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#### ASX ANNOUNCEMENT

#### Actinogen announces capital raising of up to \$8.9 million<sup>1</sup>

Highlights:

- Binding commitments for a share placement to sophisticated and professional investors of \$5.0 million
- A non-renounceable 1 for 15 entitlement offer (entitlement offer or offer) to eligible shareholders to raise up to \$3.9 million (before costs), plus 1 new option for every 2 new shares issued under the entitlement offer
- CEO & MD Dr Steven Gourlay will take up an entitlement related to his privately held and incentive loan shares, representing an investment of \$120,000
- Independent Directors will take up their full entitlements including those related to incentive loan shares, representing an investment of \$67,834
- Shareholders and investors can join a management presentation webinar today at 11am AEST.

**Sydney, 3 May 2024. Actinogen Medical ASX: ACW ("ACW" or "the Company")** is pleased to announce an \$8.9 million capital raising comprising a share placement of \$5.0 million (before costs) at an issue price of \$0.025 (2.5 cents) per new share, plus a non-renounceable entitlement offer to eligible shareholders on the same terms to raise up to \$3.9 million (before costs).

Both the placement and the entitlement offer include the issue of 1 new option for every 2 new shares issued at an exercise price of \$0.05 (5.0 cents) with a three-year term to expiry.<sup>2</sup>

Shareholders who subscribe for their full entitlement may also apply for any amount of additional shares, to be allocated at the Board of Directors discretion (top-up offer).

Funds raised from the capital raising will be applied to progressing the XanaMIA trial in patients with mildmoderate Alzheimer's disease beyond the interim results in the first 100 patients, expected in mid-2025 and for general working capital.

<sup>1</sup> Unless stated otherwise, all financial data is quoted in Australian dollars

<sup>&</sup>lt;sup>2</sup> Expiry date of options is 31 May 2027

#### Management webinar today

CEO Dr Steven Gourlay and CFO Mr Will Souter will present a webinar today on the capital raising commencing at **11am AEST**. Pre-register or join the event using the following link, or paste the address into your browser: <u>https://actinogenmedical.zoom.us/webinar/register/WN\_ap5B9p6QRiKEY7GiOgItfg</u>

The slide presentation pack to be used in this morning's webinar is attached to this announcement.

A recording of the webinar will be made available as soon as possible after the conclusion of the event on the Company's website and YouTube channel.

#### Dr Steven Gourlay, Actinogen's CEO and MD, said:

"We are delighted to announce this capital raising that secures funding beyond two important clinical trial milestones in the next 18 months and offers eligible shareholders an opportunity to participate at an attractive valuation. The Board acknowledges the support from current and new shareholders participating in the placement along with existing shareholders participating via the entitlement offer.

"Our near-term clinical milestone is the results for the XanaCIDD phase 2a trial in patients with cognitive impairment and depression due in early Q3 this year. Confirmatory cognitive results for the primary endpoint will read through to our other program in Alzheimer's disease, plus to other dementias and schizophrenia, where cognitive impairment can be crippling. Xanamem's ability to improve other symptoms of depression will also be explored by a number of secondary endpoints.

"Our second clinical program will report interim results for the first 100 patients in the phase 2b trial of Alzheimer's disease by mid-2025. The extensive clinical data generated on safety and activity to date indicate that these trials have relatively high probabilities of success. An effective and novel treatment mechanism in these diseases could revolutionize the lives of patients."

#### Further details of the share placement

The placement (which also includes the issue of 1 option for every 2 new shares issued under the placement) will be made from the Company's existing Listing Rule 7.1 capacity and will not be subject to shareholder approval.

The placement and the entitlement offers are not underwritten, but will be managed by Forrest Capital Pty Ltd and McFarlane Cameron Pty Ltd (Lead Managers).

#### Further details of the entitlement offer to eligible shareholders

ACW is undertaking a non-renounceable entitlement offer to eligible shareholders to subscribe for one new share for every 15 shares held as at the record date of 10 May 2024 at an offer price of \$0.025 (2.5 cents) per new share plus 1 option for every 2 new shares issued under the offer, to raise up to \$3.9 million (before costs) by the issue of up to 155 million new shares and up to 77.6 million options. No shareholder approval is required for the issue of securities under the entitlement offer.

Shareholders who subscribe for their full entitlement will also be able to subscribe for additional shares at the same price and will also be issued 1 new option for every 2 additional shares issued to them under the top-up offer. Fractional entitlements under all offers will be rounded up to the nearest whole number.

The table below summarizes key parameters of the placement and entitlement offer. Full details will be in the prospectus.

Placement	Key parameters
Amount raised	\$5.0 million

Entitlement offer	Key parameters
Record date	10 May 2024 (7:00pm AEST)
Approximate total capital raise target	\$3.9 million No minimum amount Non underwritten
Total number of new shares	155 million
Non-renounceable entitlement offer and price PLUS Options offer and price	<ul> <li>1 new share for every 15 shares held as at the Record date at a price of 2.5 cents per new share</li> <li>1 unlisted option for every 2 new shares at an exercise price of 5.0 cents each and expiry date 31 May 2027</li> </ul>
Top-up offer for shareholders who subscribe for their full entitlement	Right to subscribe for additional shares at the same price (top-up offer), and will also be issued 1 new option for every 2 additional shares issued to them under the top-up offer
Fractional entitlements under all offers	Rounded up to the nearest whole number
Directors right to place shortfall	Rights reserved for up to 3 months after the close of the offer to place the balance of any new shares and accompanying options not taken up by eligible shareholders
Offer opens	15 May 2024
Offer closing date	29 May 2024 (5:00pm AEST)
Legal & listing summary	Issues of new shares and options under this entitlement offer will be made pursuant to a prospectus anticipated to be lodged with ASIC and the ASX on 7 May 2024 issued in accordance Section 713 of the Corporations Act and therefore will not affect the Company's current Listing Rule 7.1 capacity. No shareholder approval is required for the entitlement offer. The new shares will be fully paid ordinary shares and will rank equally with the Company's existing issued shares. The Company will make an application to the ASX for the official quotation of the new shares.

