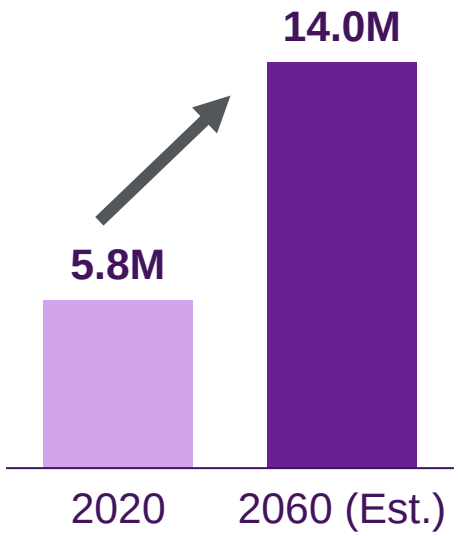
Scientific rationale

- Cortisol levels are elevated in brain fluid in early AD
- Chronic corticosteroid treatment leads to hippocampal atrophy and cognitive impairment
- Elevated cortisol levels are associated with clinical progression
- Alzheimer's disease mouse model: 30–60% inhibition of 11β-HSD1 provides full neuroprotection
- AD Phase 2a trial shows slowed disease progression in biomarker-positive patients
- MDD Phase 2a trial shows benefits in depression

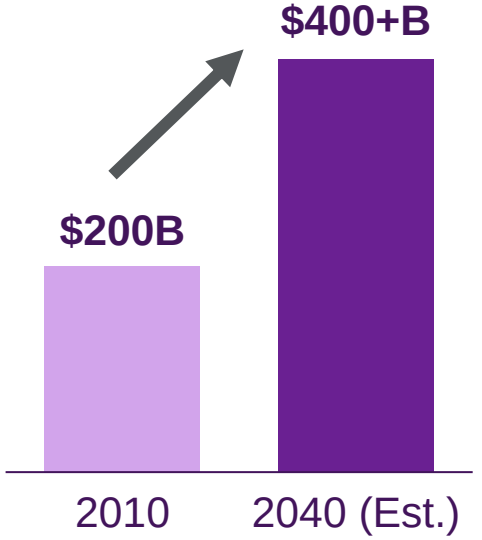
Alzheimer's Disease market – U.S.

Large unsatisfied and growing market

# of patients

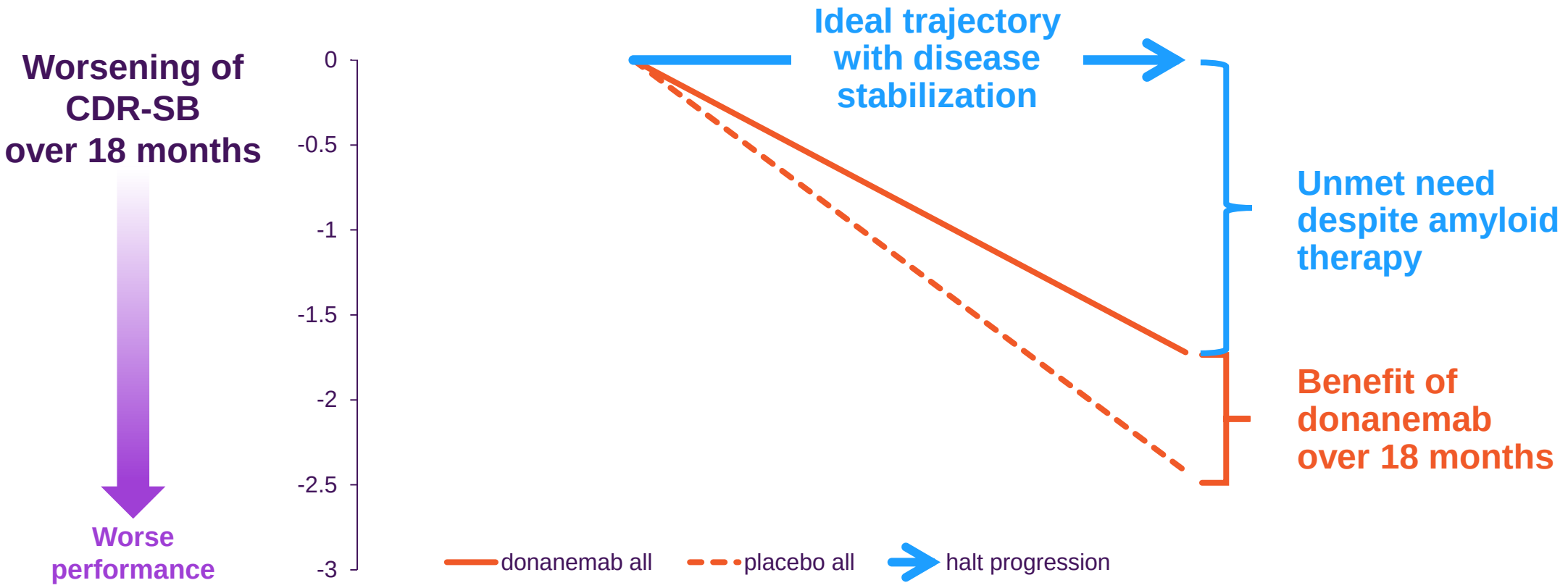


Cost to treat



Anti-amyloid therapy modestly slows AD progression

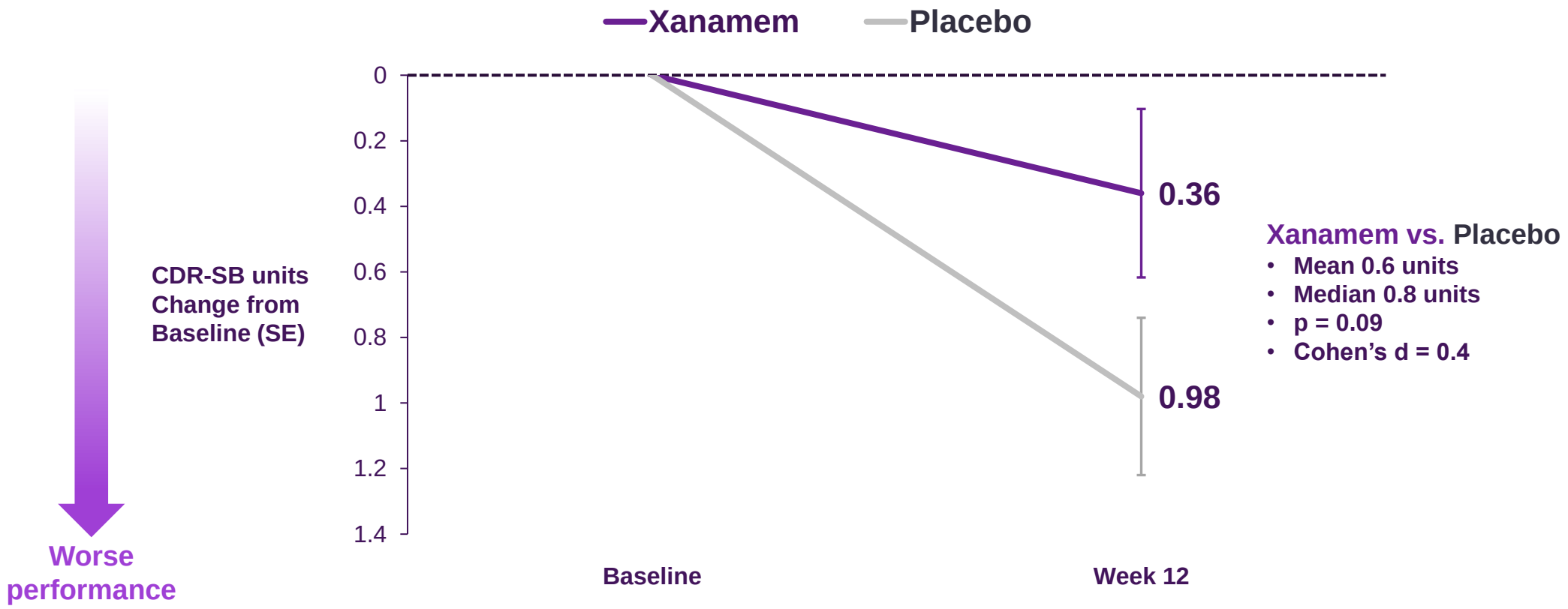
Ideally patients with AD would not worsen on treatment at all



Drugs targeting other mechanisms like Xanamem are needed

Xanamem slows AD progression markedly

Phase 2a data in biomarker-positive patients with mild AD (n=34)[1]

