



AdAlta
next generation protein therapeutics

i-body: a unique drug discovery platform

February 2020

AdAlta Limited (ASX:1AD)

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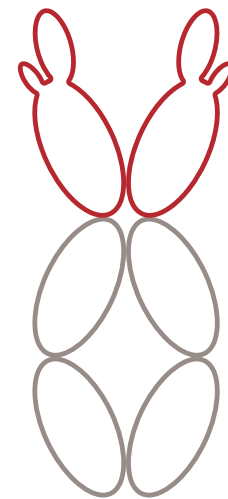
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AdAlta's purpose

AdAlta Limited (ASX:1AD) is a late pre-clinical stage biotechnology company using a promising new class of single domain antibodies, known as i-bodies, to discover and develop novel therapeutics for treating a wide range of human diseases

AdAlta summary

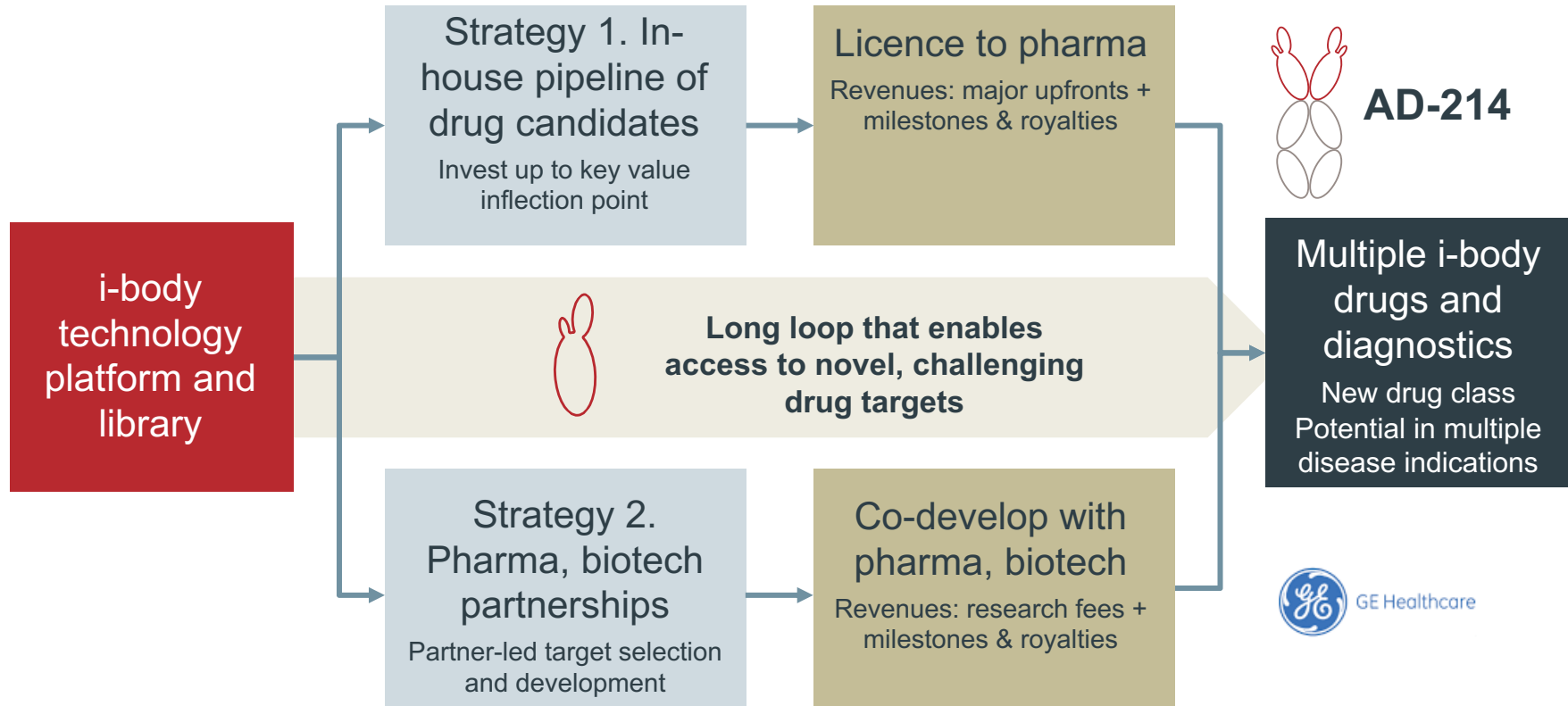
- ▶ **i-body platform for generating multiple products against “difficult” targets**
 - Novel structure (small scaffold, long binding loops) provides new way to access unique epitopes on tough biological targets such as GPCRs and ion channels that can be difficult to access with conventional approaches
 - Human based single domain scaffold
- ▶ **First in class lead internal program, AD-214, due to commence human Phase 1 clinical trial in mid-2020**
 - Targeting fibrosis of the lungs (Idiopathic Pulmonary Fibrosis), a clinical indication with high unmet medical need and early transaction potential, and other fibrotic diseases
 - USA FDA Orphan Drug Designation and strong pre-clinical data
- ▶ **Collaborations, providing additional opportunities to leverage the i-body platform**
 - Recently secured licensing deal with global medical technology firm, GE Healthcare, to develop i-bodies for diagnostic imaging
- ▶ **Experienced drug development team driving strategic focus on pipeline expansion**