The table below sets out, for illustrative purposes only, the existing share capital structure (before the placement and entitlement offer) together with the impact of the issue of the new shares under the entitlement offer and the new shares under the placement. It assumes that no options are exercised prior to the record date.

Shares	Number
Existing shares as at date of the placement and entitlement offer	2,326,920,711
Shares issued pursuant to the placement	200,000,000
Maximum number of new shares issued under the entitlement offer*	155,128,047
Total issued shares following completion of the offer and placement (assuming full subscription under the offer and no exercise of any of the options)	2,682,048,758
Ontions	
Options	Number
Existing options at the date of the placement and entitlement offer	Number 200,601,897
Existing options at the date of the placement and entitlement offer	200,601,897

\* Subject to rounding adjustments

Full details of the entitlement offer will be sent to eligible shareholders in a prospectus to be lodged with the Australian Securities Exchange (ASX) on Tuesday 7 May 2024, and to be dispatched to shareholders on or around Wednesday 15 May 2024.

The following is an indicative timetable for the entitlement offer:

Indicative Rights Issue Event Timetable <sup>1</sup>	
Entitlement offer announcement and Company resumes trading	3 May 2024
Lodgement of prospectus with ASX and ASIC	7 May 2024
Record Date	7:00pm AEST 10 May 2024
Dispatch of prospectus and entitlement offer opens	15 May 2024
Closing of entitlement offer	5:00pm AEST 29 May 2024
Allotment and issue of new shares under entitlement offer	5 June 2024
Expected normal trading of new shares under entitlement offer 6 June 20	
1 Dates / times are indicative and subject to change	

1. Dates / times are indicative and subject to change

#### **ENDS**

#### Investors

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#### 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 cognition & depression trial** is a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 167 patients. Participants are evenly randomized to receive Xanamem 10 mg once daily or placebo, in some cases in addition to their existing antidepressant therapy, and effects on cognition and depression are assessed.

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 effects on cognition, function and progression of Alzheimer's disease are assessed. Thus, Xanamem is being assessed in this trial for its potential effects as a both a cognitive enhancer and a disease course modifier.

#### About Xanamem

Xanamem's novel mechanism of action is to block the production of cortisol inside cells through the inhibition of the 11β-HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cognitive impairment is also a feature in Depression and many other diseases. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in working memory and attention, compared with placebo, in healthy, older volunteers in two consecutive trials and clinically significant improvements in functional and cognitive ability in patients with biomarker-positive mild AD. Previously, 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. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterize Xanamem's therapeutic potential.

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<sup>®</sup> is a trademark of Actinogen Medical.

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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.

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Capital raising presentation Up to a total of \$8.9 million in new funds – cash runway to late 2025

99 : RP

Presented by CEO Dr Steven Gourlay & CFO Mr Will Souter 3 May 2024

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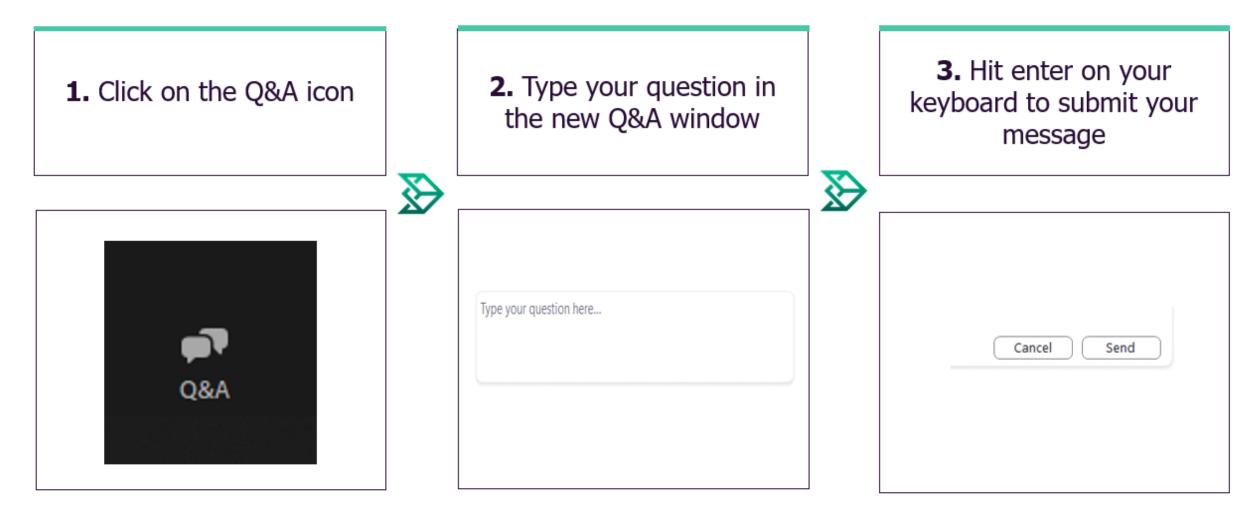
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## **Online Q&A**



