Actinogen

Strategic Update & Capital Raising Investor Presentation

Dr. Steven Gourlay MBBS PhD MBA: CEO & MD, CMO

November 25, 2021

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Actinogen

After many years of working in the biopharma industry, I am excited by the huge potential of Actinogen.

In my last major role at Principia Biopharma as Chief Medical Officer, I steered two small molecules from a microcap company valuation, through successful Phase II development and into Phase III, resulting in a significant value appreciation for shareholders when the company was acquired for US$3.7B.

I find Actinogen to be a similar investment opportunity: excellent science, a promising Phase II molecule for multiple indications, with an attractive valuation, and so accepted the role as CEO / MD and personally invested A$330K into the company prior to my appointment.

We are now planning for multiple shots on goal and strongly believe the upcoming trials are designed to achieve informative and positive outcomes. I look forward to working with the team to further develop Xanamem as we progress the development pipeline.

- Dr Steven Gourlay, Actinogen CEO / MD on appointment in March 2021

Actinogen is a neurotherapeutics developer realising a revolutionary therapy so neurology patients can live their best lives

Capital Raising & Strategic Update

Actinogen announce capital raising of approximately $15m to fund its programs until the end of 2023.

Highlights associated with the capital raising:

- Actinogen will **pursue Depression associated with cognitive impairment as a third indication,** initiating a Phase 2 study in Australia
- **Fragile X Syndrome trial is being expanded to sites in North America** to accelerate enrollment timelines and involve key, global thought leaders. A dose-ranging 5mg arm is being added to the original design (25 extra patients for a total of 75)
- **Retrospective analysis of biomarker data** read-out from previous XanADu mild Alzheimer's Disease trial brought forward to H2 CY2022
- **Last patients to be enrolled imminently in XanaMIA Part A, results due Q2 CY2022**
- **Actinogen will now have 3 fully funded Phase 2 trials in 3 CNS indications reading out in 2022/3.** Pivotal trials would follow in each successful Phase 2 program

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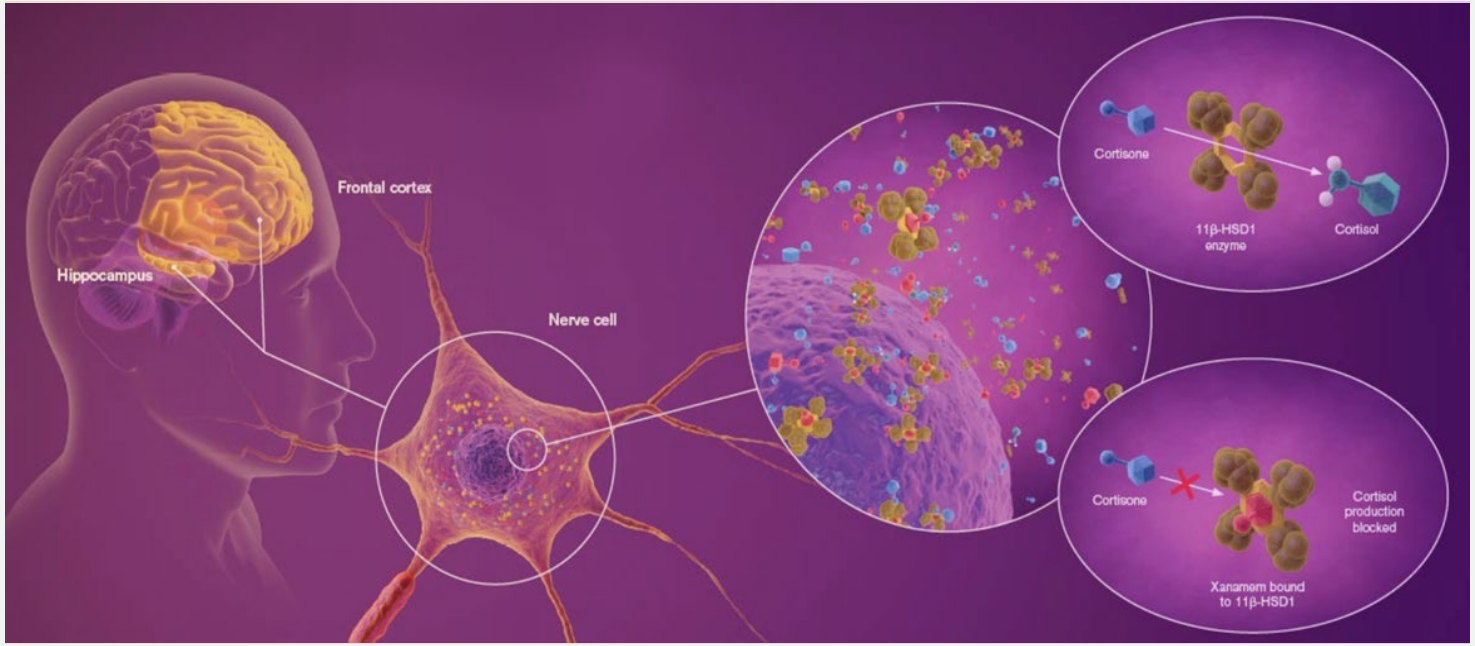
Xanamem: oral treatment and novel mechanism