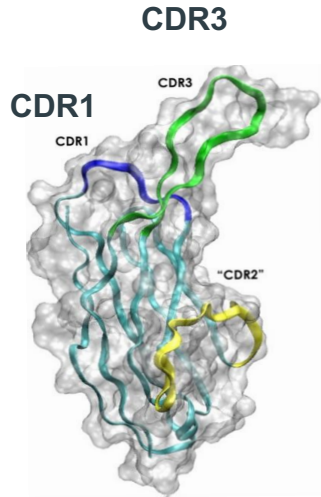
AD-214



AdAlta strategy and business model to create value

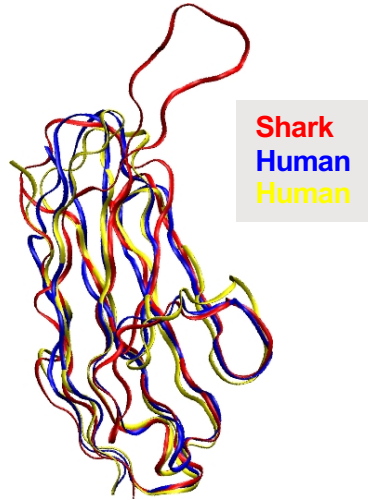


i-bodies: human single domain antibodies



Shark VNAR*

Basic research on
unique shark
immune system ...



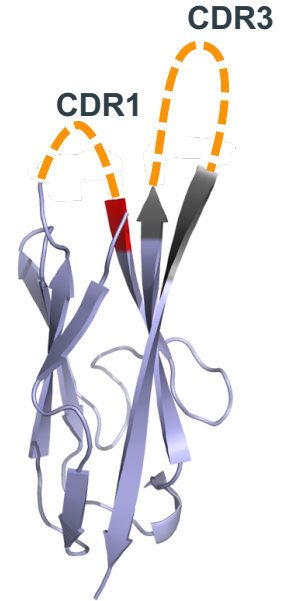
Ribbon overlay

... led to discovery of
human proteins with
same scaffold
structure ...



hNCAM Domain 1

... leading to choice
of human NCAM-1
as best mimic ...