### \$8.9m<sup>1</sup> Capital Raising Overview



Company summary	<ul> <li>~\$80m market cap</li> <li>2,326m ordinary shares on issue</li> <li>194m unlisted options 3.75 cents, expiry Sept 2026</li> <li>Current cash (pre-raise) \$6.3m<sup>2</sup> with no debt</li> <li>Anticipated higher R&amp;D rebate this year in Q4 CY24 (FY23 rebate: \$4.8 million)</li> </ul>
Offer structure	<ul> <li>\$8.9m via Placement and Rights Issue</li> <li>\$5.0m Placement to institutional and sophisticated investors of 200m shares</li> <li>Rights Issue of up to 155m new shares to raise up to a further \$3.9m from existing shareholders on the same terms</li> <li>1 for 2 unlisted options exercisable at 5 cents with 36-month expiry (31 May 2027)</li> </ul>
Offer pricing	<ul> <li>2.5 cents, representing a 21% discount to the 30-day VWAP of 3.2 cents</li> </ul>
Rights issue	<ul> <li>Right for eligible shareholders to subscribe for new shares on a 1:15 basis, on the same terms, with the opportunity to apply to top up<sup>3</sup></li> <li>Directors pre-committed to take up their rights<sup>4</sup></li> <li>Record date for holdings 7pm Friday 10 May</li> </ul>
Use of funds	<ul> <li>Progress XanaMIA phase 2b Alzheimer's trial through interim results in mid-2025 (n=100) and working capital, cash runway to late 2025</li> </ul>
1 Unless stated otherwise, all financial data is	in Australian dollars 4 Total commitment of \$187,834

3 Subject to availability under the maximum shares to be issued in the Rights Issue of 155m, and at the Company's discretion

2 As at 31 March 2024

## **Market Exclusivity**

#### Strong IP portfolio





Strong patent position with up to 12 years market exclusivity based on "composition of matter" patents in all major markets

Other patents extend potential patent life protection including "methods of use" patents, patient selection with biomarkers, manufacturing and formulation patents

Latest international patent publication teaches the use of the blood biomarker pTau for the selection of patients for Xanamem<sup>®</sup> treatment



## Strong M&A and licensing activity in the CNS sector

Target/Partner	HIRANUNA Bristol Myers Squibb	©cerevel abbvie		ကြာrothena ( <sup>III</sup> Bristol Myers Squibb'	SOSCI	◆ Sumitomo Pharma		Sage Therapeutics*	Roche
Drug	KarXT	Emraclidine	BPN-14770	PRX-005	NBI-1117567	ulotaront, SEP- 378614 and others	AL-001	BIIB-124	Bepranemab
Phase	Phase 3	Phase 2	Phase 2	Phase 1	Phase 2	Phase 3	Phase 3	Phase 3	Phase 1
Indication	Schizophrenia	Schizophrenia/ Other	Fragile X Syndrome/ Alzheimer's	Alzheimer's (tau antibody)	Schizophrenia	Schizophrenia/ Depression	Dementias (progranulin target)	Depression	Alzheimer's Disease (tau antibody)
Deal Type	Acquisition	Acquisition	Acquisition*	Licensing*	Licensing	Licensing	Licensing	Licensing	Licensing
Upfront Consideration	US\$14.0b	US\$8.7b	US\$0.04b	US\$0.1b	US\$0.1b	US\$0.3b	US\$0.7b	US\$1.5b	US\$0.1b
Earnout	n/a	US\$460	US\$0.46b	US\$2.1	US\$2.6b	US\$0.6b	US\$1.5b	US\$UNK	US\$2.0b
Total Consideration	US\$14.0b	US\$8.7b	US\$0.5b	US\$2.2b	US\$2.7b	US\$0.9b	US\$2.2b	>US\$1.5b	US\$2.1b
Date	Dec-23	Dec-23	May-20	Jun-21/Oct-23	Nov-21	Sep-21	Jul-21	Nov-20	Jun-20

\* By exercise of previously negotiated option during earlier development

## **Experienced Leadership and Management**





...with an experienced Board



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

PRINCIPIA Genentech BIOPHARMA

30+ years' experience in development of novel therapeutics

Former founding CMO at **US-based** Principia Biopharma Inc

**Dana Hilt Chief Medical Officer** MD



25+ vears of drug development experience, primarily CNS drugs

Chief Medical Officer at various pharmaceutical companies



Talented management team...

Will Souter Chief Financial Officer BComm, LLB

Extensive experience in

advisory, executive and

Particular experience in

transactions

private and public markets

IPOs, capital markets and

non-executive roles in





RN. M Health Law

30 years experience in

Clinical Operations and

10 years as Regional Head

Asiapac in rare diseases

Medical Affairs

ALEXION

MERCK SERONO

Fujun Li

SANOFI **PRINCIPIA** 

Head of Manufacturing Head of IR and Comms B.Ec (Hons), CPA, FIN PhD

BIDPHARMA

30+ years experience in

drug development and

Held multiple executive

level roles in CMC and

technical operations

manufacturing

Brambles

**Michael Roberts** 

LION NATHAN

30 years in finance & communications ASX Top 50 investor relations at Brambles. Lion and Foster's Group