Brain penetrant 11β-HSD1 small molecule enzyme inhibitor reduces cortisol inside brain cells - modulating signalling pathways and underlying disease processes[1,2]



1. Xanamem® is a CNS (Central Nervous System) penetrant small molecule based on human PET evidence and 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

Actinogen snapshot

Actinogen Medical (ASX:ACW) is developing a novel oral treatment with rapid onset of clinical activity to address a range of central nervous system (CNS) diseases

Favourable pharmaceutical properties

- ✓ Demonstrated target engagement in brain and HPA axis in human trials
- ✓ Low dose, ≤10mg
- ✓ Low drug-drug interaction potential

Substantial clinical data

- ✓ >250 subjects or patients safely treated
- ✓ Large Phase 2 safety database with 12 weeks therapy (N=185)
- ✓ Cognitive enhancement activity shown in healthy older volunteers

Attractive first target indications and rationale

- ✓ Strong cortisol rationale for treatment of early stages of Alzheimer's Disease
- ✓ Strong cortisol rationale for multiple symptom domains of Fragile X Syndrome
- ✓ Strong cortisol rationale for treatment of depression and related cognitive impairment

Protected and funded

- ✓ Molecule in-licensed from U Edinburgh in 2014
- ✓ Comprehensive patents in place[1]
- ✓ Pro-forma cash A$26.8M[2] at 30 Sep 2021 plus A$1.4M R&D Tax Incentive rebate Oct 2021

1. Composition of matter to 2031 plus 5-year extension in most countries, new patents in process
2. Assumes $15m capital raising is fully subscribed

Strong 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

…with a talented management team in place

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-company/#about-us

Jeff Carter

Chief Financial Officer

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

Tamara Miller

Vice President Drug Development & Strategy

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

Therese Russell

Head of People & Infrastructure

Dr Christian Toouli

Head of Business Development

PhD; GAICD

Esteemed Advisory Boards

World-leading, premier academics involved in the development of Xanamem

Xanamem Clinical Advisory Board
Deeply experienced in Alzheimer's Disease drug development

Prof. Craig Ritchie

Chair

THE UNIVERSITY of EDINBURGH

- World-leading authority on dementia; senior investigator on 30+ drug trials
- Chair of the Scottish Dementia Research Consortium; Professor of the Psychiatry of Ageing' Director of the Centre for Dementia Prevention (University of Edinburgh)

Prof. Colin Masters

AO

THE FLOREY INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH

THE UNIVERSITY OF MELBOURNE

The Royal Melbourne Hospital

- 35+ years research on Alzheimer's Disease and other neurodegenerative diseases
- Laureate Professor of Dementia Research and Head, Neurodegeneration Division at The Florey Institute (UniMelb)

Prof. Jeffrey Cummings

Cleveland Clinic

- World-renowned Alzheimer's researcher and leader of clinical trials
- MD, ScD; Founding Director of the Cleveland Clinic Lou Ruvo Center for Brain Health
- Recognised for his work through various awards

Scientific Advisory Board
Combining deep understanding of endocrinology, 11β-HSD1 and drug discovery

Prof. Jonathan Seckl

THE UNIVERSITY of EDINBURGH

- Undertaken extensive research in endocrinology
- Senior VP at the university of Edinburgh; Chaired Panels for MRC, Innovate UK and Wellcome Trust
- MBBS UCL, PhD (London)

Prof. Brian Walker

Newcastle University

- 20+ years research in the area of disease
- Extensive experience advising for pharmaceutical R&D
- Pro Vice Chancellor for Research Strategy & Resources at Newcastle University, UK