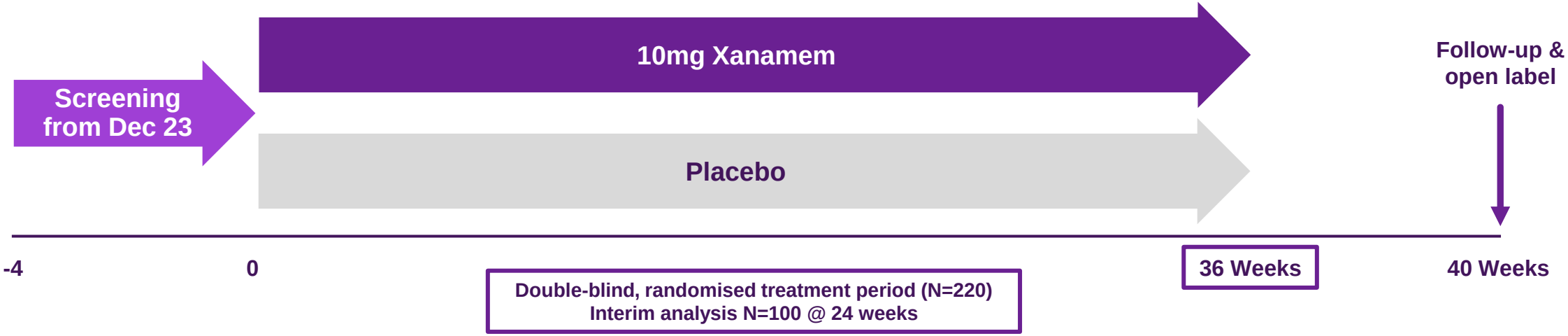


Xanamem benefits extrapolated to 18 months would be ~8x anti-amyloid drugs

1. Taylor et al. 2024, biomarker is pTau181 measured in blood

XanaMIA phase 2b/3 trial in Alzheimer's disease

Interim results mid 2025, final results mid 2026



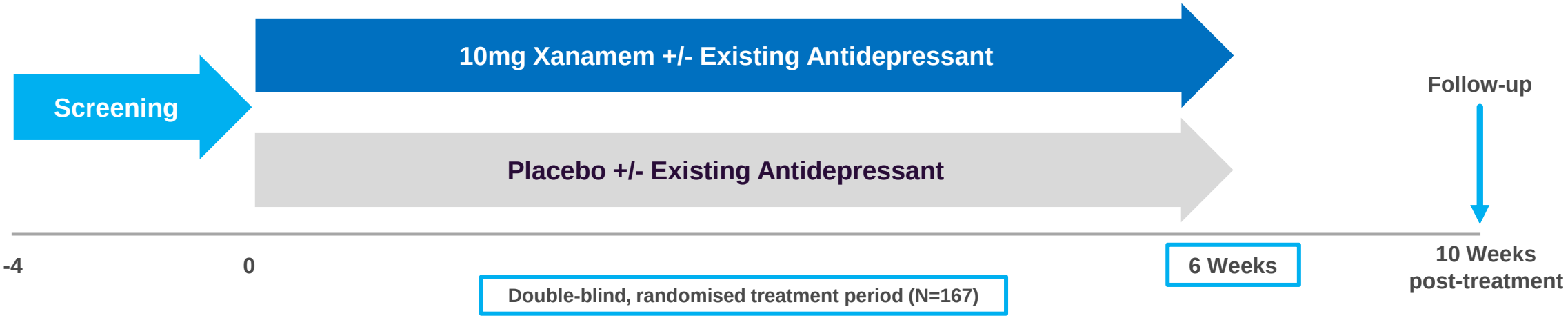
Key Inclusion Criteria	Primary Endpoint	Key Secondary Endpoints	Implementation
• Blood pTau biomarker positive • Mild-moderate Alzheimer's by NIA-AA criteria	• **CDR-SB (functional and cognitive measure)**	• Amsterdam Activity of Daily Living (functional measure) • Cognitive Test Battery (7 cognitive measures well-validated in the Alzheimer's field)	• **To-be-marketed tablet formulation** • Enrolment at 15 Australian sites • Currently **expanding to US** • Interim analysis when 100 people complete 24 weeks

NIA-AA=National Institute of Aging - Alzheimer's Association; **CDR-SB** Clinical Dementia Rating Scale – Sum of Boxes

Positive phase 2a depression data

XanaCIDD trial design

Phase 2a, double-blind, proof-of-concept controlled trial to assess safety and efficacy



Primary Endpoint	Key Secondary Endpoints
• **Cogstate Cognitive Test Battery Attention Composite** (attention and working memory)	• Montgomery-Åsberg Depression Rating Scale (**MADRS**) • Patient Global Impression-Severity **(PGI-S)** • Executive Function Cognitive Composite **(EFC)** • Memory Function Cognitive Composite **(MC)**

Results summary

- ***Clinically and statistically significant treatment benefits on depression symptoms***
- Cognition improved markedly in both Xanamem and placebo groups without evidence of greater Xanamem benefit vs. placebo
- Xanamem was safe and well tolerated (n=165 treated)
- The trial was well-conducted, with excellent data quality, no major differences between Australia and the UK or at high enrolling clinical sites

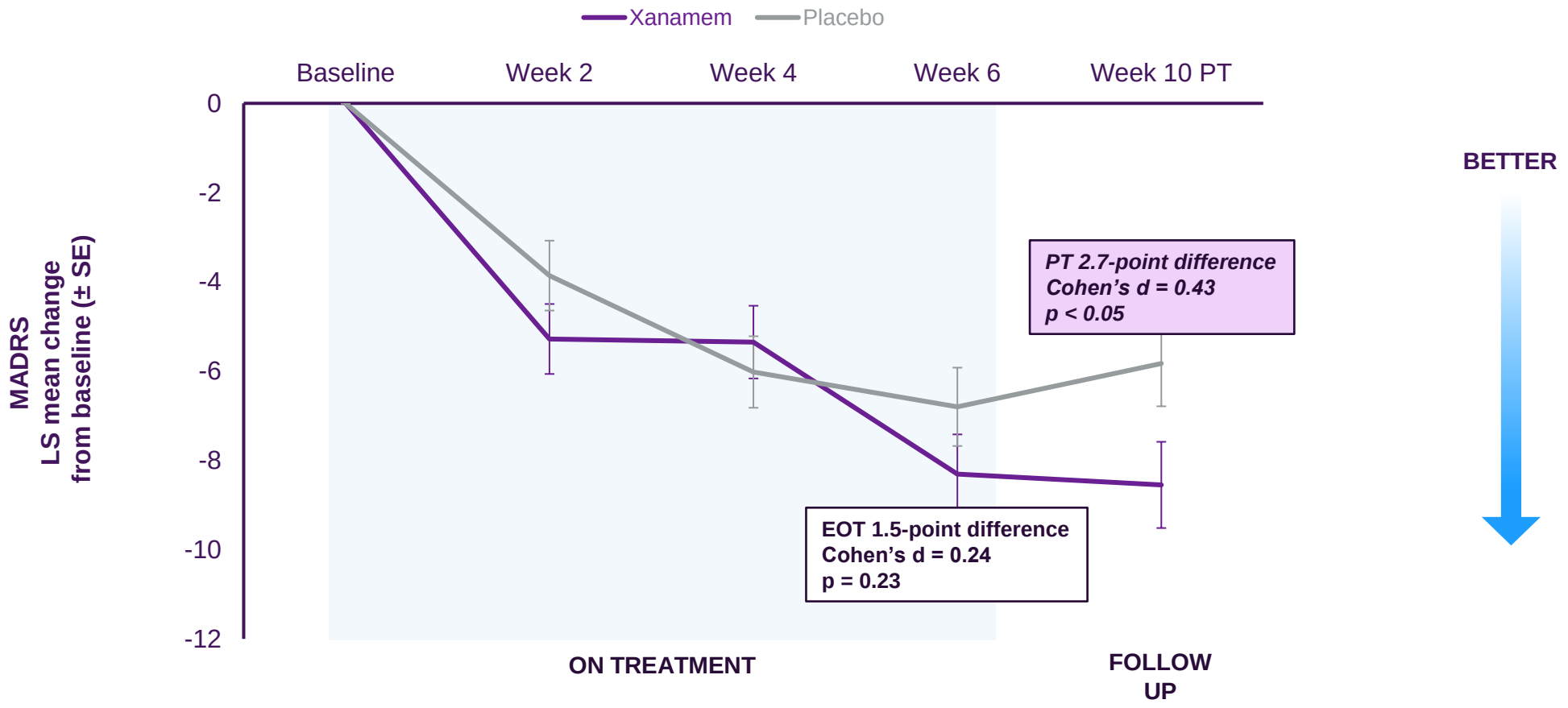
MADRS & PGI-S depression benefits

Montgomery-Åsberg Depression Rating Scale, Patient Global Impression-Severity

- Xanamem treatment performed better than placebo, to a clinically, and in many cases, statistically significant extent:
  - ✓ In all patients (n=165) a clinically significant MADRS benefit was seen at the end of 6 weeks treatment and a clinically and statistically significant benefit four weeks post-treatment at Week 10 ($p < 0.05$)
  - ✓ Xanamem showed higher response rates e.g. achieving 50% MADRS reduction (34% vs. 22%) and 50% higher remission rates (26% vs. 17%)
  - ✓ PGI-S curves separated earlier than MADRS and favored Xanamem at all timepoints
  - ✓ Subgroup analysis showed broadly consistent MADRS and PGI-S activity also with maximal effect at Week 10