Dr. Geoff Brooke Chairman MBBS: MBA



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



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



Dr. Nicki Vasquez **Non-Executive Director** PhD



## **Attractive product profiles in Depression and Alzheimer's**

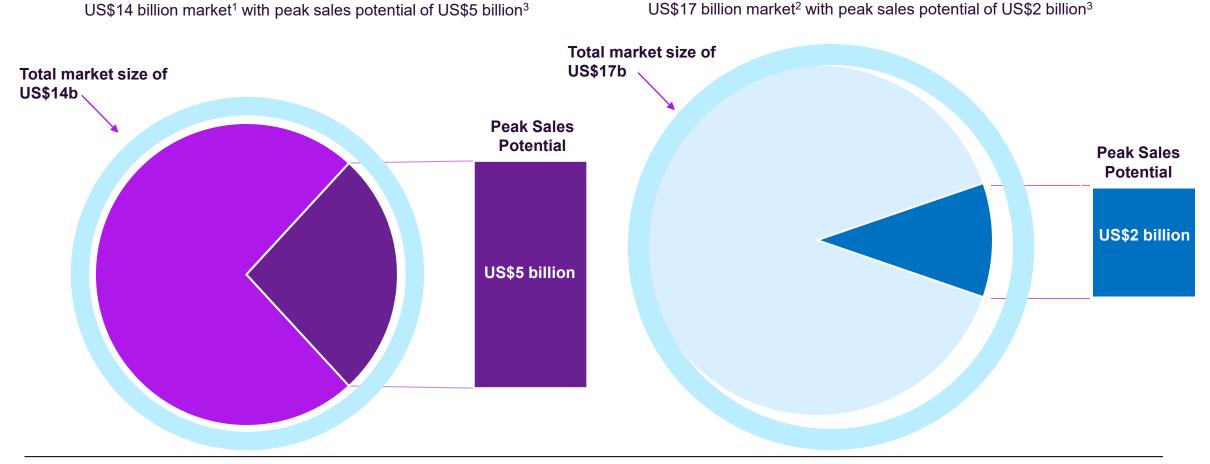
Rapidly acting oral therapy with dual action on cognitive impairment / depression

Cognitively enhancing and disease modifying oral therapy for all stages of Alzheimer's disease

## **Opportunity across two key markets**

Significant market opportunity across both Alzheimer's disease (AD) and Depression

#### Alzheimer's Disease Market



1. https://www.futuremarketinsights.com/reports/depression-treatment-market

2. https://www.futuremarketinsights.com/reports/alzheimers-diagnostics-and-therapeutics-market

3. Peak sales 2034 https://www.edisongroup.com/research/pressing-forward-with-xanamem



**Depression Market** 



## The science and the trials

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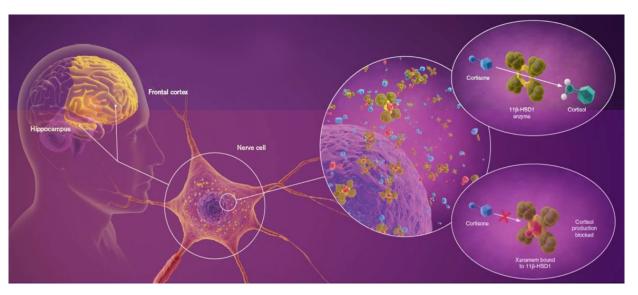


## Xanamem: Oral, once-a-day treatment with a unique mechanism

Xanamem is a brain penetrant 11β-HSD1 small molecule enzyme inhibitor which **reduces** brain tissue cortisol<sup>3,4</sup>

Potential to be:

- Rapidly cognitive enhancing
- Disease-modifying (slowing progression)<sup>1,3</sup>
- Anti-depressant effects



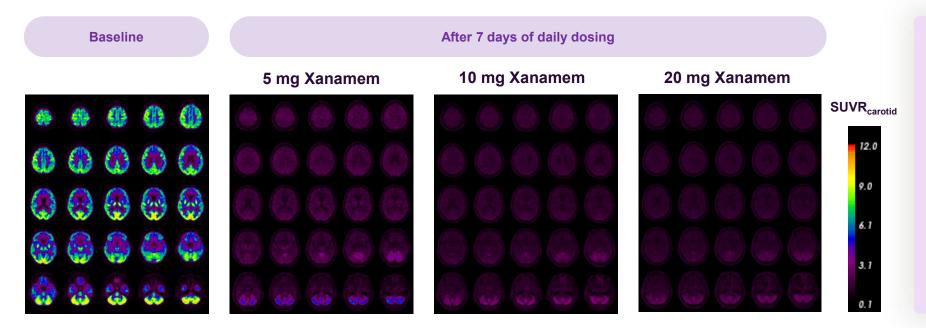
## Mouse experimental studies, brain cortisol levels & human clinical trials validate cortisol as a target for the treatment of AD<sup>1-5</sup>

<sup>1.</sup> Sooy et al. 2015 showing effects on amyloid plaque reduction in an aged mouse model after 28 days associated with increases in insulin degrading enzyme – at 13 month cognitive protection was independent of continued amyloid deposition; 2. Popoli et al. 2011 microglial cell modulation in rats, effects on glutamate, cannabinoid and other signalling pathways; 3. Hilt, D. Oral symposium AD/PD International Conference 2023; Actinogen website: <u>Actinogen – News</u>; 4. based on human PET scan evidence (data on file), Webster et al. 2017 Selection and early clinical evaluation of the brain-penetrant 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor UE2343 (Xanamem<sup>TM</sup>); 5. CTAD conference Oct 2023



## PET data shows full target engagement in the brain at low doses

**Previous enzyme inhibitors<sup>1</sup> have not achieved adequate brain concentrations** 



PET data<sup>2</sup> demonstrates that 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.

