



ASX ANNOUNCEMENT

Actinogen CEO presentation to ShareCafe investor webinar

Sydney, 21 October 2022. Actinogen Medical ASX: ACW (“ACW” or “the Company”) is pleased to announce its participation in the ShareCafe Small Cap *Hidden Gems* investor webinar, to be held **today** from 12:30pm AEDT / 9:30am AWST.

The webinar can be viewed live via Zoom and will provide investors with the opportunity to hear from and engage with Actinogen’s CEO and Managing Director Dr Steven Gourlay and representatives of other leading ASX-listed micro/mid cap companies.

Dr Gourlay will provide an overview of Actinogen and focus on the Company’s recent positive Alzheimer’s Disease (AD) Phase 2a trial results that showed a strong clinical effect from its lead compound Xanamem¹ and a major validation of the ‘cortisol hypothesis’ for AD.

To access further details of the free webinar and to register for the event, please copy and paste the following link into your internet browser:

https://us02web.zoom.us/webinar/register/WN_8hqY8k0nTketqbFfslCgiw

A copy of Dr Gourlay’s presentation slides is attached.

A recorded copy of the webinar will be made available following the event on the Actinogen and ShareCafe websites.

ENDS

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Announcement authorised by the Board of Directors of Actinogen Medical

¹ Xanamem is a registered trademark of Actinogen Medical Limited

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.

About Xanamem

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

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease, and Xanamem has shown the ability to enhance cognition in healthy, older volunteers. 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 11 β -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 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® is a trademark of Actinogen Medical.

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



New Alzheimer's Disease Phase 2a trial results show strong clinical effect Major validation of 'cortisol hypothesis'

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD

Presented at Sharecafe Hidden Gems webinar 21 October 2022

Authorised by the Board of Directors of Actinogen Medical Limited

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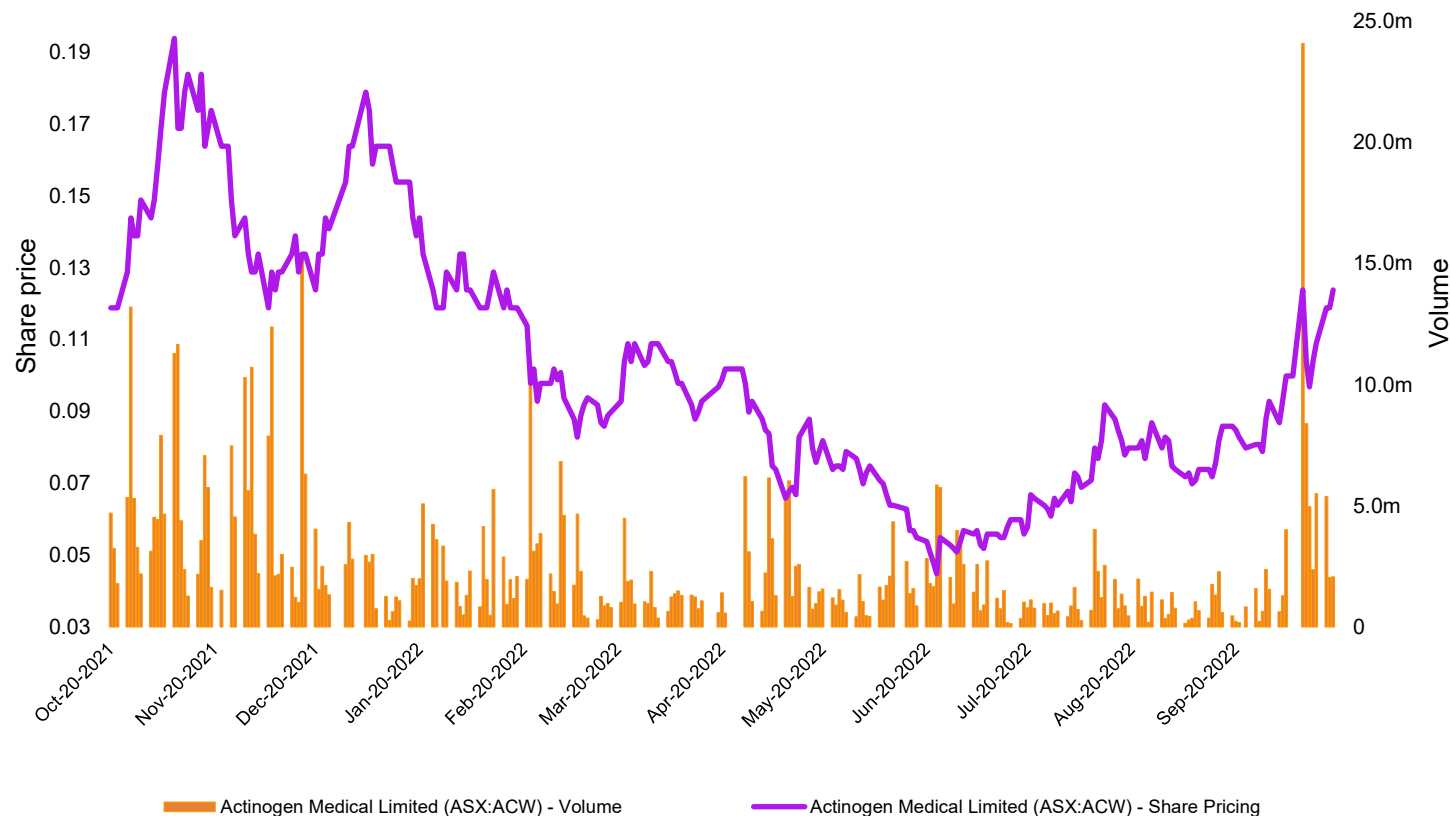
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ACW top stockholders and stock price