Xanamem MADRS separation from Week 6

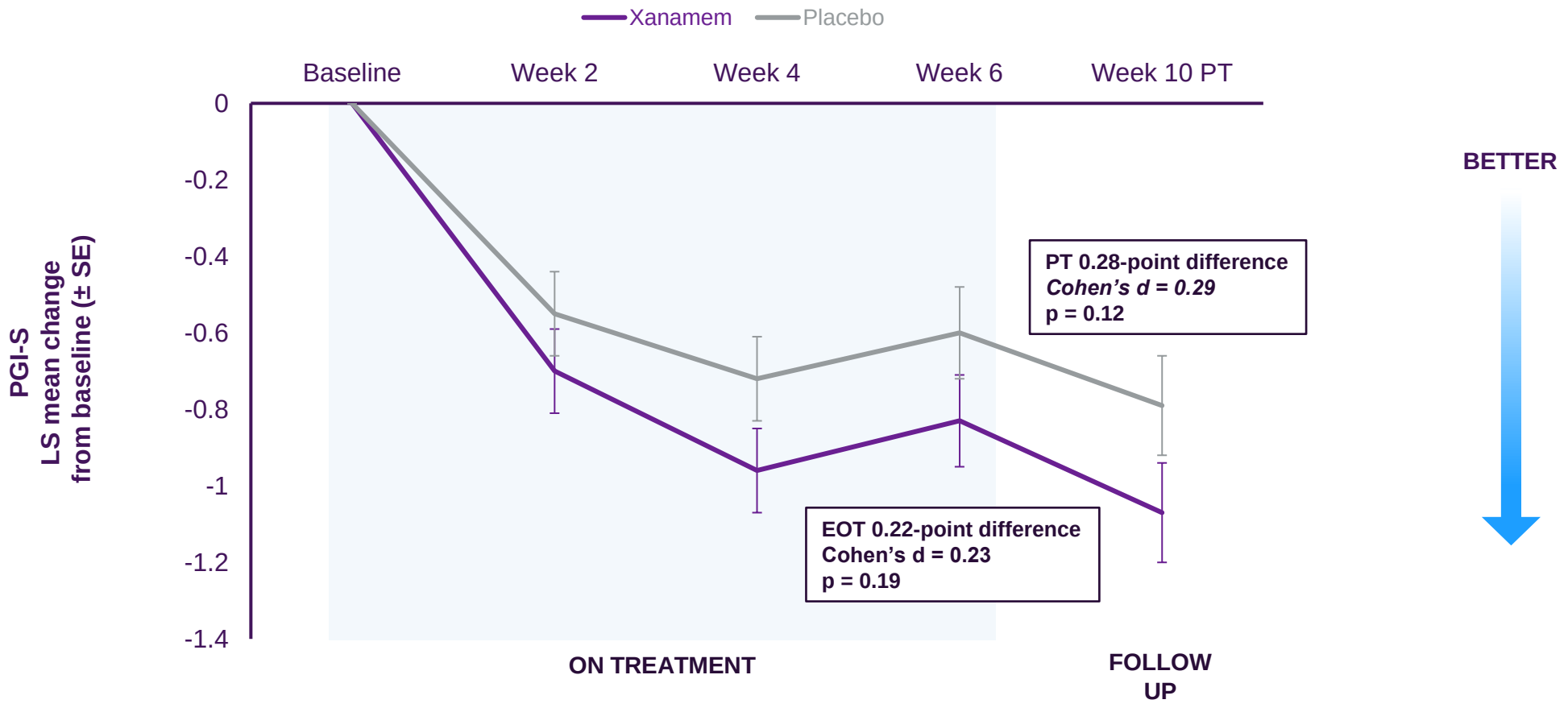
All randomized participants (n = 165)



Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale

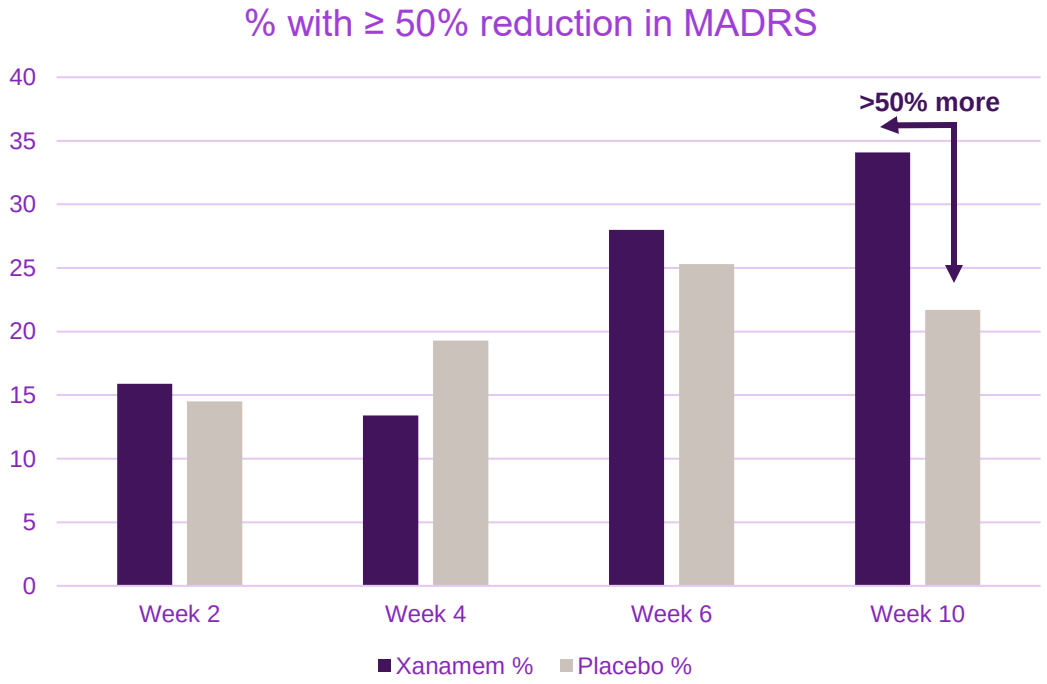
Xanamem PGI-S separation from Week 2

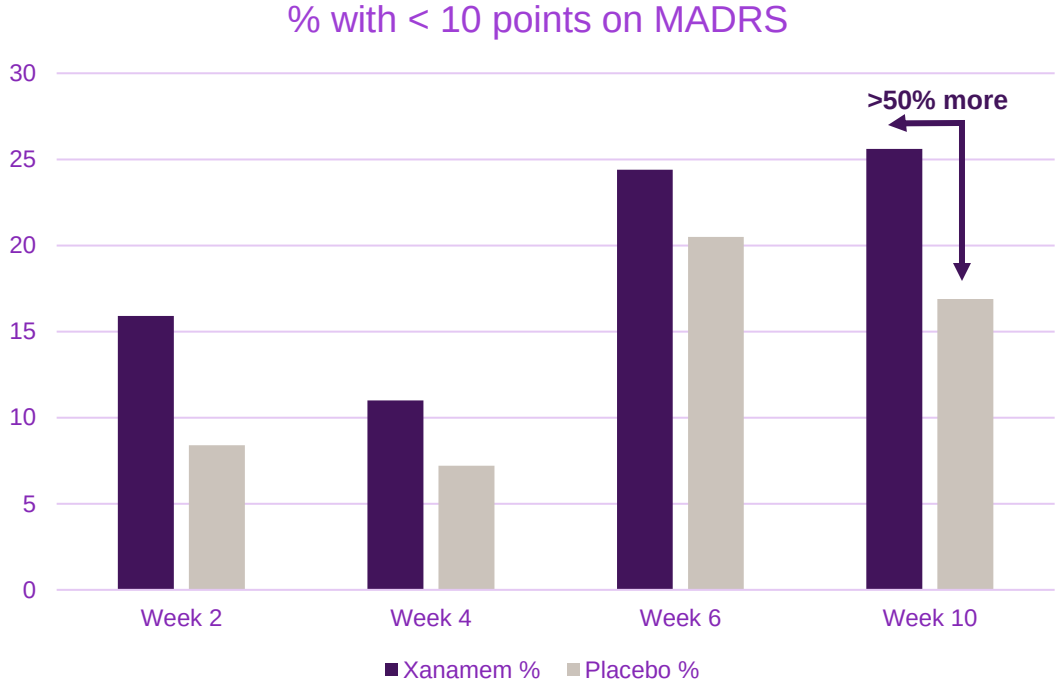
All randomized participants (n = 165)