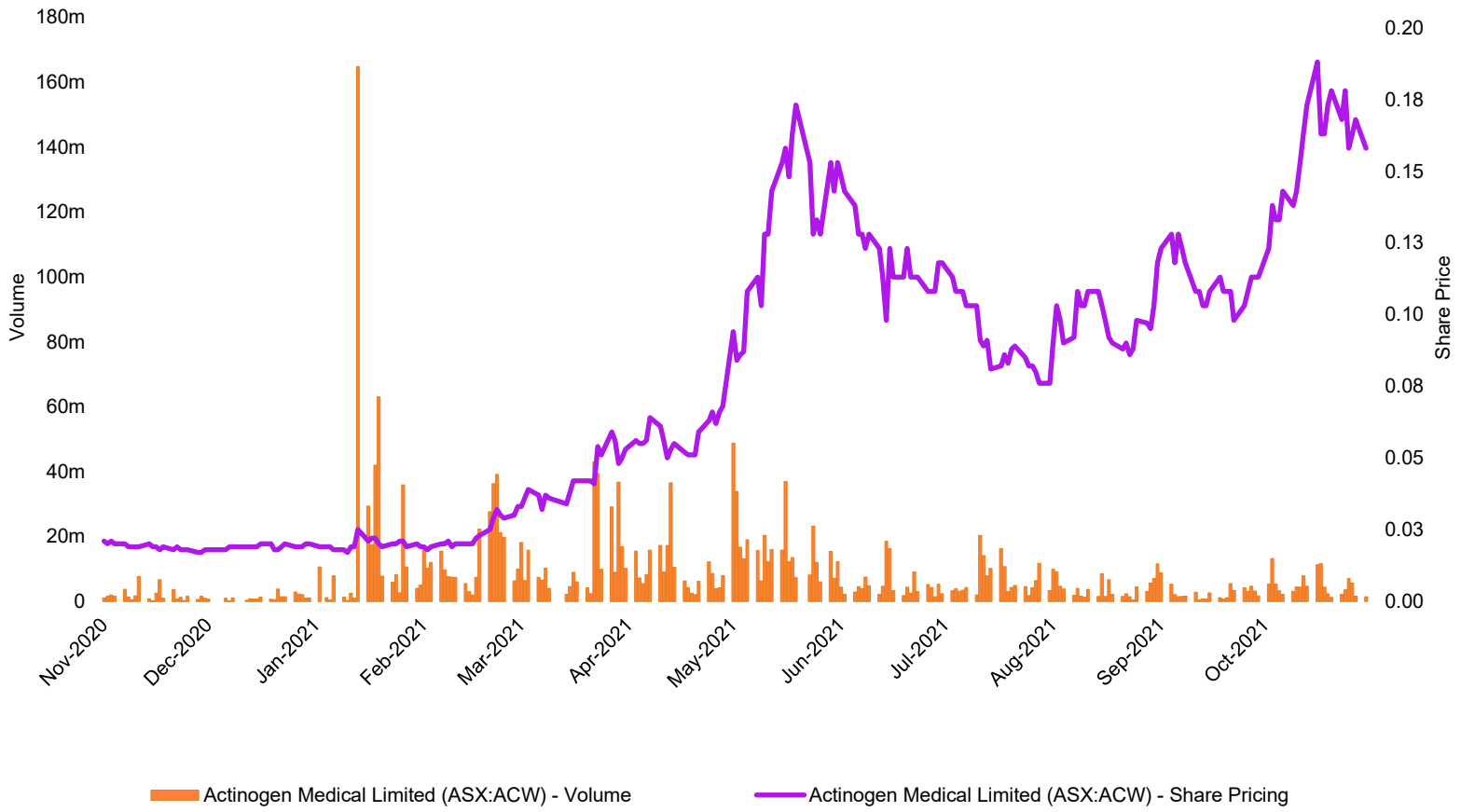
Prof. Scott Webster

THE UNIVERSITY of EDINBURGH

- Chair of Medicines at the Centre of Cardiovascular Science, University of Edinburgh
- Former positions across both biotech and academia
- Founder and Chief Scientific Officer at Kynos Therapeutics

ACW stock performance 12 months

Share price chart at 24 Nov 2021

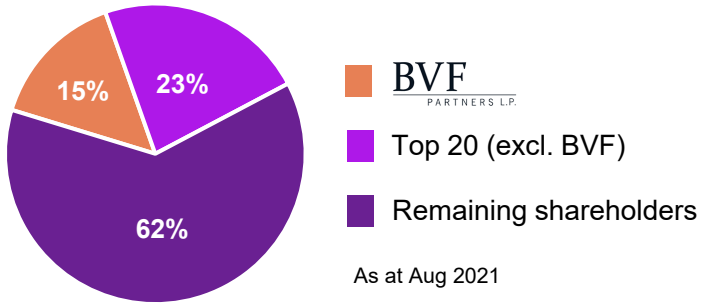


Trading Information

52 week high	A$0.20
52 week low	A$0.02
Number of shares	1,660.6M
Market capitalisation (24 Nov 2021)	A$268.3M
Pro-forma cash at 30 Sep[1,2]	A$26.8M

Major Shareholders

BVF Partners	14.9%
Steven Gourlay	3.8%
Edinburgh Technology Fund	2.9%



As at Aug 2021

1. Does not include A$1.4M R&D Tax Incentive rebate received Oct 2021
2. Assumes $15m capital raising is fully subscribed