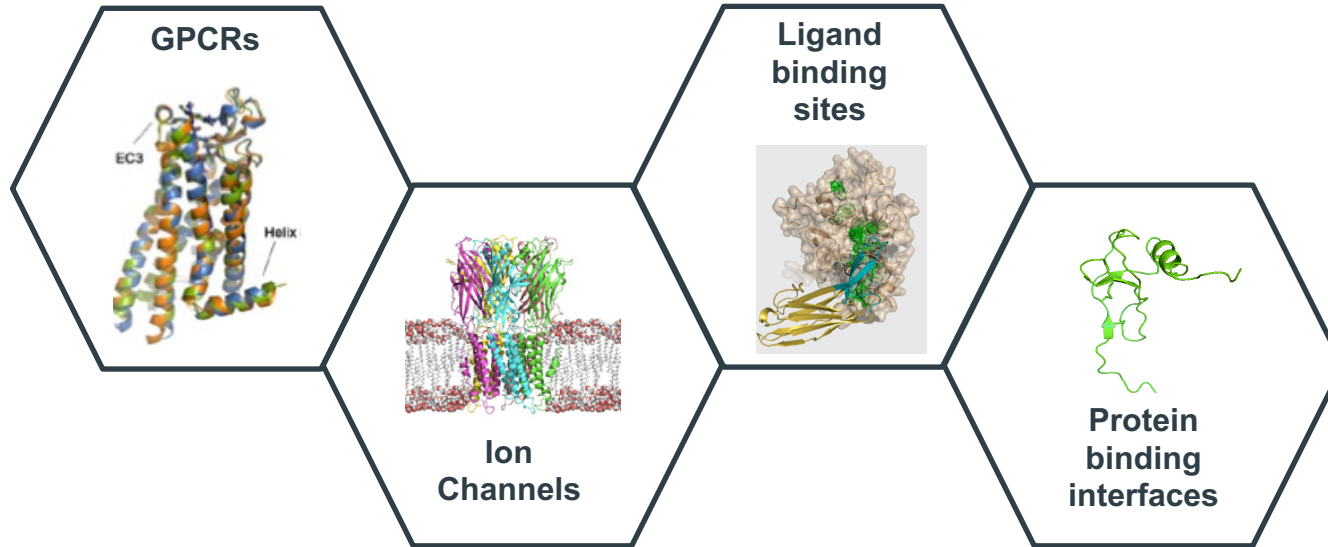


i-body library

... and invention and
patenting of i-bodies by
adding randomized
VNAR-like binding loops
to NCAM-1

i-bodies: targeting “difficult to drug” targets

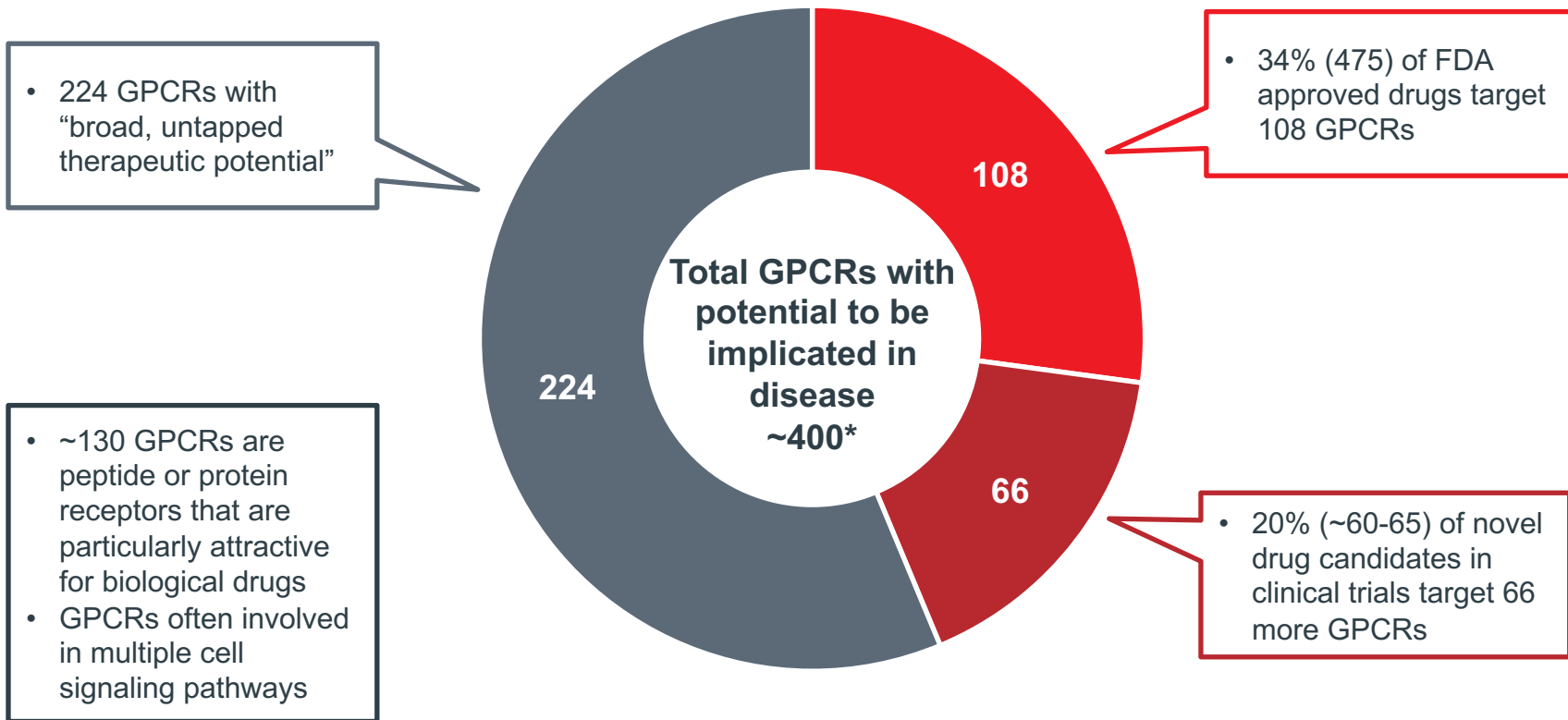
Small size, long loop of i-body can access unique epitopes