Xanamem major improvement in depression response

Increased rates of remission (MADRS < 10) and large (50%) improvements





Broad & durable subgroup effects - MADRS & PGI-S

Measured at Weeks 2, 4, 6 & 10 (green favors Xanamem, red placebo)

Response/variable	All (n=165)	*No anti-D (n=31)	Yes anti-D (n=134)	*MADRS < 26 (n=81)	MADRS ≥ 26 (n=83)	*Cog. < 0.07 (n=82)	Cog. ≥ 0.07 (n=82)
MADRS (Cd ≥ 0.3) (week)	10	2,6	10	2,6,10	(4),10	2,6,10	-
MADRS (p < 0.05) (week)	10	-	10	6	-	2,10	-
PGI-S (Cd ≥ 0.3) (week)	-	6,10	4,6,10	4,6,10	6,10	4,6,10	-
PGI-S (p < 0.05) (week)	-	-	10	-	-	10	-
Selected demographics:							
Mean age (SD)	49 (14)	50 (13)	49 (14)	49 (14)	50 (13)	53 (13)	45 (13)
% female	62%	45%	66%	62%	63%	66%	59%
Mean HAM-D (SD)	21 (3)	21 (4)	21 (3)	20 (3)	23 (3)	22 (3)	21 (3)
% on anti-D therapy	81%	0%	100%	79%	83%	79%	83%
Mean boxfiller (SD)	21 (5)	22 (6)	21 (5)	22 (5)	21 (6)	20 (5)	23 (5)

Excellent safety profile consistent with prior trials

Summary of Treatment-Emergent Adverse Effects (TEAE)

	Xanamem N = 82	Placebo N = 83	Overall N = 165
Any TEAE	69 (84.1%)	67 (80.7%)	136 (82.4%)
TEAE related to trial drug	27 (32.9%)	24 (28.9%)	51 (30.9%)
Serious adverse event	0	1 (1.2%)	1 (0.6%)
Related TEAE discontinuation or interruption of drug	3 (3.7%)	1 (1.2%)	4 (2.4%)
TEAEs with incidence ≥ 5% overall			
Headache	11 (13.4%)	16 (19.3%)	27 (16.4%)
Fatigue	6 (7.3%)	5 (6.0%)	11 (6.7%)
Nasopharyngitis	4 (4.9%)	6 (7.2%)	10 (6.1%)
Upper respiratory tract infection	5 (6.1%)	5 (6.0%)	10 (6.1%)

There remains significant unmet need in depression

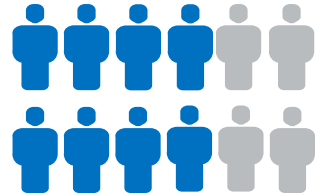
Xanamem's unique mechanism and safety differentiate it from older drugs

Scientific rationale

- More than 50 years of research associates cortisol with depression
- Elevated CSF and plasma cortisol levels associated with diagnosis, treatment outcomes and relapse
- Positive effects of cortisol receptor antagonism reported with mifepristone[3]
- ***Now positive phase 2a data on depressive symptoms for Xanamem***

U.S. Depression market large unmet need

- 21M patients have had ≥ 1 MDD episode



- Two-thirds with an episode **with severe impairment** in the past year
- 61% of adults with MDD episodes receive treatment with existing drugs (that have many side effects)
- ≥365 M prescriptions per year

A safe, effective and combinable small molecule is an attractive product profile for depression

3. Ding et al 2021

Offer Summary

Capital raising overview

Actinogen is seeking to raise up to approximately A$11.1m via a Placement and SPP

Placement	▪ Institutional Placement to raise approximately A$7.0m under Actinogen's existing L.R. 7.1 placement capacity (**Institutional Placement**) and; ▪ Placement to Directors of $1.1m, including CEO, Dr Steven Gourlay for $1.0m, subject to shareholder approval (**Director Placement**) (together, the Institutional Placement and Director Placement are the **Placement**) ▪ Approximately 270.2 million new fully paid ordinary shares in Actinogen (**New Shares**) to be issued under the Placement, representing approximately 10.0% of Actinogen's current shares on issue
Share Purchase Plan	▪ The Company intends to offer eligible shareholders the opportunity to participate in a Share Purchase Plan (**SPP**) and apply for up to $30,000 of New Shares, to raise up to an additional $3 million ▪ Record date for determining eligibility for the SPP is 7:00pm on Tuesday, 17 September 2024 ▪ The Company reserves the right to increase the size of the SPP or to scale back applications in its absolute discretion ▪ Further details in relation to the SPP including the timetable will be provided to eligible shareholders in an SPP booklet expected to be released following the Placement. The SPP is subject to shareholder approval and is not underwritten.
Offer Pricing	▪ New Shares issued under the Placement and SPP will be issued at an offer price of A$0.03 per share (**Offer Price**), which represents: – A discount of 14.3% to the last close of A$0.035 per share on 16 September 2024 – A discount of 18.2% to the 5-day VWAP of A$0.0375 per share to 16 September 2024 – A discount of 30.6% to the 15-day VWAP of A$0.0436 per share to 16 September 2024
Attaching Options	▪ New Shares will be offered under the Placement and SPP with three free attaching options (intended to be listed on the ASX) for every four New Shares issued (**Options**) subject to shareholder approval at the upcoming EGM ▪ The Options will have an exercise price of $0.05 and will expire on 30 September 2027
Director participation	▪ Directors Steven Gourlay, Geoff Brooke, George Morstyn and Malcolm McComas will participate in the Placement for $1.13m. This includes a subscription of $1.0m by CEO Steven Gourlay. Director participation is subject to shareholder approval at an extraordinary general meeting.
Ranking	▪ New shares under the Placement and SPP will rank pari passu with existing ordinary shares in Actinogen
Joint Lead Managers	▪ Bell Potter Securities Limited and MA Moelis Australia Advisory Pty Ltd

Use of funds

XanaMIA phase 2b/3 trial and other activities

Details	A$m
Full enrolment of phase 2b/3 XanaMIA trial for 220 participants	
▪ Additional site and patient costs	9.5
▪ Additional data management, data monitoring committee and statistical costs	0.5
▪ Additional quality activities	0.5
▪ Offer costs	0.6
Total	**11.1**

Offer timetable

Indicative capital raising timetable[1]	Date
Trading halt	Monday, 16 September 2024
Record Date for SPP	Tuesday, 17 September 2024
Placement and SPP announced, and trading halt lifted	Wednesday, 18 September 2024
Settlement of Placement Shares	Monday, 23 September 2024
Allotment of Placement Shares and SPP Opens	Tuesday, 24 September 2024
SPP Closes	Tuesday, 8 October 2024