Share price chart at 19 October 2022

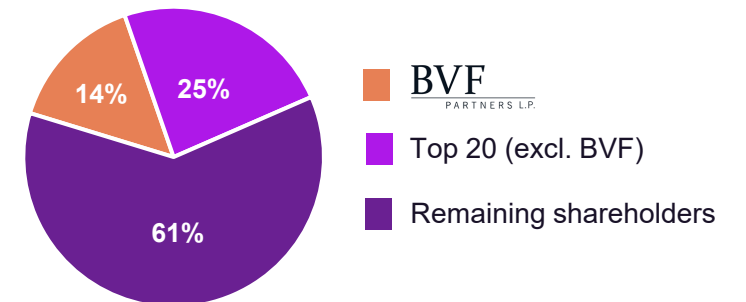


Trading Information

52 week high	A\$0.20
52 week low	A\$0.04
Number of issued shares	1,796M
Market capitalisation (19 Oct 2022)	A\$216M
Cash Balance at 30 Jun 2022	A\$20M ¹

Major Shareholders

BVF Partners	13.9%
Steven Gourlay	3.7%
Edinburgh Technology Fund	2.7%



¹ Including receivable of A\$4.1 million for R&D tax credit

Leadership and Management



Extensive drug development and commercial experience

Experienced Board of Directors...



Dr. Geoff Brooke

Chairman

MBBS; MBA



- 30+ years experience in the healthcare investment industry
- Founder and MD of Medvest Inc and GBS Ventures, Chairman of Cynata Therapeutics, Board Member of Acrux



Dr. George Morstyn

Non-Executive Director

MBBS; PhD; FRACP; MAICD



- 25+ years experience in biotech investment and drug development
- Board member of Cancer Therapeutics and SymBio



Mr. Malcolm McComas

Non-Executive Director

BEc, LLB; FAICD; SF Fin



- 25+ years experience in the financial services industry
- Chairman of Pharmaxis and Fitzroy River Corporation



Dr. Steven Gourlay

CEO & MD

MBBS; FRACP; PhD; MBA



- 30+ years experience in development of novel therapeutics
- Former founding CMO at US-based Principia Biopharma Inc