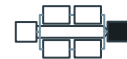


Additional unique i-body properties










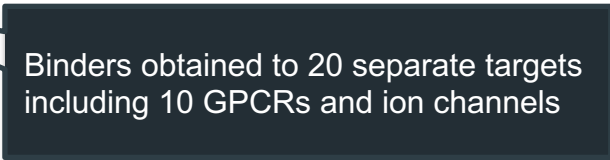
- Novel, tunable pharmacology
- Flexible half-life
- Stability to pH and temperature cycling
- Multiple potential routes of administration

Many potential “difficult to drug” targets: G-protein coupled receptor (GPCR) example





AdAlta pipeline

Partner	Product/ Indication	Target	Class of Target	Discovery	Preclinical	Manufact- uring	IND enabling studies	Phase I
 AdAlta <small>next generation protein therapeutics</small>	AD-214: Idiopathic Pulmonary Fibrosis	CXCR4	GPCR					
 AdAlta <small>next generation protein therapeutics</small>	AD-214: Other fibrotic indications (kidney, eye, liver, skin)	CXCR4	GPCR					
 Excellerate BIOSCIENCE	Not disclosed	Not disclosed	GPCR					
 GE Healthcare	Diagnostic agents	Granzyme B + others	Serine protease					
 AdAlta <small>next generation protein therapeutics</small>	i-body discovery engine	Various						



Fibrosis: significant unmet medical need

- ▶ Fibrosis is the build-up of connective tissue
- ▶ Results from repeated inflammation and uncontrolled wound healing
- ▶ Causes scarring of vital organs such as the lung, liver, skin, eye, heart and kidney
- ▶ Leads to irreparable damage and eventual organ failure



Fibrosis contributes to the pathophysiology of **45-50%** of diseases
There is **no clinically satisfactory therapeutic** approach to fibrosis

Market opportunity for IPF (lung fibrosis)

Idiopathic Pulmonary Fibrosis (IPF) is an irreversible, unpredictable and incurable disease

THE STATISTICS

People living with IPF
300,000

People die from IPF every year
40,000

Median length of survival after IPF diagnosis
3.8 years

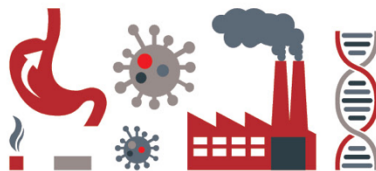
IPF incidence



of sufferers die within 2 to 3 years following diagnosis

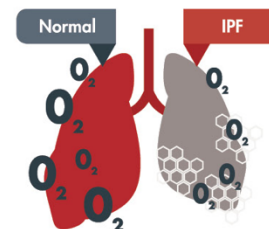


Causes



The cause is unknown but risk factors may include: smoking, environmental exposures, chronic viral infections, abnormal acid reflux and family history of the disease.

Pathology



Resultant scarring/honeycombing in the lung restricts breathing and oxygen exchange.

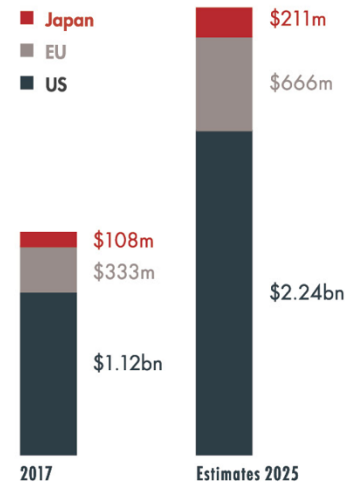
Current IPF treatments

Pirfenidone

Nintedanib



IPF Therapy Sales (US\$)