Xanamem Clinical Development Pipeline

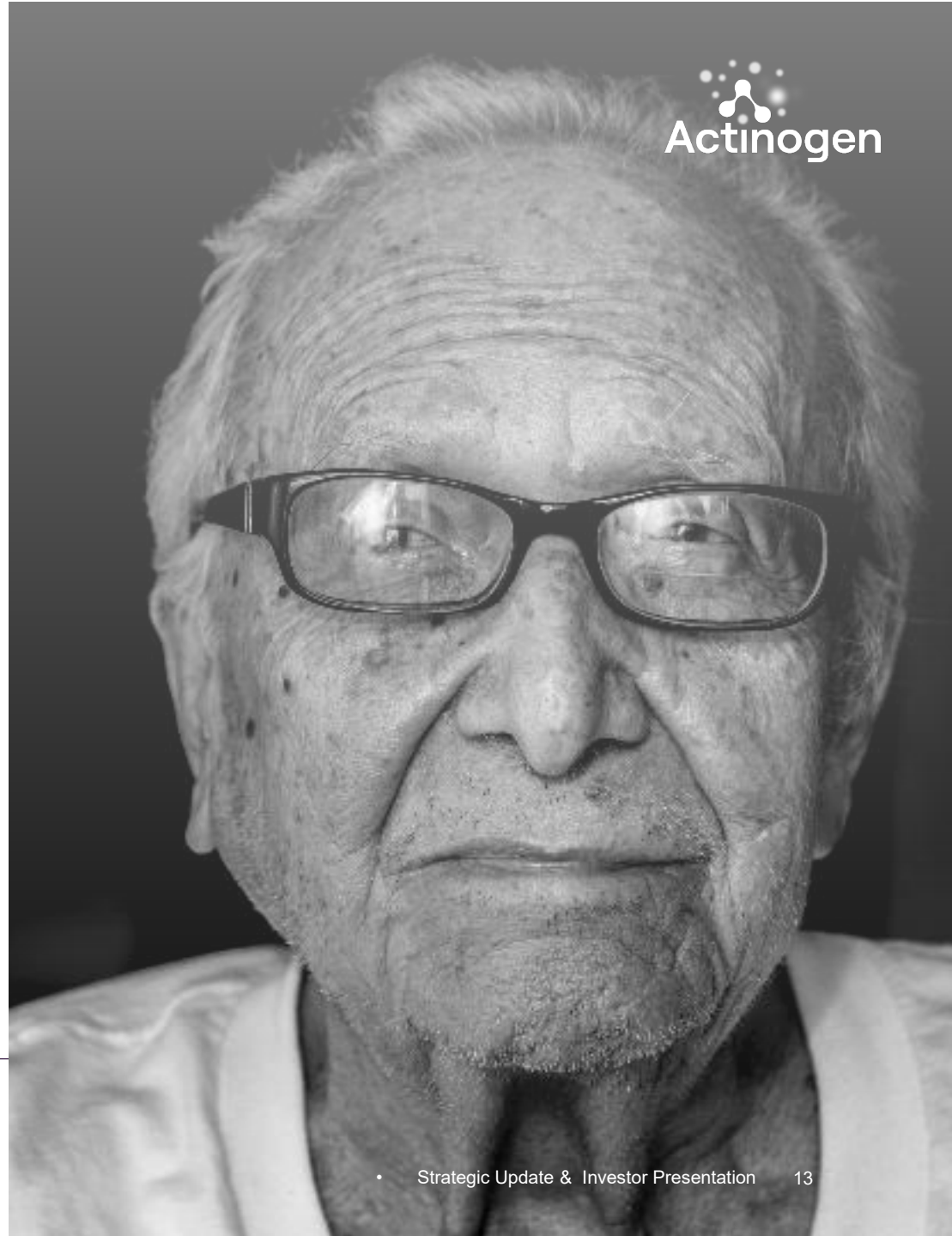
Diseases to be studied in 2021/2022	Phase 2 Pathway	Outlook
Mild cognitive impairment due to **Alzheimer's disease**	**XanaMIA** **Part A:** 10mg, 5mg, Placebo Older Volunteers: cognition **Part B:** Patients with MCI due to AD: cognition & biomarkers	*"Big-to-market"* *Multiple Phase 2b/3 trials*
Anxiety, sleep & behavioural problems in **Fragile X Syndrome**	**FDA Pre-IND Meeting** **XanaFX** Phase 2 trial	*"Fast-to-market" single pivotal Phase 3*
Depression with cognitive impairment	**Study preparation** **XanaMDD** Phase 2 randomised trial	*Portfolio diversification and optionality*

Alzheimer’s Disease

Targeting cognitive enhancement and disease-modification in the early stages of disease

Science Behind the Xanamem AD Program

- ✓ Cortisol is toxic to monkey brain cells[1]
- ✓ Cortisol impairs animal cognition[2]
- ✓ Cortisol & hippocampal volume/memory[3]
- ✓ Higher blood cortisol & cognitive decline[4]
- ✓ Higher CSF cortisol & cognitive decline[5]
- ✓ 11β-HSD1 Alzheimer's mouse model[6]
- ✓ Xanamem & improved human cognition[7]



1. Implant in hippocampus, Sapolsky et al. 1990; increased amyloid proteins, Green et al. 2006
2. Literature review, Ouanes et al. 2019
3. Human study with MRI and cognitive assessment, Lupien et al. 1998
4. Morning cortisol & cognitive decline, Cernansky et al. 2006; Pietrzak et al. 2017
5. Longitudinal human study with multivariate modelling, Popp et al. 2015
6. 11β-HSD1 inhibition reduced amyloid and cognitive decline, Sooy at al. 2015
7. Xanamem placebo-controlled trial working memory & attention (Actinogen data on file)