Note: 1. The timetable is indicative only and is subject to change

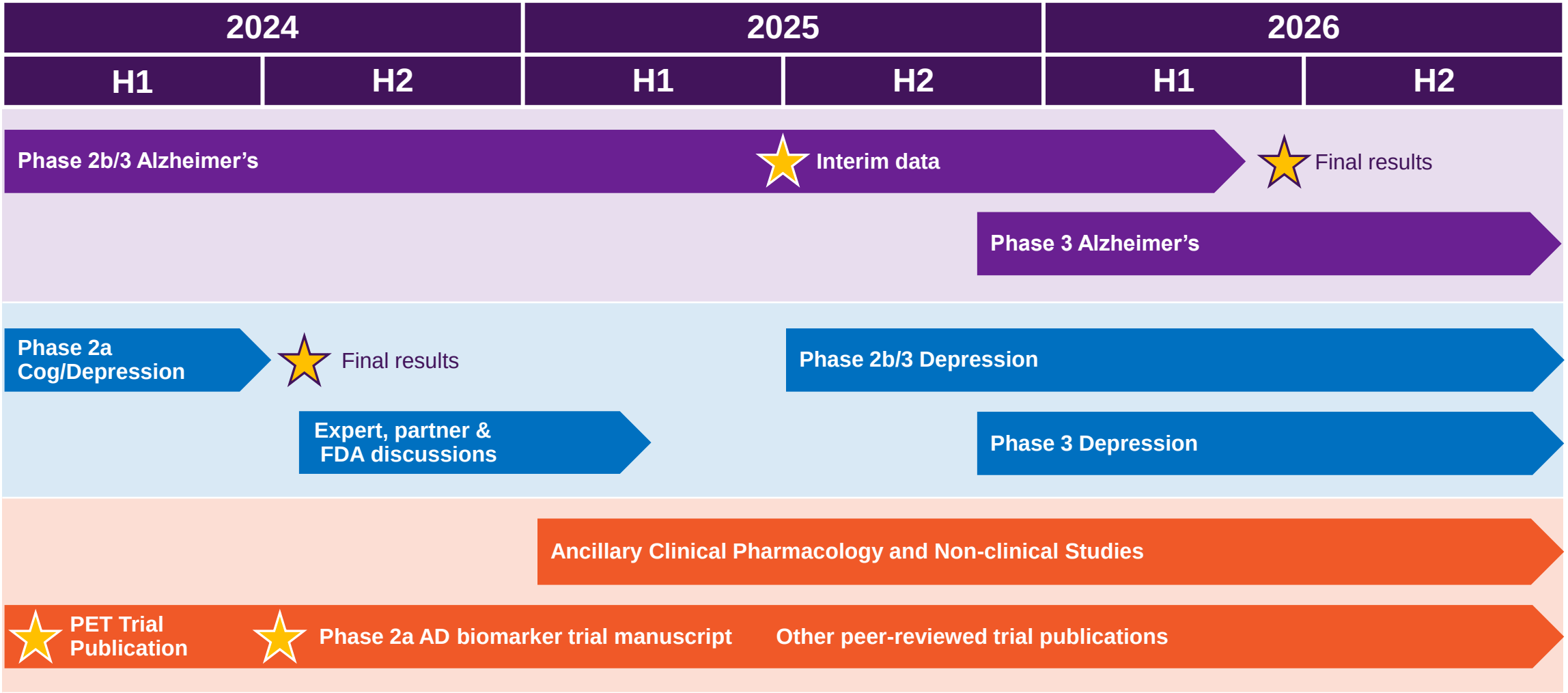
Conclusions

Controlling brain tissue cortisol really works!

Proof of 11β-HSD1 as a therapeutic target is a *major scientific and clinical advance*

- Clinically, statistically significant and durable treatment benefits on depression
- Xanamem was safe and well tolerated; no significant safety issues were observed
- Durability of Xanamem benefits for four weeks after the end of treatment suggests underlying biological modification due to cortisol control has occurred
- Depression data suggest higher probability of success for XanaMIA phase 2b/3 trial

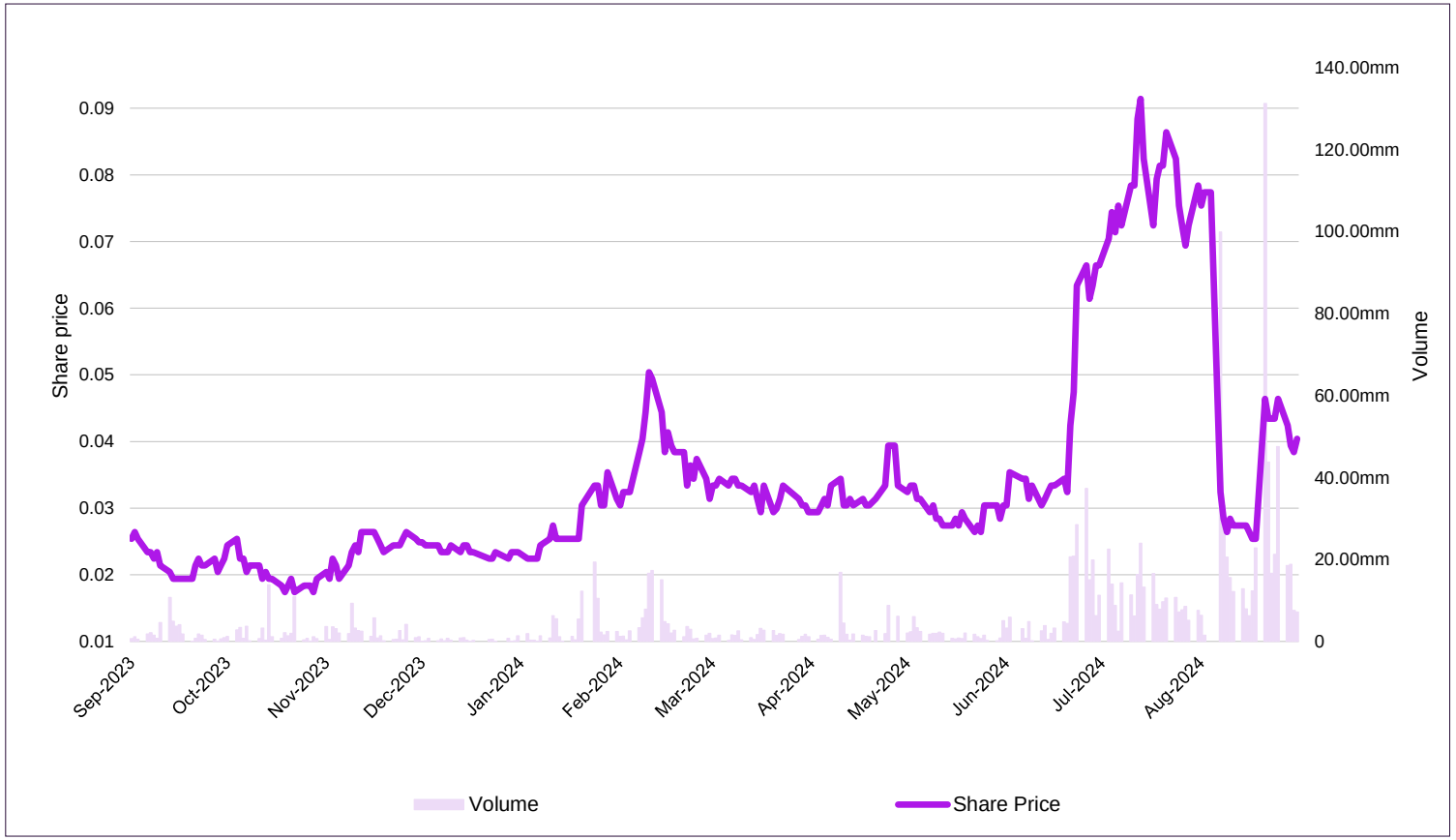
Two promising late-phase clinical programs



Appendix – corporate

Stock price and key shareholders*

ASX: ACW – Last 12 months



Key data

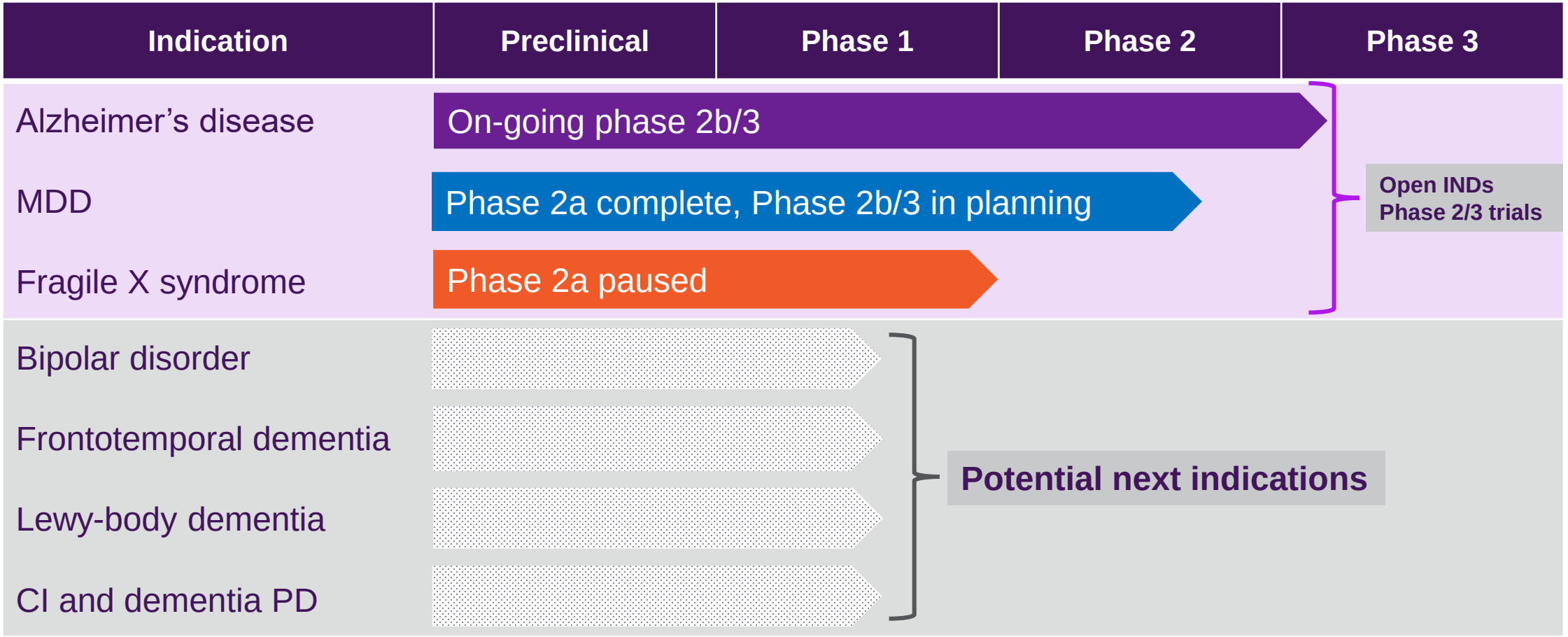
52 Week Range	$0.015 - $0.099
YTD CY24 change	+75%
Shares on issue	2.7Bn
Unlisted options	349m
Closing price	$0.035
Closing market cap*	$94.9m
30 June cash balance	$9.45m