Source: GlobalData 2018

AD-214 targets CXCR4, a GPCR involved in fibrosis and other disease states

- ▶ CXCR4 is important in maintaining stem cells in bone marrow
- ▶ HIV-1 uses CXCR4 as a co-receptor for viral entry into host cells
- ▶ CXCR4 has been associated with more than 23 types of cancers
- ▶ CXCR4 has more recently been recognised as a critical player in development of fibrosis including in:
 - Lung
 - Kidney
 - Heart
 - Eye
 - Skin



 **mozobil**
(plerixafor injection)

Mozobil (plerixafor or AMD3100)* is only approved drug targeting CXCR4

- ▶ Indicated for stem cell mobilization (is also anti-fibrotic)
- ▶ Indicated for single use only (toxicity prevents chronic use)

**AD-214 is a first in class
anti-fibrotic**

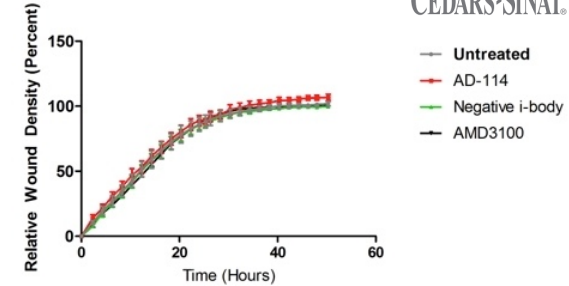
AD-114* specifically reduced migration/invasion with IPF lung fibroblasts *in vitro*



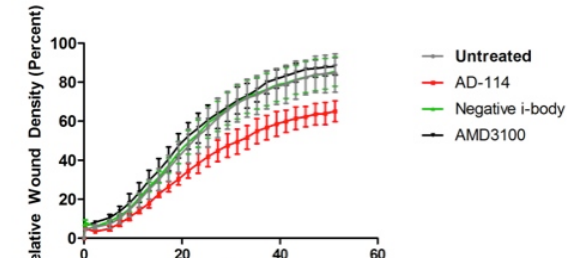
AD-114

- Specifically inhibited migration of fibroblasts from slow and rapidly progressing IPF patients but did not affect fibroblasts from normal subjects
- Has greater *in vitro* efficacy in this assay than approved therapies Nintedanib and Pirfenidone
- Also reduced soluble collagen 1 deposition

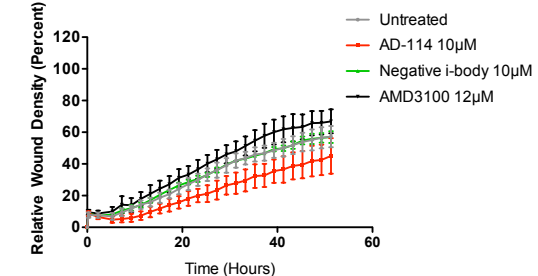
Normal fibroblasts



Slow/stable IPF progressor fibroblasts



Rapid IPF progressor fibroblasts

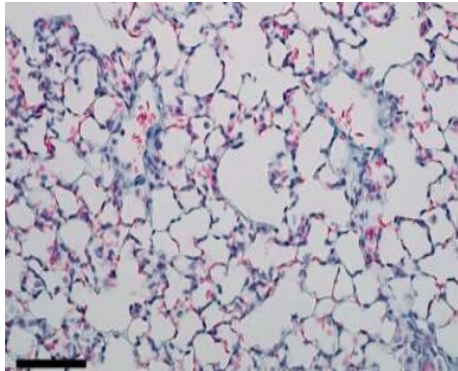


	MIGRATION	No effect on normal fibroblasts	Inhibits IPF fibroblast migration
i-body AD-114		✓	✓
Nintedanib (Boehringer)		✗	✓
Pirfenidone (Roche)		✓	✗
Other CXCR4 drug (Sanofi)		✓	✗

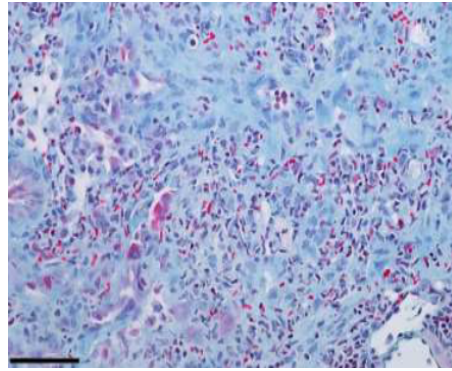
AD-114* *in vivo* activity in Bleomycin-induced mouse model of lung fibrosis