PET data supports a low Xanamem dose ≤10mg daily

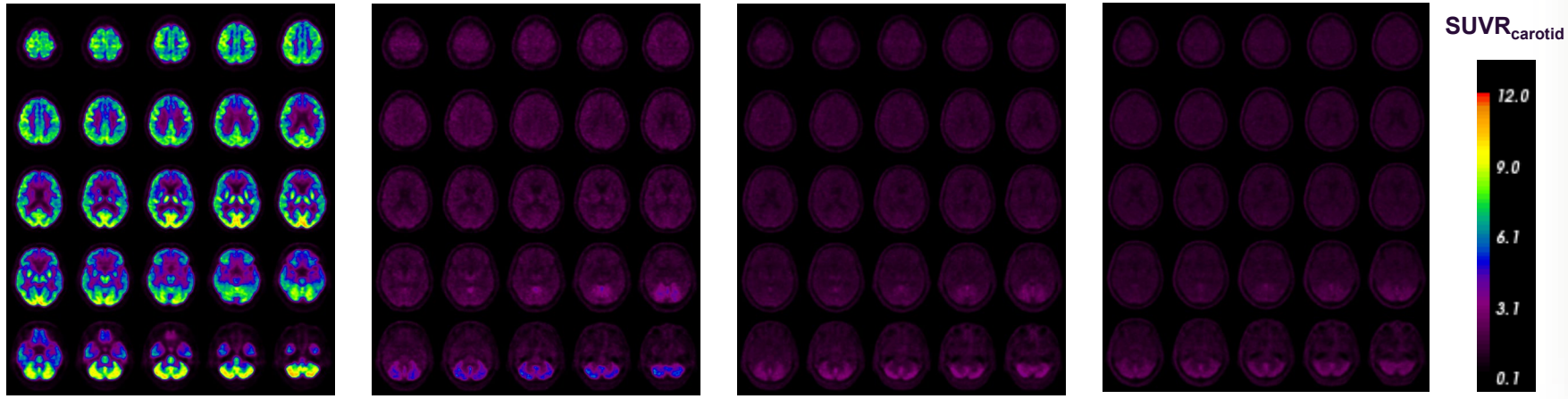
Baseline

After Dose

5mg Xanamem

10mg Xanamem

20mg Xanamem



PET data 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 5mg dose.

This is consistent with full hormonal pharmacodynamic activity seen with 10mg in clinical trials.

Note: Study population consisted of ~50% healthy subjects (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.

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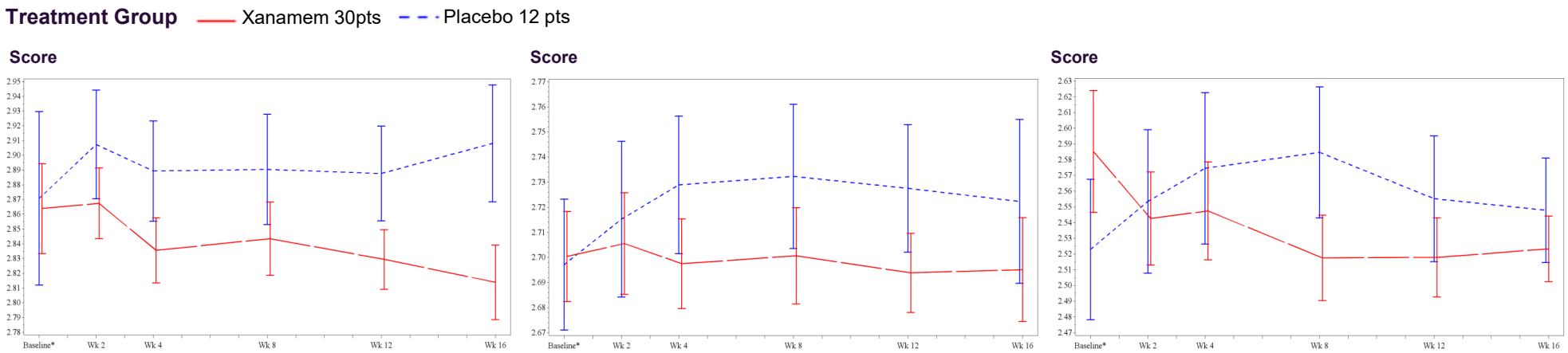
Cognitive improvement demonstrated

Phase 1 XanaHES study demonstrated statistically significant cognitive efficacy signal in multiple cognition domains based on Cogstate Cognitive Test Battery as early as 2 weeks[1]



P<0.01

Working memory (One Back Test)

Strongly statistically significant result

P=0.05

Visual attention (Identification Test)

Statistically significant result

P=0.09

Psychomotor function (Detection Test)

Good trend to a positive result

Large effect sizes seen in working memory and attention, trends in other domains

1. XanaHES Phase 1 clinical trial treated healthy elderly patients with 20mg Xanamem daily (n=30 active, n=12 placebo). All values are the means of observed data. p values were calculated with an ANCOVA (analysis of covariance) model using Baseline values as a covariate.

Bridging Phase 1 cognition data to patients

No functional Impairment

XanaMIA Trial

XanaMIA Part A → **XanaMIA Part B**

Functional Impairment stages in Alzheimer's disease

XanaHES

Healthy elderly

MCI* patients

- Disease biomarkers
- Computerised cognitive testing
- DSST

XanADu

Mild

- 2015 design
- Only 12 weeks
- New biomarker analysis
- N=185

Moderate

Severe

Multi-billion dollar market alone or as combination therapy

* Mild Cognitive Impairment (MCI): memory, executive function deterioration with retained functional abilities

XanaMIA Phase 1b/2 trial data in 2022 & 2023

Targeting the first stages of Alzheimer's Disease

XanaMIA - Part A

H12022: minimum effective dose on cognition

- **Healthy older subjects** - with normal cognition, ≥50 years of age (same as XanaHES trial)
- **Sensitive endpoints and testing criteria** - highly sensitive cognition tests (Cogstate, iDSST)
- DSST used for vortioxetine **regulatory cognitive** claim
- **Dose ranging** - 5mg, 10mg vs. placebo