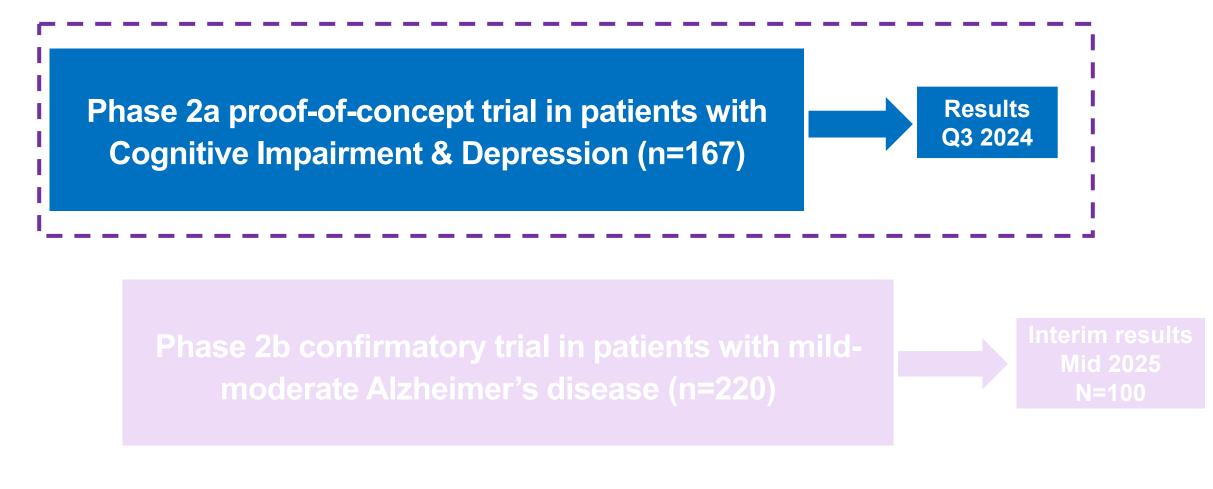
#### Validates 10mg dose in efficacy trials

 ABT-384 was claimed to have brain penetrant ability based on likely hepatic effects on deuterated cortisol (Katz et al. 2013), negative 12-week AD trial (Marek et al. 2014)
 Study population consisted of ~50% healthy older subjects who were cognitively normal and ~50% with Alzheimer's disease. Subjects dosed for seven days. Baseline: Mean of baseline scans of patients in that dose group; After dose: Mean of post-dosing (7 days) scans in that dose group.



## **Actinogen Xanamem Phase 2 trials underway**

Supported by extensive existing clinical data from four previous trials of Xanamem 10mg



### Targeting brain tissue cortisol with Xanamem is a promising strategy in cognitive impairment & depression

- Elevated cortisol associated with severe, melancholic depression<sup>2</sup>
- Cortisol levels associated with treatment outcomes, relapse, & cognition<sup>3</sup>
- 80-90% of MDD patients report neurocognitive symptoms<sup>1</sup>
- Cognitive symptoms often persist during remission<sup>1</sup>
- Positive effects with GR receptor antagonism with mifepristone<sup>4</sup>
- ✓ Meta-analysis of clinical cortisol approaches<sup>5</sup>

Xanamem has improved human cognition in 2 trials with same cognitive endpoint to be used<sup>6</sup>

3. Depression literature review, Malhi & Mann 2018; HPA axis in major depression, Keller et al. 2016

 GR, glucocorticoid receptor; Combined analysis of mifepristone for psychotic depression, Block et al. 2018; mifepristone effects on depression in biopolar disorder, Young et al. 2004; Evidence from clinical studies with CRH<sub>1</sub> receptor antagonists, Holsboer & Ising 2008
 Meta-analysis of prior trials aimed at reducing cortisol, Ding et. al 2021



<sup>1. 3-</sup>year prospective study and review, Conradi et al. 2011

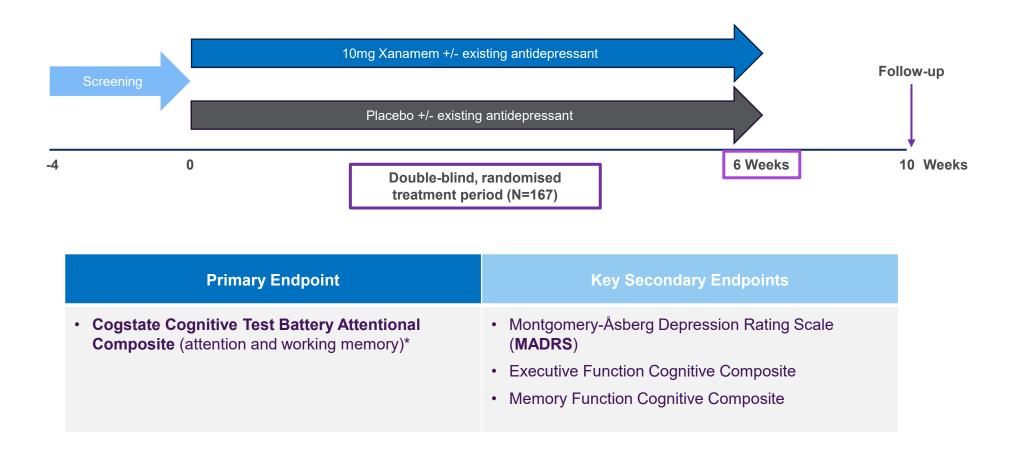
<sup>2.</sup> Quantitative summary of four decades of research, Stetler & Miller 2011

<sup>6.</sup> Two Xanamem placebo-controlled trials showing improved working memory & attention (Actinogen data on file)