Prophylaxis setting

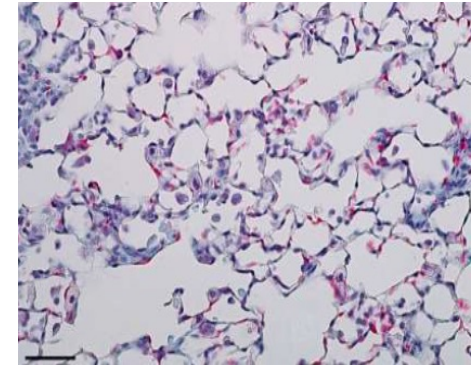
AD-114 has demonstrated in vivo activity (reduced collagen content, reduced inflammatory cell infiltration, improved tissue architecture) in a bleomycin-induced mouse model of lung fibrosis



**Normal mouse
lung tissue**



**IPF mouse lung tissue
(21 days after bleomycin)**



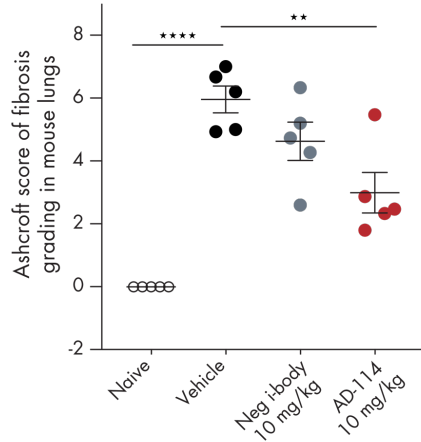
**IPF mouse lung tissue +
AdAlta anti-CXCR4 i-body
AD-114 dosed for 21 days**

Blue staining represents collagen, a hallmark of fibrosis

AD-114* prevents fibrosis in 21-day bleomycin-induced mouse lung fibrosis model

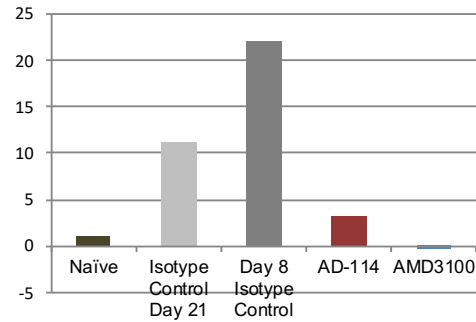
Prophylactic setting

Ashcroft score

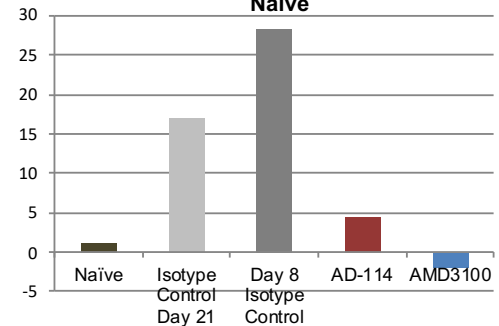


Fibrotic gene expression

Col1A1 Fold Change as Compared To Naïve



Col3A1 Fold Change as Compared To Naïve



Protocol



From single domain antibody to AD-214

When combined, the i-body and Fc fragment create a superior drug, which will be better for patients and for potential commercial partners

Monoclonal Antibody



AD-114

Binds to CXCR4 on the cell surface and has anti-fibrotic activity

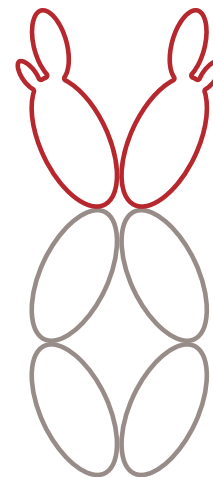
Proof of concept molecule: used PASylation for half-life extension



Fc Fragment

Binds to cells expressing the Fc receptor (FcRn) to extend the half life

AD-214



i-body binds to CXCR4 to have anti-fibrotic activity

Fc fragment binds to extend half life

Therapeutic candidate: Fc fusion for half-life extension, manufacturability

AD-214 safe in 4-week toxicology study

RECENT DATA

- ▶ 3 non-human primate studies completed
- ▶ Most recent: a Good Laboratory Practice (GLP) study to evaluate safety and toxicology prior to initial human studies
 - 10mg/kg, 30mg/kg and 100mg/kg multiple doses over four weeks plus recovery (human equivalent dose 32mg/kg)
 - AD-214 well tolerated with no deaths, no AD-214-related clinical signs, no changes in a panel of clinical observations, and only slight transient and completely reversible haematology changes