XanaMIA - Part B

2023: disease-modifying potential on biomarkers

- Targeting subjects with **mild cognitive impairment** due to Alzheimer's disease (confirmed using positive serum biomarkers)
- **Cognitive endpoints** - highly sensitive cognition tests (Cogstate, iDSST)
- Prospectively measuring disease-modifying potential with change in **Alzheimer's Disease biomarkers** over 12 weeks treatment
- **One or more** doses depending on Part A

Planned retrospective analysis of Phase 2 plasma samples for Alzheimer's Disease biomarkers

Bringing disease biomarker data readout forward into 2022

XanADu Phase 2 trial

- 185 patients (n=91 active, n=94 placebo)
- 10mg daily
- Mild Alzheimer's disease without biomarker or imaging confirmation

Preliminary feasibility completed for biomarker analysis extension study

- Upwards of 50 patients/guardians sought to be reconsented
- Most sites willing to participate
- Established relationship with analytical laboratory
- Biomarkers assessed will include Aβ1-40, Aβ1-42, T-tau, Tau 181, NfL, and GFAP

Fragile X syndrome

An inherited disorder caused by the FMR1 mutation on the X chromosome with no approved treatments

Fragile X Syndrome has high unmet medical need

Unmet medical need

- Commonest genetic cause of intellectual disability, predominantly males
- Management of FXS is often complex, with **life-long treatment** required for patients

Strategic benefits

- Xanamem in FXS has been awarded **Rare Paediatric Disease Designation**, and eligible for **Orphan Drug** Designation
- **Broadens range of partners** in orphan space

Fast-to-market path

- Moderate sized, **comprehensive proof-of-concept** Phase 2
- Anticipate **single Phase 3** for approval

Valuable commercial opportunity[1]

- Estimated **global market size of ~US$250M**
- Related indications such as Autism Spectrum Disorder
- **Priority Review Voucher value ~US$100-125M**

FMR1: Fragile X mental retardation 1

1. FXS market in 2026. GlobalData analyst report 2018. Projection for 7 major markets: US, France, Germany, Italy, Spain, UK, Japan

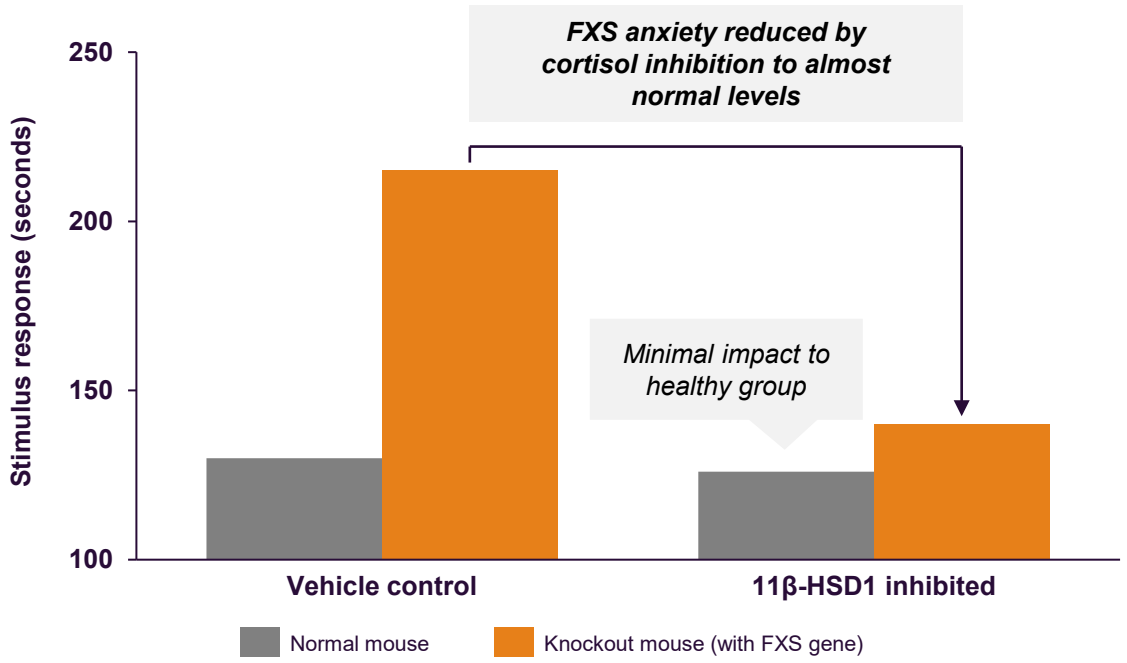
Science Behind the Xanamem FXS Program

- ✓ Elevated blood cortisol in patients[1]
- ✓ Elevated cortisol & human symptoms[2]
- ✓ Glutamate linked to cortisol response[3]
- ✓ FMR1 KO mice show raised cortisol[4]
- ✓ Elevated 11β-HSD1 in FXS mouse[5]
- ✓ 11β-HSD1 Fragile X mouse model[6]

1. Hessl et al. 2002; Wisbeck et al. 2000
2. Elevated cortisol correlates with symptoms, Hessl et al. 2002; Hardiman & Bratt 2016
3. Mouse FMR1 mutation model of Fragile X & glutamate, cortisol mechanism Ghilian et al. 2015
4. Mouse cortisol (corticosterone), Lauterborn et al. 2004
5. FMR1 deficiency promotes age-dependent alterations in the cortical synaptic proteome, Tang et al., 2015
6. Normalisation of anxiety with 11β-HSD1 inhibition, Vanderklish & Francesconi 2019