## XanaCIDD proof-of-concept Phase 2a trial in Cognitive Impairment & Depression



Results early Q3 2024, primary endpoint validated in prior trials of Xanamem



### XanaCIDD trial blinded data review: methods



- Blinded analysis to ensure data quality just prior to end of trial enrolment
- Analysis used all available data from up to 148 participants\*
- Trial data is pooled, meaning that treatment assignment was not unblinded (decoded)
  - Company and trial personnel will not know who received active vs. placebo treatment until the end of the trial
  - No Xanamem effect can be directly evaluated from pooled data
- Primary endpoint is the "Attention Composite" made up of three computerized, reaction time tests
- Secondary endpoints include the Montgomery-Asberg Depression Rating Scale (MADRS), other cognitive composites and responder analyses

\* Sensitivity analyses using completing participants showed similar results, data are preliminary and not final

### Trial is progressing well with pooled data trending in the right direction, results due in early Q3 2024



#### OBSERVATIONS

- Assessment of data quality found no concerning trends by country or clinical site
- Clinical safety profile remains excellent, with no serious adverse events related to Xanamem
- Improvement seen in **all three computerized tests** that make up the primary endpoint "Attention Composite"
  - Improvements greater than in prior trial placebo groups<sup>1,2,3</sup>
  - Improvements of ≥30% of a baseline standard deviation are potentially clinically significant in the field of cognition<sup>4</sup>
- 32% change-from-baseline improvement in the MADRS scores in the range reported for active & placebo groups in prior trials<sup>5</sup>

<sup>1.</sup> Detection test no change in depressed patients over 12 weeks: LaMonica et al 2018 doi: 10.1371/journal.pone.0203343

<sup>2.</sup> Stability over 12 weeks in older cognitively normal people and those with Alzheimer's: Lim 2013 et al. Archives of Clinical Neuropsychology 28 (2013) 320–330

<sup>3.</sup> Cognitively normal older volunteer data - Actinogen data on file

<sup>4.</sup> Acetycholinesterase inhibitor Cohen's d (change as a % of baseline standard deviation) range 0.2 to 0.3 (20 to 30%): Rockwood 2004

<sup>5.</sup> Placebo group depression trial response rate reviews: Stone et al. 2022 BMJ 2022;378:e067606 Jones et al. 2021 doi:10.1001/jamanetworkopen.2021.25531



## **Actinogen Xanamem Phase 2 trials underway**

De-risked by extensive existing clinical data from four previous trials of Xanamem 10mg

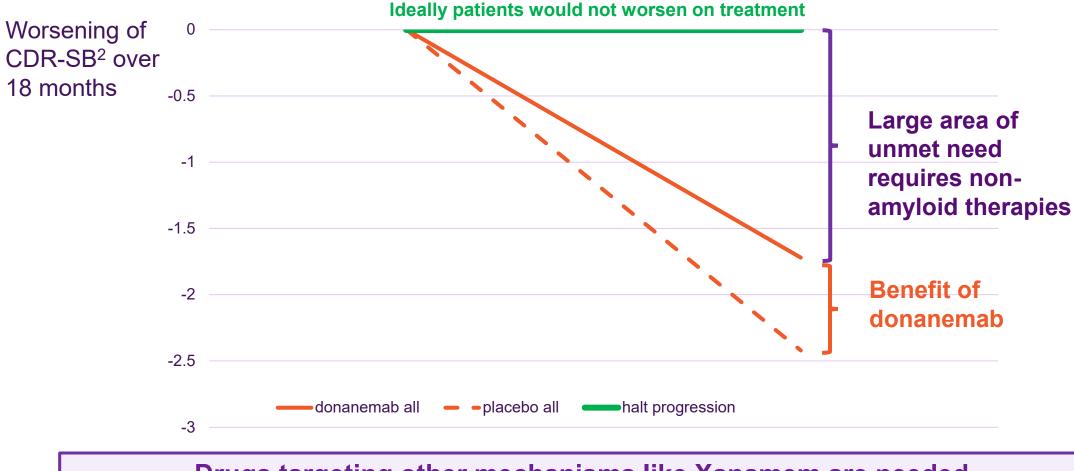
Phase 2b confirmatory trial in patients with mildmoderate Alzheimer's disease (n=220)

Interim results Mid 2025

N = 100

## Newer anti-amyloid "immunotherapy" antibodies shown to slow but not halt progression of AD<sup>1</sup>





#### **Drugs targeting other mechanisms like Xanamem are needed**

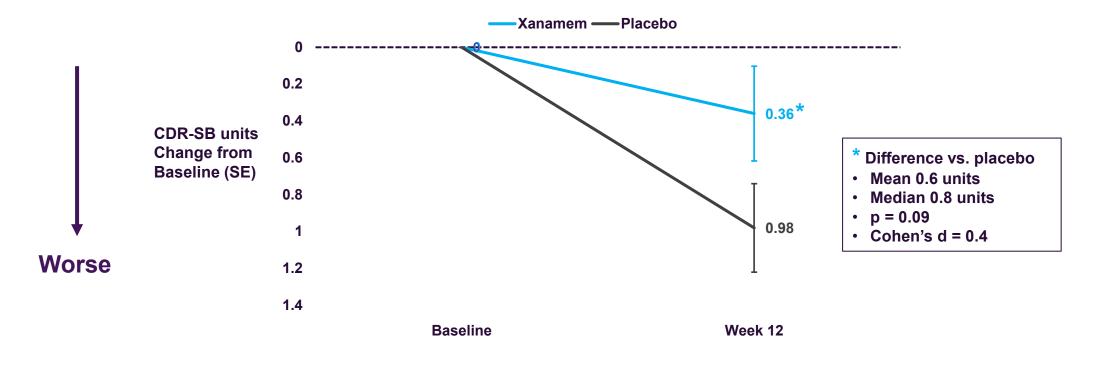
 Donamemab is an anti-amyloid antibody given as an intravenous infusion every 4 weeks until amyloid clearance (Sims JR at al. JAMA. Published online July 17, 2023. doi:10.1001/jama.2023.13239 Data shown are for whole population studied with absolute difference to placebo of 0.7 points, intermediate tau population difference also 0.7 points