See full team and bios at:
<https://actinogen.com.au/our-team/>

...with a talented management team in place



Jeff Carter

Chief Financial Officer

B. Fin Admin; M. App. Fin; CA



Tamara Miller

SVP Product Development

M.Med Sci; BSc; MSc; PMP; CPPM



Dr Paul Rolan

Chief Medical Officer

MD, FRACP



Cheryl Townsend

VP Clinical Operations

RN, M Health Law



Dr Christian Toouli

Head of Business Development

PhD; GAICD



Michael Roberts

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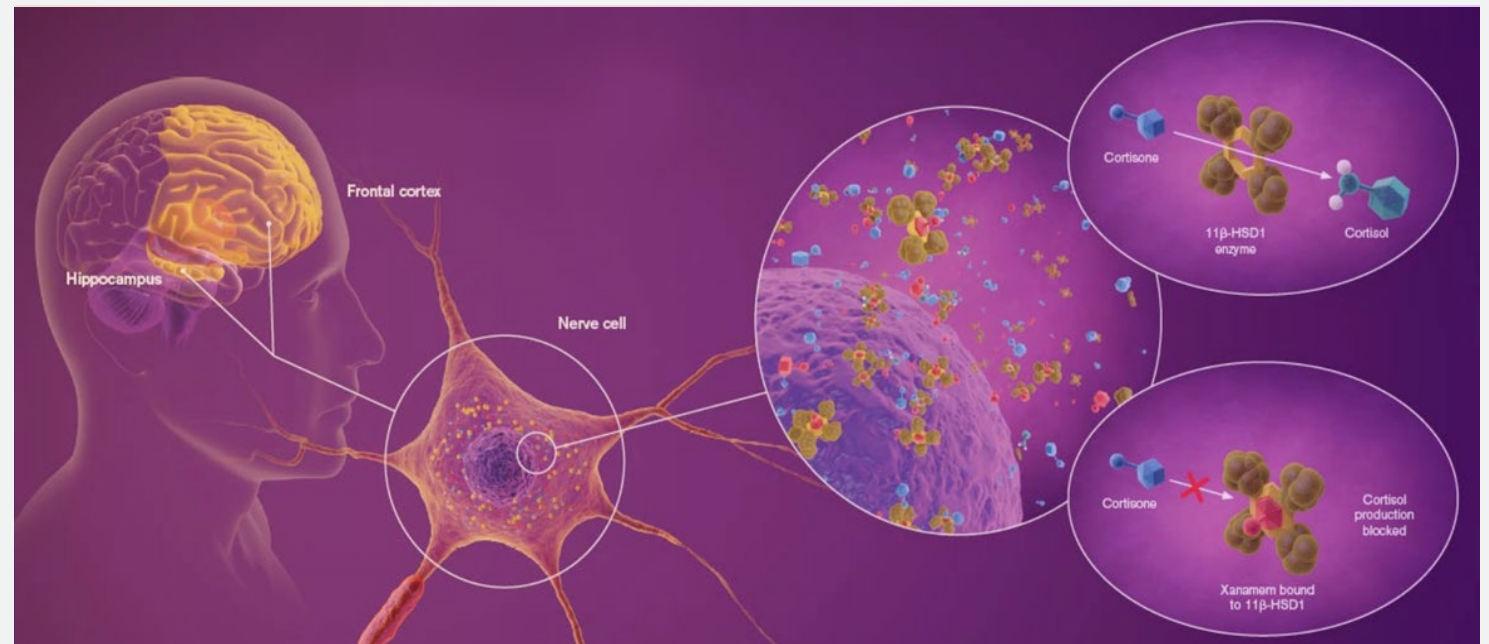
BEc Hons, CPA, FFin

Xanamem: Oral, low dose, once-a-day treatment with a unique non-amyloid mechanism

Brain penetrant 11β -HSD1 small molecule enzyme inhibitor reduces cortisol inside brain cells - modulating signaling pathways and underlying disease processes^{1,2}

Potential to be:

- Rapidly cognitive enhancing
- Disease-modifying (slow or halt progression) in AD
- Anti-depressant




1. Xanamem® is a CNS (Central Nervous System) penetrant small molecule based on human PET scan evidence and cerebrospinal fluid (CSF) measurements
2. 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; Popoli et al. 2011 microglial cell modulation in rats, effects on glutamate, cannabinoid and other signalling pathways

ACW Xanamem program – current status

- ✓ 300 people safely tested in trials using Xanamem
- ✓ Positive attention and memory (cognition) results in two trials
- ✓ Last week – large therapeutic effect in early-stage Alzheimer's Disease (AD) patients
- ✓ FDA approved endpoints

Commencing in coming months:

-  Phase 2 XanaCIDD Depression trial
-  Phase 2b XanaMIA Alzheimer's Disease trial

Recent clinical results in AD patients validate and de-risk Xanamem program

Xanamem doubled rate of disease stabilization



Response analysis in Alzheimer's Disease patients:¹

- *Twice as many patients in the Xanamem group had stable or improved disease compared with placebo²*
- *56% of patients treated with Xanamem were stable or improved*
- *60-80% relative reduction of disease progression vs. placebo*