Xanamem may treat multiple symptom domains in FXS

Normalisation of anxiety in the FXS KO mouse[1]



Symptoms of Fragile X syndrome are all potentially amenable to Xanamem therapy

XanaFX trial target symptoms

- Anxiety[2]
- Cognitive impairment
- Behaviour problems/ hyper-reactivity

Other FXS symptoms potentially amenable to Xanamem therapy

- Sleep problems
- Learning disabilities
- Speech and language deficits

1. Pre-clinical FMR1 knock-out mouse model using BVT 2733 as the 11β-HSD1 inhibitor showed highly significant results (***p<0.0001). Normal mouse is a wild-type mouse. (Source: Vanderklish PW. 2019. Compounds for treatment of emotional/psychological symptoms in fragile x syndrome, WO 2019/075394 Al.)
2. ~90% of FXS patients suffer symptoms of anxiety

Major Depressive Disorder associated with Cognitive Impairment

Targeting dual cognitive enhancement and anti-depressant activity

Market characteristics of Major Depressive Disorder (MDD)

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MDD is common[1,2]

~5% prevalence globally, 1 in 7 lifetime risk

Neurocognitive symptoms are a typical feature (>80%)[3]

Difficulty thinking and concentrating, unable to make decisions

Only one anti-depressant has a cognitive benefit claim

Vortioxetine sales US$500m[4]

1. World Health Organization, Depression. 2021.
2. Kessler & Bromet 2013
3. Conradi et al. 2011, *Psychol Med,* 41(6):1165-74.
4. Lundbeck financial reports 2020

Science Behind the Xanamem Depression Program

- ✓ 80-90% report neurocognitive symptoms[1]
- ✓ Cognitive symptoms often persist during remission[1]
- ✓ Elevated cortisol associated with severe, melancholic depression[2]
- ✓ Cortisol associated with treatment outcomes, relapse, & cognition[3]
- ✓ Positive effects with GR receptor antagonism with mifepristone[4]
- ✓ Xanamem & improved human cognition[5]

1. 3-year prospective study and review, Conradi et al. 2011
2. Quantitative summary of four decades of research, Stetler & Miller 2011
3. Depression literature review, Malhi & Mann 2018; HPA axis in major depression, Keller et al. 2016
4. 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_1 receptor antagonists, Holsboer & Ising 2008
5. Xanamem placebo-controlled trial working memory & attention (Actinogen data on file)

Clinical/Regulatory – established endpoints & regulatory path

Initial trial will be placebo-controlled Phase 2 of 6-weeks treatment

- MDD endpoints used by other programs
  - Trintellix endpoints: MADRS[1] and HAM-D[2] scores
  - Spravato (esketamine) endpoints: MADRS score
  - Zulresso endpoints: HAM-D score
- Cognitive endpoints used by other programs
  - Trintellix label claim for cognition largely based on DSST[3] score
  - Xanamem XanaHES study showed response in working memory & attention with Cogstate
  - Spravato also included cognition tests as safety endpoints in both short-term and long-term study, as ketamine is known to result in cognitive dysfunction
    - Used Cogstate Battery and HVLT-R[4]

[1] Montgomery-Asberg Depression Rating Scale
[2] Hamilton Depression Rating Scale
[3] Digit Symbol Substitution Test
[4] Hopkins Verbal Learning Test - Revised

Commercial opportunity is large, even at Phase 2

Global Big Pharma strong M&A interest in acquiring or partnering and licensing assets with novel mechanisms of action where depression is the lead/key indication.

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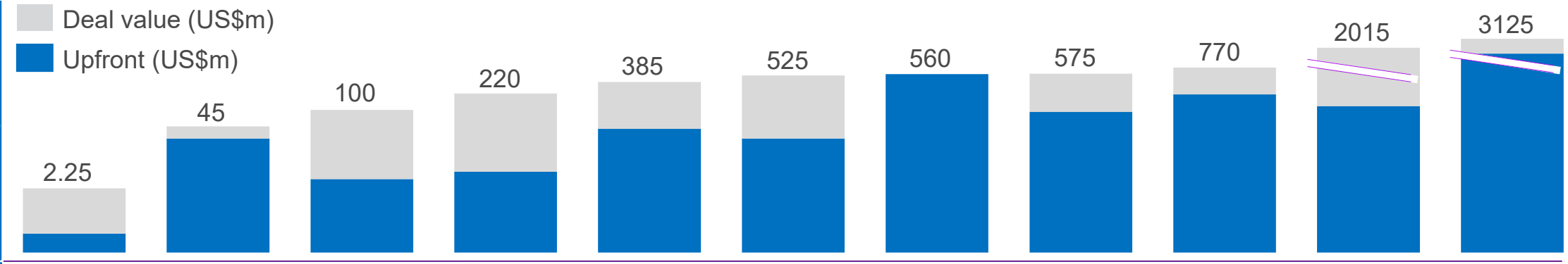