2. CDR-SB is an 18-point scale measuring functional and cognitive status, patients in the donanemab trial had an average baseline score of 4 ± 2 points



## Xanamem significantly slows the rate of functional decline (CDR-SB) in patients with mild AD\*

Patients with elevated plasma pTau181 indicating progressive, amyloid-positive disease (n=34)



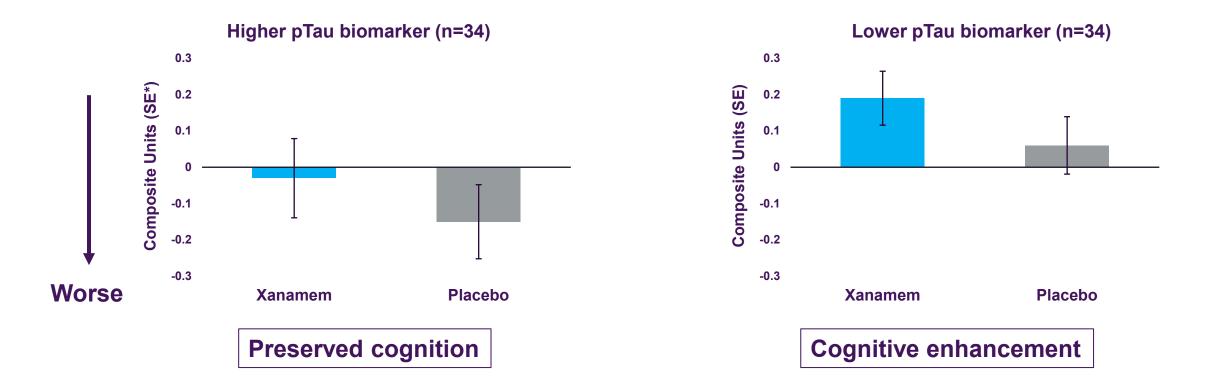
#### Xanamem benefits extrapolated to 18 months would be ~8x anti-amyloid drugs

\* CDR-SB Clinical Demetia Rating Scale – Sum of Boxes is a measure of patient function and is an endpoint used by the FDA; Patients with a pre-treatment plasma pTau181 level greater than the prespecified median of 6.74 pg/mL to indicate AD pathology and likelihood of progressive disease; similar effect size for pTau >10.2 pg/mL cutoff; extrapolated effect size 8-10 times greater than 0.4-0.45 reported for lecanemab (USPI Leqembi 2023 & van Dyck et al. 2022; DOI: 10.1056/NEJMoa2212948) if extrapolated to 18 months; no treatment effect detected in ADASCog-14 or ADCOMS

## Cognitive improvements suggest potential clinical benefits across dementia patient sub-types\*



Positive trends in both high and low plasma pTau biomarker groups



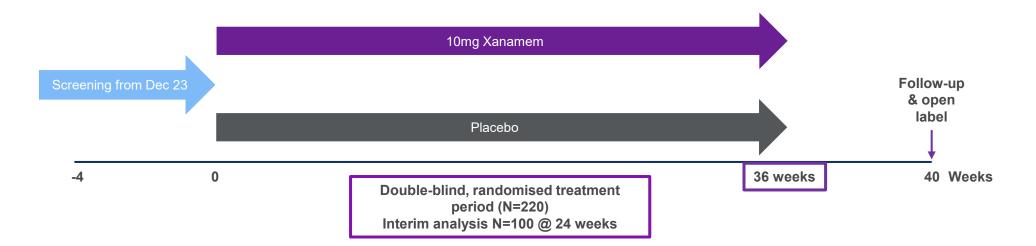
#### Consistent with Xanamem activity as a cognitive enhancer & disease-modifier

\* Post hoc analysis of composite of word recall & recognition, CFT & COWAT tests (p=NS), error bars show Standard Error of the Mean; low pTau patients less likely to have amyloid-positive disease, results consistent with volunteer data shown in Slide 7

### XanaMIA Phase 2b trial in Alzheimer's Disease



#### Initial, interim results in mid 2025, final results H1 2026



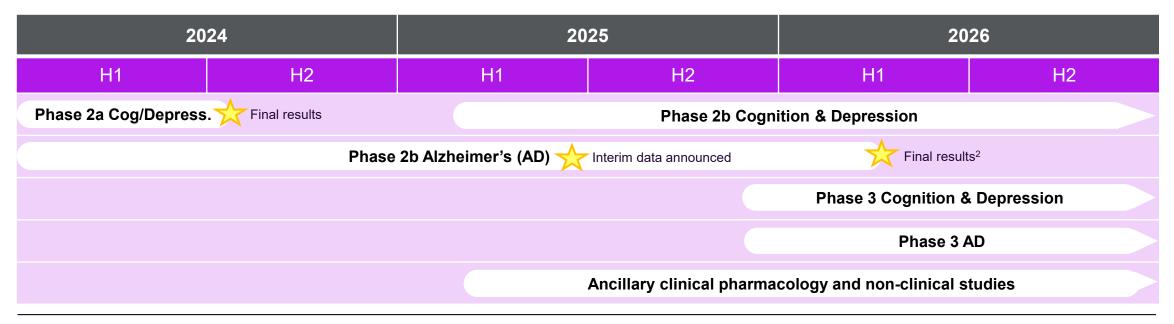
Key inclusion criteria	Primary Endpoint	Key Secondary Endpoints	Implementation
<ul> <li>Blood pTau biomarker positive</li> </ul>	<ul> <li>Cognitive Test Battery (7 cognitive measures)</li> </ul>	<ul> <li>CDR-SB (functional and cognitive measure)</li> </ul>	Commence enrolment at up to 15 Australian sites
<ul> <li>Mild-moderate Alzheimer's by NIA-AA criteria</li> </ul>		<ul> <li>Amsterdam Activity of Daily Living (functional measure)</li> </ul>	<ul> <li>Interim analysis when 100 people complete 24 weeks</li> </ul>
			Add US sites when feasible