Xanamem protected the majority of patients from AD progression

1. Identified by pTau-positive biomarker level above median value, n=34

2. Where CDR-SB decreased or was unchanged - Xanamem 9 of 16 (56%) vs. Placebo 5 of 18 (28%)

Data shows large Xanamem clinical effect in AD patients



Biomarker-positive patients likely to progress to more severe disease

	N	Clinical Dementia Rating – Sum of Boxes (CDR-SB) ¹				
Elevated pTau Group		Desired change	Xanamem	Placebo	Cohen's d	p value
pTau >6.74 pg/mL ¹ (mean)	34	Down	0.4	1.0	0.41	0.09
pTau >6.74 pg/mL (median)	34	Down	0.0	0.8	-	-
pTau >10.2 pg/mL ¹ (mean)	9	Down	0.1	0.8	0.62	0.33
pTau >10.2 pg/mL (median) ¹	9	Down	-0.3	0.5	-	-

Clinically significant effect size of CDR-SB 0.6 - 0.8 units

1. CDR-SB is an FDA-recognized endpoint for trials in patients with early Alzheimer's Disease

2. Published cutoff of 10.2 pg/mL² cutoff by Cullen et al. 2022 for progression to clinical AD. 6.74 pg/mL represents the median value of the dataset

The Xanamem opportunity in Depression

Current anti-depressants



work slowly (3 weeks) and
initial suicide risk



do not target cognition



multiple adverse effects
blood pressure, sexual function, appetite...