Key Shareholders

Biotechnology Value Fund	9.2%
CEO Steven Gourlay	3.6%
Top 20 (ex BVF/Management)	22.8%

*Data as at 16 September 2024; market cap undiluted (excludes options); cash balance excludes options converted post 30/6 and R&D tax rebate of $9m expected in Q4 FY2024

Xanamem pipeline



MDD: Major depressive disorder; **CIAS:** Cognitive impairment associated with schizophrenia; **CI:** Cognitive impairment; **PD:** Parkinson's disease

Recent neuroscience acquisitions and IPOs

	Caraway / MERCK	KARUNA THERAPEUTICS / Bristol Myers Squibb	cerevel / abbvie	ALTO NEUROSCIENCE	CONTINEUM therapeutics	rapport therapeutics
Lead Drug(s)	**TRPML1**	**KarXT**	**Emraclidine**	**ALTO-100**	**PIPE-307 PIPE-791**	**RAP-219**
Phase	Preclinical	Phase 3	Phase 2	Phase 2	Phase 2	Phase 1
Lead asset	PD, other neuro	Schizophrenia	Schizophrenia	MDD	MS & MDD	Epilepsy, BPD, other neuro
Transaction	Acquisition	Acquisition	Acquisition	IPO	IPO	IPO
Amount	US$610m*	US$14.0b	US$8.7b	US$148m	US$110m	US$174m
Date	23-Nov	23-Dec	23-Dec	24-Feb	24-Apr	24-Jun

PD: Parkinson's disease; **MDD**: major depressive disorder; **MS:** multiple sclerosis; **BPD:** bipolar disorder
* Upfront and milestones combined

Active licensing for clinical neuroscience assets

Drug	ACI – 24.060	PRX-005	NBI-1117567	ulotaront, SEP- 378614 and others	AL-001	BIIB-124	Bepranemab
Phase	Phase 1b/2	Phase 1	Phase 2	Phase 3	Phase 3	Phase 3	Phase 1
Indication	Alzheimer's (amyloid beta antibody)	Alzheimer's (tau antibody)	Schizophrenia	Schizophrenia/ Depression	Dementias (progranulin target)	Depression	Alzheimer's Disease (tau antibody)
Deal Type	Exclusive Option & License	Exclusive Option & License*	License	License	License	License	License
Upfront	US $100m	US$100m	US$100m	US$300m	US$700m	US$1.5b	US$100m
Earnout	US $2.1b	US$2.1	US$2.6b	US$0.6b	US$1.5b	US$UNK	US$2.0b
Total Consideration	US$2.2b	US$2.2b	US$2.7b	US$0.9b	US$2.2b	>US$1.5b	US$2.1b
Date	May-24	Jun-21/Oct-23	21-Nov	21-Sep	21-Jul	20-Nov	20-Jun

* By exercise of previously negotiated option agreement during early development

Appendix – other Xanamem

Controlling brain cortisol[1] has durable benefits

Xanamem inhibits local tissue production of cortisol in key regions of the brain via 11β-HSD1[2]

"STRESS" in the brain becomes "CHILL"

RAPID changes in kinases, cell function, neurotransmitters over hours to days lead to short-term "low stress" settings

"Lower stress" shorter term e.g.

- Reducing inflammation
- Improving neurotransmitter balance
- Decreasing cell death

SLOW changes in gene expression and protein synthesis over days to weeks lead to durable "low stress" settings

"Lower stress" longer term e.g.

- Improving neural circuitry
- Generating new brain cells
- Ideal receptor configurations

1. Ramamoorthy & Cidlowski 2016 2. For a comprehensive review of 11β-HSD1 see Seckl J. 2024

Human PET study shows full target engagement

Other 11β-HSD1 enzyme inhibitors have not achieved adequate brain levels

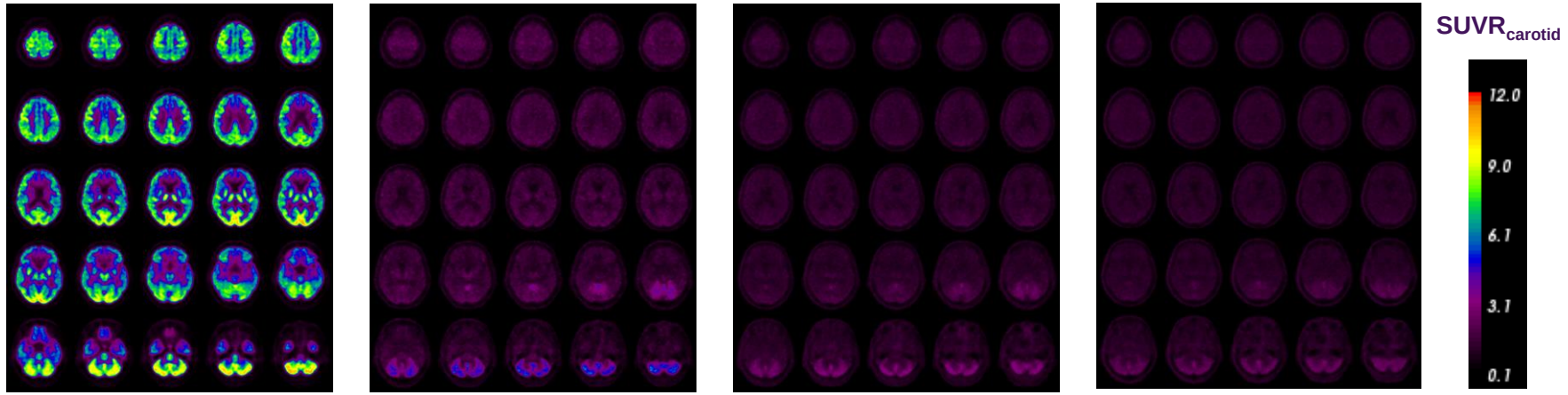
Baseline

After 7 days of daily dosing

5 mg Xanamem

10 mg Xanamem

20 mg Xanamem



Xanamem extensively binds to the 11β-HSD1 enzyme throughout the brain, with high post-treatment effects (absence of colour) after 7 days at all doses, slightly less at a 5 mg dose.

This is consistent with full hormonal pharmacodynamic activity seen in clinical trials with doses as low as 5 mg.

Validates 10mg dose in efficacy trials

Appendix – depression data

XanaCIDD statistical methods

Statistical considerations reflect industry standard for proof-of-concept trials

- Primary & secondary endpoints analyzed using a standard Mixed Model for Repeated Measures (MMRM)
- Three pre-specified subgroups for efficacy: current anti-depressant therapy (yes/no), baseline depression severity (lower/higher) and degree of cognitive impairment (lower/higher)
- p values shown are 2-sided hypothesis tests unless stated otherwise
- Effect sizes were calculated using the Cohen's d (Cd) statistic representing the effect as a % of the baseline population variability or standard deviation. This metric is frequently used in the cognition field[1] and is useful in depression[2]:
  - **> 0.2** = Potentially clinically meaningful effect size
  - **≥ 0.3** = Clinically meaningful effect size
  - **≥ 0.5** = Large and clinically meaningful effect size