## **Recent Milestones & Upcoming Catalysts<sup>1</sup>**



✓ Q1 2024	Human PET study peer-review publication	<ul> <li>Q2-4 2024</li> </ul>
✓ Q1 2024	UK Innovation Passport granted	<ul> <li>Q1 2025</li> </ul>
✓ Q2 2024	Phase 2b Alzheimer's trial first patient treated	• Mid 2025
✓ Q2 2024	Phase 2a cognition & depression full enrollment	• H1 2026
• Q3 2024	Phase 2a cognition & depression trial results	• H1 2026

Various peer-review publications, abstracts
Start cognition & depression Phase 2b
Interim analysis Alzheimer's Phase 2b
Final results Alzheimer's Phase 2b <sup>2</sup>
Start Alzheimer's Phase 3



### **Company Highlights**

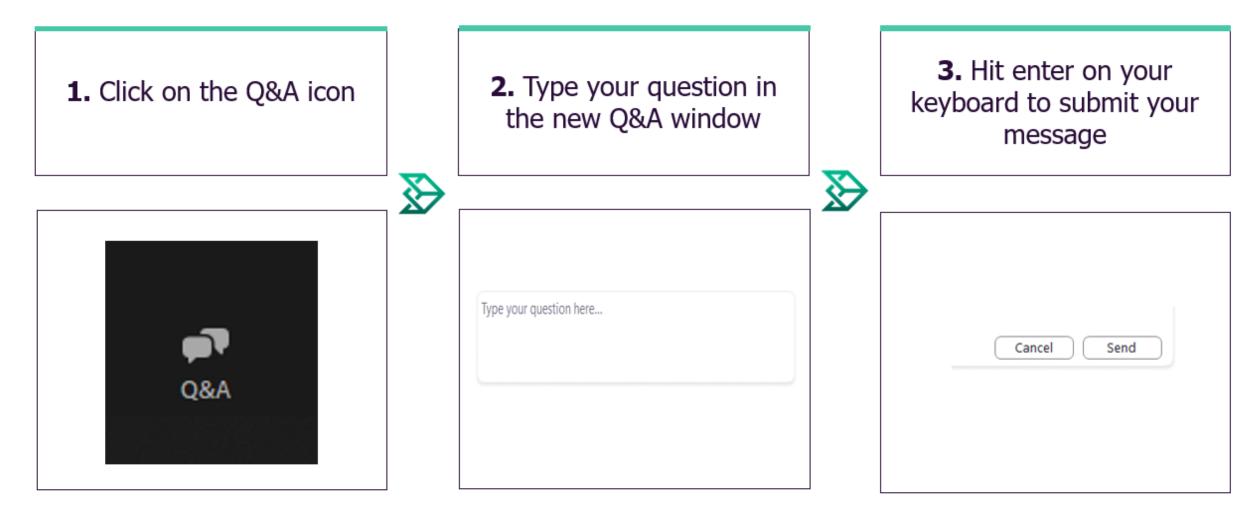
#### Positioned to leverage the wider biotech market tailwinds



Clinical-stage, advanced manufacturing	Xanamem <sup>®</sup> lowers brain cortisol and is in Phase 2 trials to treat patients with cognitive impairment associated with depression and Alzheimer's disease; to-be-marketed pill formulation completed, stable at room temperature
2 Strong biological rationale & clinical data	Elevated brain fluid cortisol is strongly associated with Alzheimer's and depression Positive clinical efficacy data from three placebo-controlled trials
3 Safe, oral, easy to use	Safely treated > 350 people to date, low oral once-daily dose, very low drug interaction potential good for combination therapy
4 Large global market opportunity	Depression: Market \$17 billion <sup>1</sup> Alzheimer's: Market \$14 billion <sup>2</sup>
5 Near-term milestone	Phase 2a depression results Q3 CY24 Peer reviewed manuscripts Q2-4 CY24 Phase 2b Alzheimer's interim results mid CY25
6 Protected	Composition of matter protection to 2036 in most markets, multiple patent families including manufacturing and use patents extend market exclusivity further
7 Experienced team	Highly experienced Board and Management with a proven track record, Dr Gourlay's last exit US\$3.7 billion M&A at Principia/Sanofi
8 Funded	Cash \$6.3 million (no debt), fundraising \$8.9 million, plus R&D rebate expected >\$4.8 million (Q4) provides cash runway to late 2025
1. https://www.futuremarketinsights.com/reports/depression	-treatment-market

2. https://www.futuremarketinsights.com/reports/alzheimers-diagnostics-and-therapeutics-market

## **Online Q&A**





# Appendix IIIIImaad O 38

## 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



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