Tox study results were in line with expectations and in keeping with previous studies

Additional pre-clinical disease model study to be completed to inform clinical dosing

AD-214 radio-labelled PET tracer to enhance clinical development

Challenge

- No good biomarker for CXCR4 blocking in patients
- Difficult to confirm AD-214 binds to CXCR4 in fibrotic tissue

Solution

- Radio-label AD-214 so it can be detected by PET imaging

Benefits

- Confirm binding of AD-214 to CXCR4 in patients
- Determine duration of binding
- Determine AD-214 tissue distribution
- Visualise severity of fibrosis
- Enable Phase I studies to include patients

Funding

- AdAlta awarded up to A\$1m from MRFF Biomedical Translation Bridge Program to cover up to 50% of development and clinical testing costs



Biomedical
TRANSLATION BRIDGE
PROGRAM

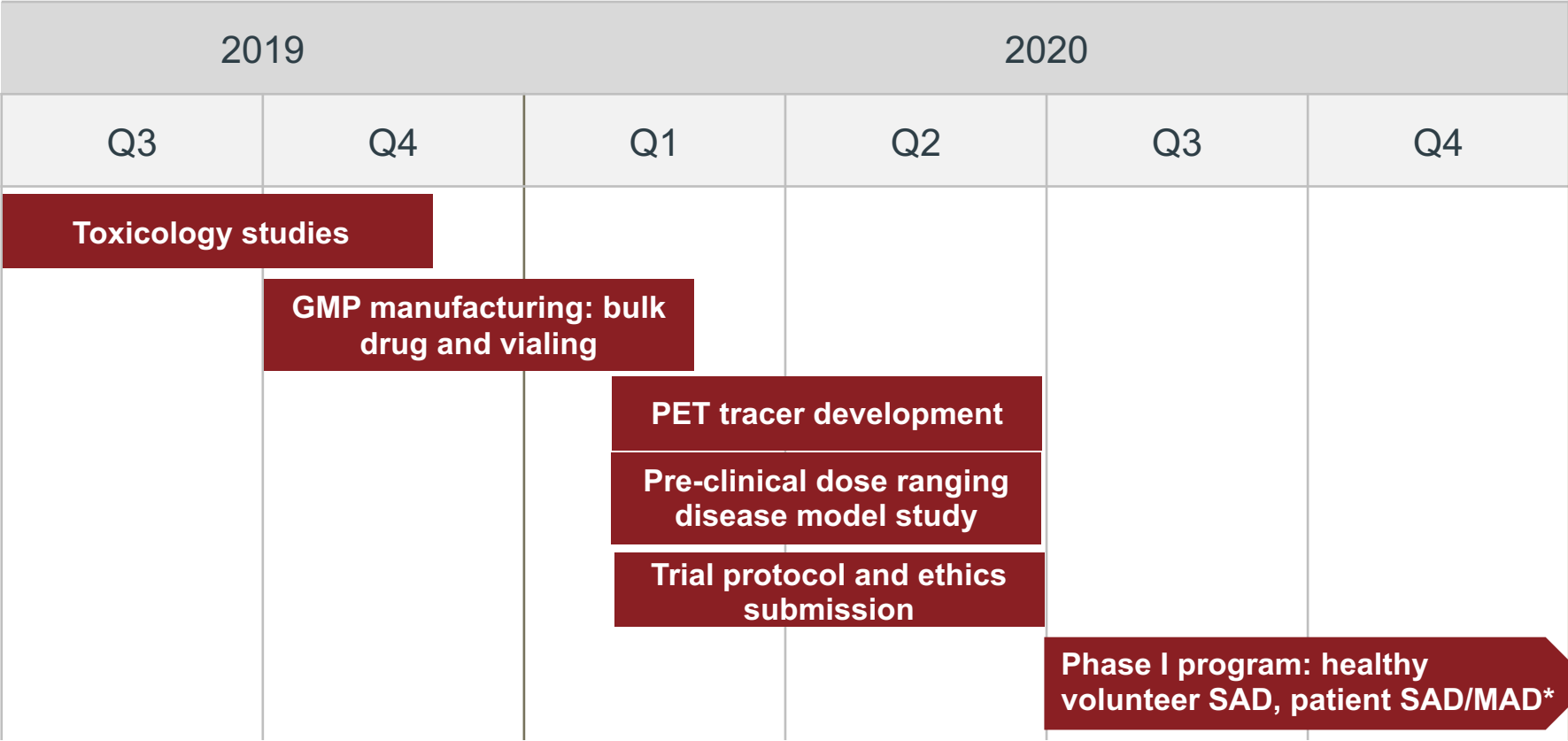
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MTPConnect
MedTech and Pharma Growth Centre