1. Cohen et al. 1992; 2. Hengartner et al. 2020

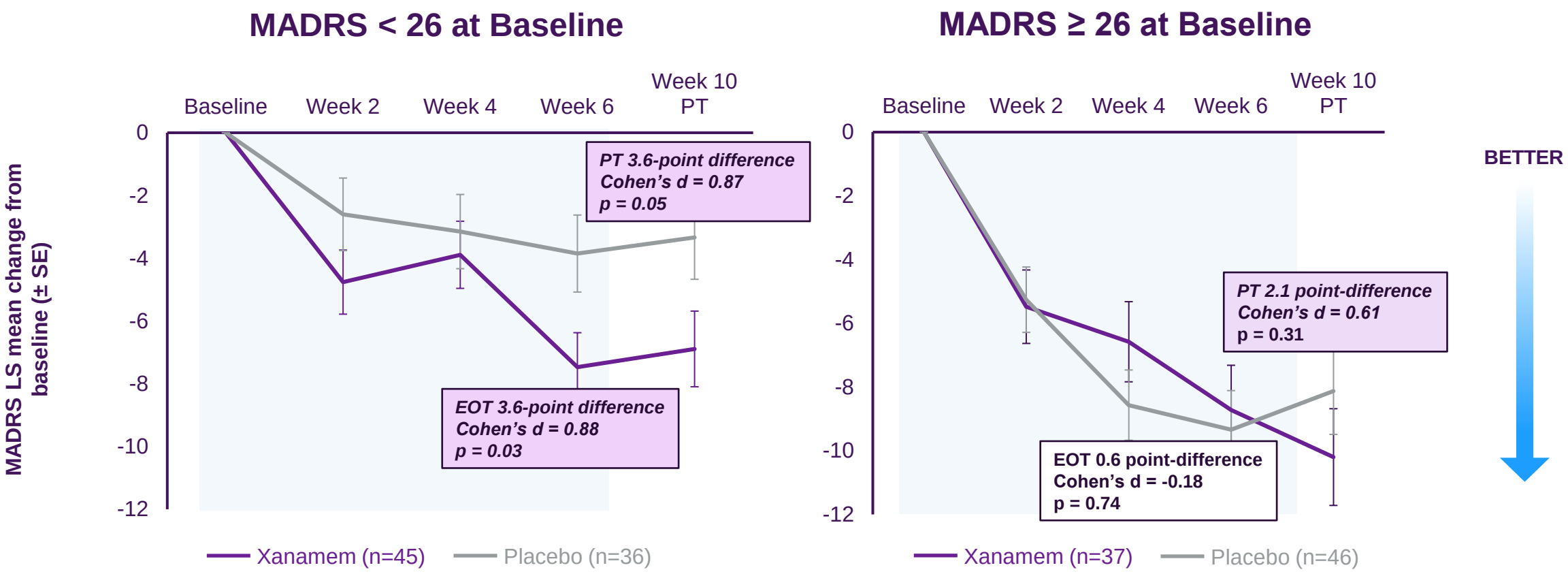
Typical, broad, moderate depression trial population

All XanaCIDD patients were either on, or previously treated with, anti-depressants

	Xanamem (n=82)	Placebo (n=83)
Mean age (SD)	49 (13)	49 (15)
% female	63	61
Mean screening HAM-D depression score (SD)	21 (3)	21 (3)
Mean MADRS (SD)	24 (6)	26 (7)
% on anti-depressant therapy	77%	86%
Mean cognition – screening Boxfiller (SD)	22 (5)	21 (6)
Mean cognition – Attention Composite (SD)	0.11 (0.77)	-0.10 (0.98)

Stronger MADRS response in patients with milder MDD

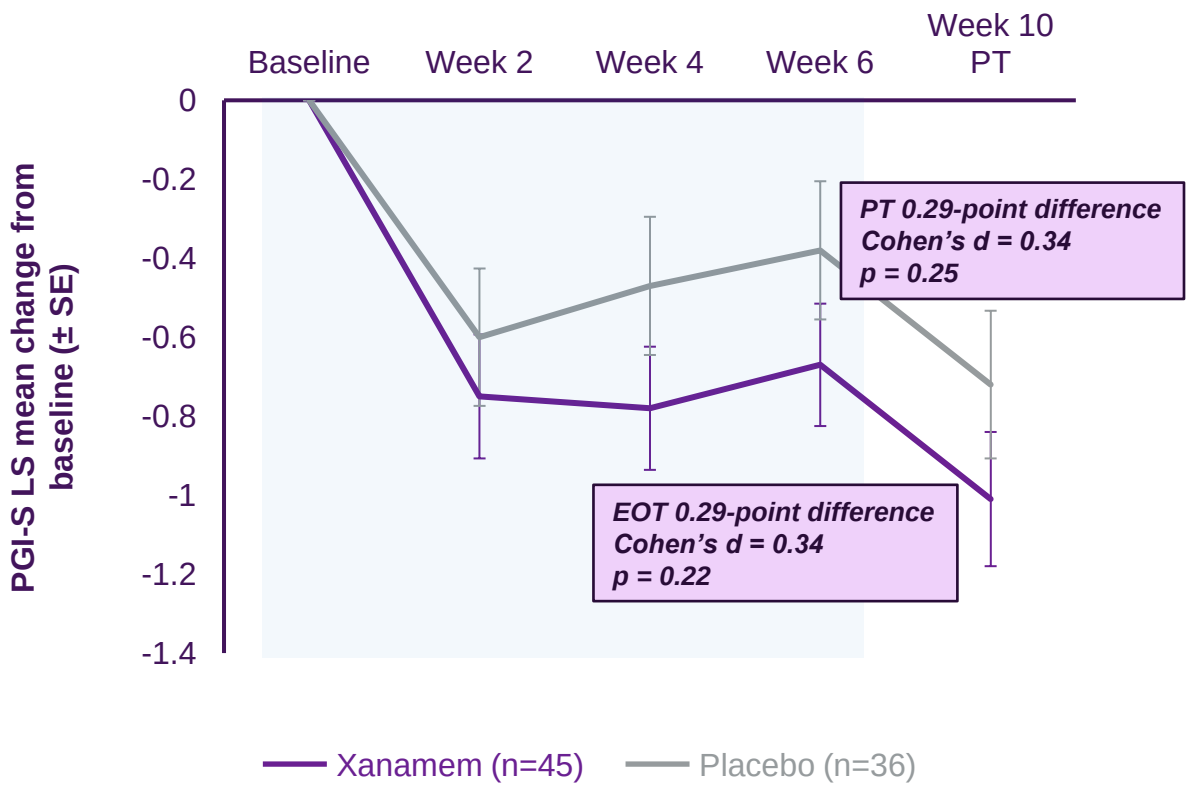
Clinically significant in both XanaCIDD subgroups at Week 10



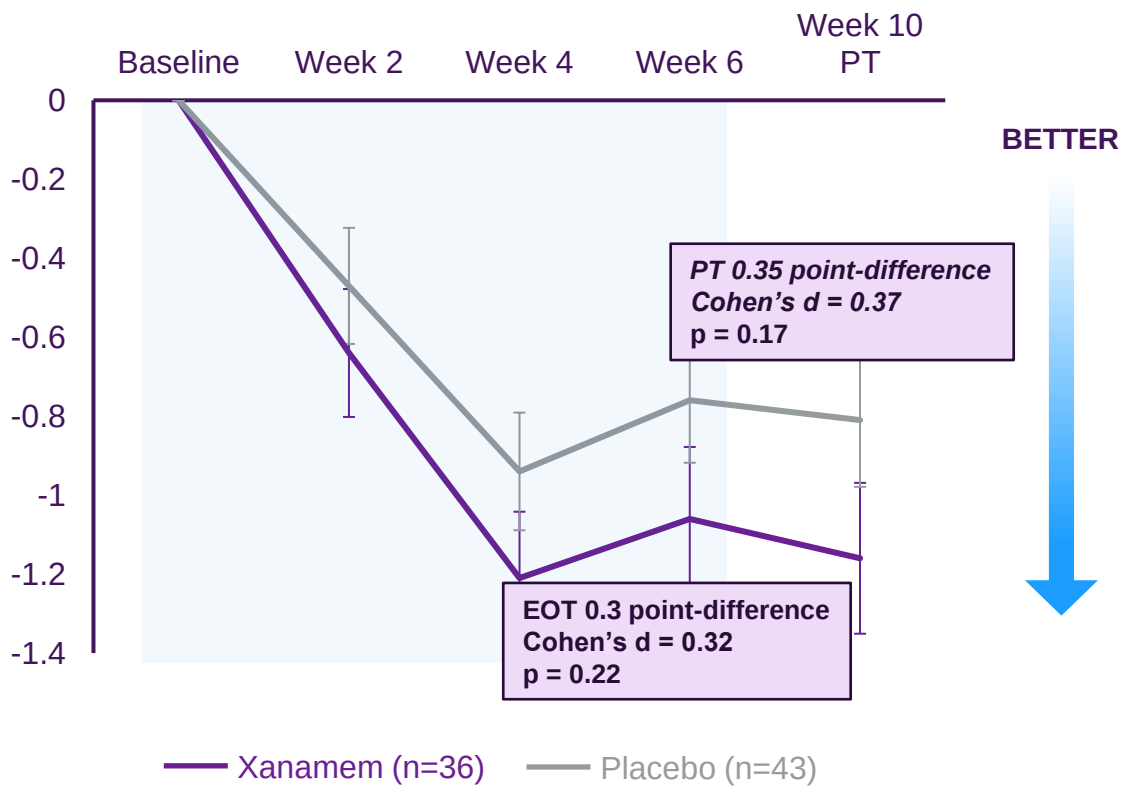
Positive PGI-S responses both MADRS groups