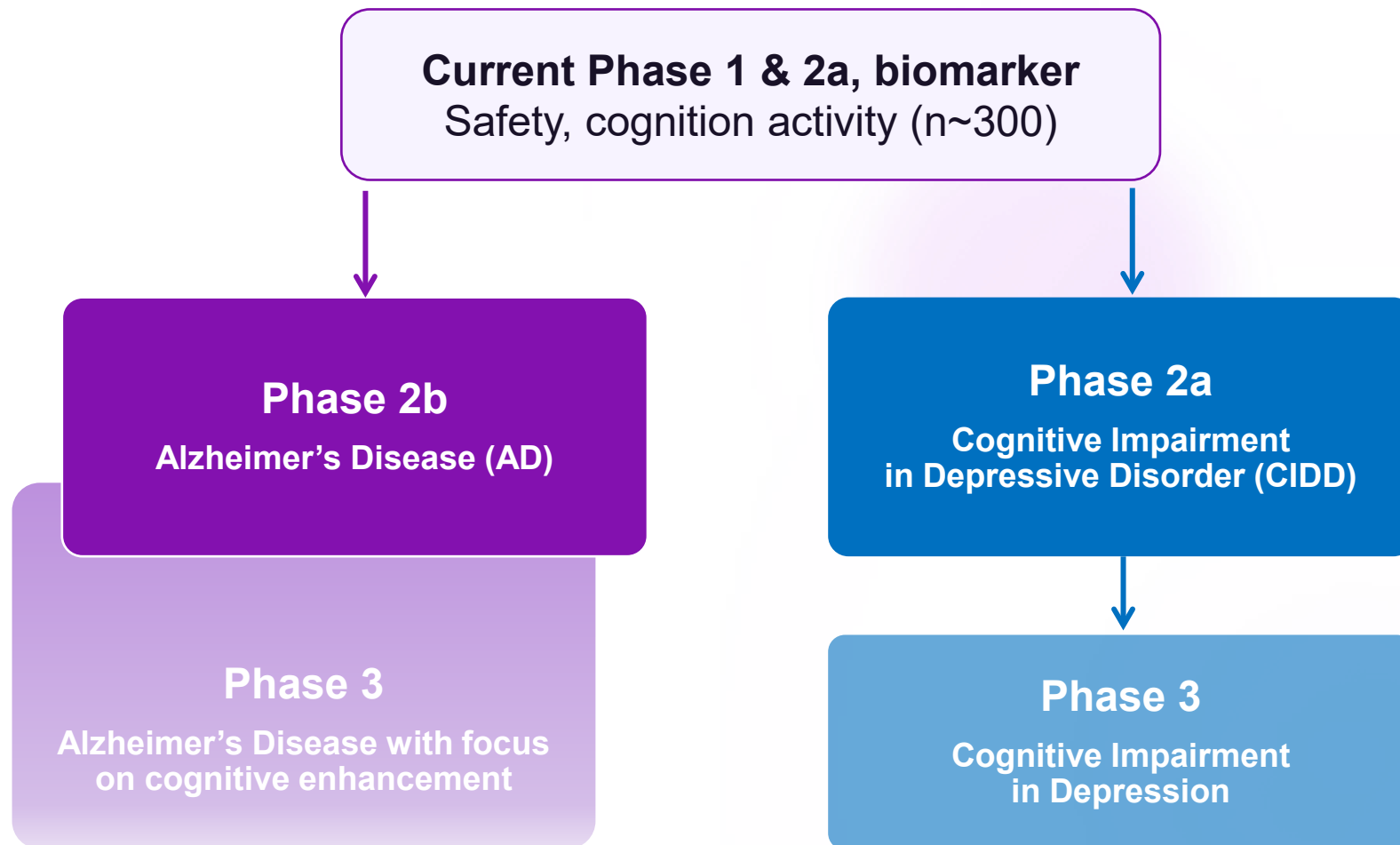


Xanamem improves cognition quickly

Xanamem may improve both depression and cognitive impairment

Xanamem Phase 2 & 3 program

Building on four independent Phase 1 and 2 studies showing activity



Actinogen strategy validated by new results



Backed by strong balance sheet and intellectual property

Accelerate clinical development

- **Focus on cognitive enhancement:**
 - Patients with early Alzheimer's Disease
 - Use pTau for patient selection
 - Phase 2b will use commercial tablets
 - Cognitive enhancement Depression Phase 2
 - Trial operations based in Australia and selected other countries

Forward planning

- Scale up and optimise **manufacturing** to prepare for commercially viable, large scale production
- **Ancillary clinical and nonclinical** studies
- **Commercial** planning

Create value from partnerships



Pharma/biotech engagement

- **Actively engage large and mid-size potential partners with new results**
 - Seek value-add partnerships
 - Evaluate regional opportunities



Regulatory engagement

- Seek early **US FDA and EMA** interactions to agree endpoints for pivotal, approvable trials in AD



Xanamem timeline & catalysts



2022

- October **multiple partnering presentations of new results**
- November **CTAD¹ XanaMIA presentation**
- Trial **enrollment starts for XanaCIDD** trial in Depression
- Key global **regulatory submissions** in AD with FDA, EMA, other
- Phase 2b XanaMIA **AD trial preparation**

2023

- **Partnering discussions**
- **XanaMIA Phase 2b** enrollment starts H1
- **XanaCIDD** enrollment ± results
- **Presentations & publications**

2024

- **XanaMIA Phase 2b results**
- **Expand Cognitive/Depression** program
- **Expand Alzheimer's Disease** program

¹ Clinical Trials in Alzheimer's Disease global conference

Questions



Thank you

If you have any questions following the webinar please contact:

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Appendix



Actinogen company snapshot



Actinogen Medical (ASX:ACW) is developing a novel oral treatment with rapid onset of clinical activity to improve cognition and quality of life



Favourable pharmaceutical properties

- ✓ Demonstrated target engagement in brain and HPA axis¹ in human trials
- ✓ **Low dose, $\leq 10\text{mg}$**
- ✓ Low drug-drug interaction potential suitable for combination therapy



Substantial clinical data

- ✓ **>300 subjects or patients safely treated**
- ✓ Cognitive enhancement activity (attention & working memory) - two trials
- ✓ Large **CDR-SB effect** in pTau-positive AD of 0.6-0.8 points - Phase 2a data



Attractive disease indications and rationale

- ✓ **Strong cortisol rationale for treatment of multiple diseases:** early stages of Alzheimer's Disease; Depression & related cognitive impairment; Fragile X Syndrome; and many others



Protected and funded

- ✓ Molecule in-licensed from U Edinburgh in 2014
- ✓ Comprehensive patents in place²
- ✓ **Cash position ~A\$20M incl. receivables at 30 Jun 2022**



High functioning semi-virtual company model

- ✓ Core team of 10 fulltime employees based in Australia
- ✓ Leveraging senior consultants in various fields in Australia, Asia, UK and USA
- ✓ **Australian-based operations gains 43.5% as cash rebate**

1. Hypothalamic-Pituitary-Adrenal axis (body's system to regulate blood levels of cortisol)
2. Composition of matter to 2031 plus 5-year extension in most countries, new patents published and in process

Selected glossary 1



11 β -HSD1 11 beta HydroxySteroid Dehydrogenase-1 enzyme

A β Amyloid beta – a type of amyloid protein associated with Alzheimer’s Disease, 42 and 40 are different forms

ACTH Adrenocorticotrophic 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

GFAP Glial Fibrillary Acidic Protein – a marker of microglial cell activation in the brain

Filamen A a protein believed to relate to amyloid toxicity

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 Glutaminy-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