Bidder / Licensee	VistaGen Therapeutics	Janssen	ABVC	biohaven pharmaceuticals	Takeda	Supernus Pharmaceuticals	Allergan	SHIONOGI	NOVARTIS	Neurocrine Biosciences	Biogen
Target / Licensor	Pherin Pharmaceuticals	CERECOR	BioLite	AstraZeneca	Lundbeck	NAVITOR PHARMACEUTICALS	Naurex	Sage Therapeutics	CADENT	Takeda	Sage Therapeutics
Year	2018	2017	2015	2016	2007	2020	2015	2018	2020	2020	2020
Deal type	Option + license	License	License	License	Partnership	Partnership + option	Acquisition + option	License	Acquisition	License	Partnership + license
Relevant candidate/s	PH100	CERC-501 (Aticapran)	BLI-1005 (ABV-1504)	Llanicemine (BHV-5000)	Vortioxetine & tedatioxetine	NV-5138	Rapastinel, apimostinel	Zuranolone (SAGE-217)	MIJ821	TAK-653, TAK-041 (seven total)	Zuranolone (SAGE-217)
MoA	Neuroactive steroid nasal spray	Oral kappa opioid receptor antagonist	Botanical reuptake inhibitor of norepinephrine	Low-trapping NMDA receptor antagonist	Serotonin modulator / triple reuptake inhibitor	Orally active mTORC1 activator	NMDA receptor modulators	Orally active $GABA_A$ receptor modulator	NMDA receptor modulator	AMPA potentiator, GPR139 agonist	Orally active $GABA_A$ receptor modulator
Phase	2	2	2	2	2	2	1 & 3	3	2	PC[2] – 2	3
Sole asset/s in deal?[1]	✗	✓	✗	✓	✗	✓	✓	✓	✗	✗	✓

1. Indicates whether listed assets were the sole target of the deal, or if additional assets for other indications were also included in deal terms; does not include agreements where an option to license future assets was secured.
2. Pre-clinical

Summary and Outlook

Significant value upside for Actinogen

Accelerate clinical development

- Commence Fragile X Syndrome trial
- Expand pipeline with depression Phase 2 program
- Create optionality for development and partnerships

Forward planning

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

Value from partnerships, peer companies

Pharma/biotech engagement

- Actively engaging with large and mid-size potential partners

Priority review and PR voucher

- Priority review granted by FDA
- PRVs recently traded for US$100M-US$125M

Peer AD company valuations reflect growth potential

- Peer companies in phase 2 or 3 for AD: valuations ~US$200M-$2.1B[1]

1. Vivoryon Therapeutics, phase 2a/b AD lead asset (EURONEXT Amsterdam: 374m euro); Athira Pharma, phase 2 AD lead asset (NASDAQ GS:~US$537m); Cortexyme, negative topline data in phase 2b/3 AD for lead asset (NASDAQ GS:~US$365m) and same drug in phase II for periodontal disease and Parkinson's disease; Cassava Sciences, AD lead asset phase 2 asset with positive biomarker and cognition data (NASDAQ GS:~US2.1B); Annovis Bio, very early phase 2 data AD, PD (NASDAQ US$202m). All companies' value primarily attributed to their lead AD asset. Market capitalisations as of November 23-24 2021.

Next steps and key catalysts

- **Clinical trials to read out in 2022 and 2023**

  Alzheimer's Disease
  - XanaMIA Part A cognition results Q2 CY2022
  - XanADu retrospective biomarker results H2 CY2022
  - XanaMIA Part B patient biomarker/cognition data 2023

  Fragile X Syndrome
  - Commenced in 2021
  - XanaFX trial results 2023

  Depression
  - Commence program immediately, results 2023
- **Publications and collaborations**
  - Focus on PET and other peer-review publications
  - Leverage academic, grant collaborations

Offer Summary

Capital Raising Overview

Actinogen is raising approximately A$15m via a Placement and Share Purchase Plan

Offer Structure	▪ Institutional Placement commitments received for A$12 million ▪ Share Purchase Plan (SPP) targeted to raise A$3 million*
Offer Pricing	▪ Placement offer price of A$0.135 per share, which represents: – A discount of 15.6% to the last close of A$0.16 per share on 22 November 2021 – SPP at the same offer price as the Placement
SPP	▪ Actinogen intends to offer eligible shareholders an opportunity to subscribe for up to A$30,000 of new Shares under a Share Purchase Plan at a price per Share equal to the Offer Price
Lead Manager	▪ Bell Potter Securities Limited

* The company reserves the right to accept oversubscriptions of up to A$2 million

Use of funds*

The capital raising will fully fund Actinogen's clinical development program through end of 2023

Details	A$m
Expanded Fragile X program to North America	7.0
Depression associated with cognitive impairment (3rd disease indication)	5.0
Early assessment of Alzheimer's Disease biomarker data	1.0
Additional GMP manufacturing	1.0
Offer costs and working capital	1.0
Total	**15.0**

* Assumes $3 million subscription under the SPP

Offer timetable

Indicative capital raising timetable[1]	Date
Trading halt	Tuesday, 23 November 2021
Record date for the SPP	Wednesday, 24 November 2021
Announcement of the Equity Raising and trading halt lifted – shares recommence trading on ASX	Thursday, 25 November 2021
Settlement of Placement	Tuesday, 30 November 2021
Allotment and commencement of trading of new shares under the Placement	Wednesday, 1 December 2021
SPP opens	Monday, 29 November 2021
SPP closes	Monday, 13 December 2021
Issue of new shares under SPP	Wednesday, 15 December 2021

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