Clinically significant XanaCIDD findings at Weeks 6 & 10

MADRS < 26 at Baseline



MADRS ≥ 26 at Baseline



Appendix – references

Key references

Other references see also https://actinogen.com.au/xanamem

11β-HSD1 inhibition

- Seckl J. 11β-Hydroxysteroid dehydrogenase and the brain: Not (yet) lost in translation. J Intern Med. 2024 Jan;295(1):20-37. doi: 10.1111/joim.13741. Epub 2023 Nov 8. PMID:37941106. https://onlinelibrary.wiley.com/doi/10.1111/joim.13741
- Cognitive and disease-modifying effects of 11β-hydroxysteroid dehydrogenase type 1 inhibition in male Tg2576 mice, a model of Alzheimer's Disease: Sooy, K., Noble, J., McBride, A., Binnie, M., Yau, J. L. W., Seckl, J. R., Walker, B. R., & Webster, S. P. 2015. *Endocrinology, 1-12.*
- Partial deficiency or short-term inhibition of 11β-hydroxysteroid dehydrogenase type 1 improves cognitive function in aging mice Sooy, K., Webster, S. P., Noble, J., Binnie, M., Walker, B. R., Seckl, J. R., & Yau, J. L. W. 2010. *Journal of Neuroscience, 30(41), 13867-13872.*

Xanamem clinical trials

- Plasma pTau181 Predicts Clinical Progression in a Phase 2 Randomized Controlled Trial of the 11β-HSD1 Inhibitor Xanamem® for Mild Alzheimer's Disease Taylor J, Jaros M, Chen C, Harrison J, Hilt D *J Alz Dis 2024; 100: 139-150*
- Brain 11-Hydroxysteroid Dehydrogenase Type 1 Occupancy by Xanamem™ Assessed by PET in Alzheimer's Disease and Cognitively Normal Individuals Villemagne VL, Dore V, Chong L, Kassiouf M, Mulligan, R, Feizpoura A, Taylor J, Roesner M, Miller T, Rowe CC *J Alz Dis 2024: 97: 1463–1475*
- Selection and early clinical evaluation of the brain-penetrant 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor UE2343 (Xanamem™) Webster, S. P., Ward, P., Binnie, M., Craigie, E., McConnell, K. M., Sooy, K., Vinter, A., Seckl, J.R. & Walker, B. R. 2007. *Bioorganic & medicinal chemistry letters, 17(10), 2838-2843.*
- Various podium and poster presentations on website

Technical references

- CDR-SB Clinical Dementia Rating Scale – Sum of Boxes is an 18-point, 6-domain measure of patient cognition and function and is a common endpoint used by regulators. Patients in the Xanamem biomarker phase 2a analysis had a baseline of approximately 4 points, similar to that in the donanemab phase 3.
- Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155–159. https://doi.org/10.1037/0033-2909.112.1.155
- Hengartner MP, Jakobsen JC, Sørensen A, Plöderl M (2020) Efficacy of new-generation antidepressants assessed with the Montgomery-Asberg Depression Rating Scale, the gold standard clinician rating scale: A meta-analysis of randomised placebo-controlled trials. PLOS ONE 15(2): e0229381. https://doi.org/10.1371/journal.pone.0229381

Alzheimer's disease and cortisol

- Plasma Cortisol, Brain Amyloid-β, and Cognitive Decline in Preclinical Alzheimer's Disease: A 6-Year Prospective Cohort Study Pietrzak RH, Laws SM, Lim YY et. al. for the Australian Imaging, Biomarkers and Lifestyle Research Group 2017. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 2017; 2(1):45-52
- Decrease in cortisol reverses human hippocampal atrophy following treatment of Cushing's disease Starkman, M. N., Giordani, B., Gebarski, S. S., Berent, S., Schork, M. A., & Schteingart, D. E. 1999. *Biol psych*, *46(12), 1595-1602.*

Depression and cortisol

- Ding et. al. Front. Pharmacol 2021 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8461240/
- Effect of glucocorticoid and 11β-hydroxysteroid-dehydrogenase type 1 (11β-HSD1) in neurological and psychiatric disorders Dodd S, Skvarc D R, Dean OM, Anderson A, Kotowicz M, Berk M *Int J Neuropsychopharmacol* 2022; 25(5):387-398
- Depression and Hypothalamic-Pituitary-Adrenal Activation: A Quantitative Summary of Four Decades of Research Stetler C, Miller GE *Psychosom Med* 2011; 73(2):114-26

Market & cost of treatment estimates

- Matthews, K. A., Xu, W., Gaglioti, A. H., Holt, J. B., Croft, J. B., Mack, D., & McGuire, L. C. (2018). Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015–2060) in adults aged≥ 65 years. Alzheimer's & Dementia. https://doi.org/10.1016/j.jalz.2018.06.3063
- Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. *NEJM*. 2013;368(14):1326-34.
- https://www.cdc.gov/aging/aginginfo/alzheimers.htm#treated
- https://www.nimh.nih.gov/health/statistics/major-depression
- Symphony Health and ICON plc Company, Metys® database full year 2023

Currencies

- Currencies are in Australian dollars unless otherwise stated

Selected Glossary 1

- **11β-HSD1 –** 11 beta HydroxySteroid Dehydrogenase-1 enzyme. Selectively expressed in brain, liver, adipose.
- **Aβ –** Amyloid beta – a type of amyloid protein associated with Alzheimer's Disease, 42 and 40 are different forms
- **ACTH –** Adrenocorticotropic hormone that regulates blood levels of cortisol
- **ADAS-Cog –** Alzheimer's Disease Assessment Score - Cognition
- **ApoE4 –** Apoprotein genotype associated with genetic risk of Alzheimer's Disease
- **ATN –** Amyloid, Tau, Neurodegeneration
- **Clinical Scales –** Measure how a patient feels, performs and functions
- **CDR-SB –** Clinical Dementia Rating "Sum of Boxes" scale measuring cognition and function on an 18-point scale (high worse)
- **CNS –** Central nervous system
- **CSF –** Cerebrospinal fluid
- **CTAD –** Clinical Trials on Alzheimer's Disease (conference)
- **CTB –** Cognitive Test Battery of computerized tests
- **Double-blind –** Investigators, participants and company do not know who has active vs placebo treatment during a trial
- **EMA –** European Medicines Agency
- **FDA –** US Food & Drug Administration
- **Filamen A –** A protein believed to relate to amyloid toxicity
- **GFAP –** Glial Fibrilliary Acidic Protein – a marker of microglial cell activation in the brain
- **IDSST –** International Digit Symbol Substitution Test of cognition

Selected Glossary 2

- **IQCODE –** Informant Questionnaire on Cognitive Decline in the Elderly
- **MCI –** Mild Cognitive Impairment – memory, executive function deterioration with retained functional abilities
- **MDD –** Major Depressive Disorder
- **MMSE –** Mini Mental State Examination – a 30-point scale of simple questions to assess mental abilities
- **NfL –** Neurofilament Light – a nerve protein in the brain and rest of the body too
- **NIA-AA –** National Institutes of Aging and Alzheimer's Association
- **NMDA –** A type of receptor for glutamate in the brain
- **NPI –** Neuropsychiatric Inventory to assess psychiatric symptoms
- **NTB –** A Neurologic Test Battery, in this presentation one designed to measure executive function aspects of cognition
- **PET –** Positron Emission Tomography – a type of body scan
- **Placebo controlled –** Non-active treatment for double-blind design
- **p-Tau181 or 217 AD –** Biomarker of phosphorylated Tau protein
- **QPCT –** Glutaminyl-peptide cyclotransferase is an enzyme proposed to create toxic amyloid species
- **RAVLT –** Rey Auditory Visual Learning Test
- **RBANS –** Repeatable Battery for the Assessment of Neuropsychological Status (a test of mental abilities)
- **ROC AUC –** Receiver Operating Curve Area Under the Curve (1.0 ideal) – a type of statistical test to compared two methods of measurement
- **Tau –** A brain protein
- **Ttau –** Total tau levels including both phosphorylated and non-phosphorylated tau

Contacts

Michael Roberts
Investor Relations
P: +61 2 8964 7401
M: +61 423 866 231
E. michael.roberts@actinogen.com.au

Steven Gourlay
CEO & Managing Director
P: +61 2 8964 7401
E. steven.gourlay@actinogen.com.au