In partnership with



AD-214 development: key milestones

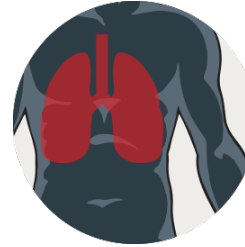


AD-214 has broad application in treating fibrosis

AdAlta data suggests that AD-214 can improve fibrosis across a range of fibrotic diseases

- ▶ **LUNG:** Idiopathic Pulmonary Fibrosis
- ▶ **KIDNEY:** Chronic kidney disease
- ▶ **EYE:** Wet-Age Related Macular Degeneration
- ▶ **LIVER:** NASH
- ▶ **SKIN:** Hypertrophic scar

AdAlta has demonstrated broad anti-fibrotic and anti-inflammatory effects in several animal models of disease and with human tissues with its lead i-body candidate.



Lung
IPF



Eye
Wet-AMD & PVR



Liver
NASH & CIRRHOSIS



Kidney
RENAL FIBROSIS



Skin
SCLERODERMA



GE Healthcare licensing deal: i-body platform

Overview:

- ▶ Agreement with global medical technology and diagnostics firm, GE Healthcare
- ▶ AdAlta will screen its novel i-body library on a number of targets in order to identify i-bodies that GE can use as imaging agents, starting with Granzyme B

Summary of commercial terms:

- ▶ Upfront payment of GBP100,000 and initial research fee received following target selection
- ▶ GE Healthcare will pay AdAlta research fees on staged basis
- ▶ Further milestone payments and royalties expected if development successful

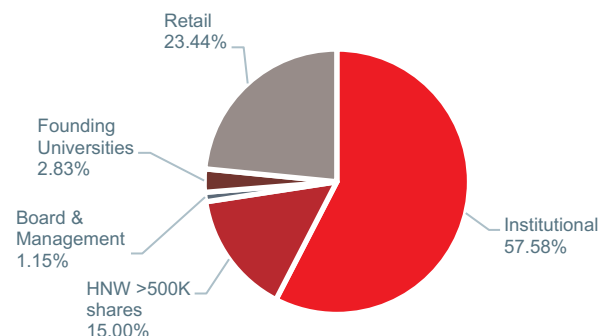
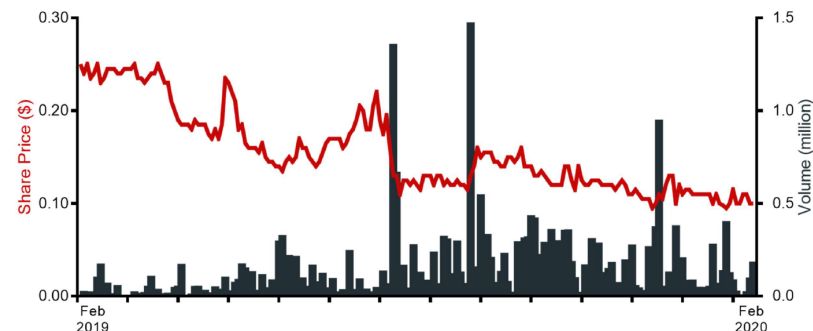
AdAlta aims to develop a range of therapeutic and diagnostic partnerships

Financial position

Key financial details	
ASX code	1AD
Share price (3 February 2020)	AUD\$0.10
Market capitalisation	AUD\$16.39m
Ordinary Shares	163,945,613
Listed Options	23,348,803
Unlisted Options	7,514,067
Current cash (31 December 2019)	AUD\$5.03m
Trading range (last 12 months)	AUD\$0.085 to \$0.27
Average daily volume	103,880

Major shareholders	%
Yuuwa Capital LP	32.97
Platinum Asset Management	8.66
Brispot Nominees Pty Ltd	4.79
CS Fourth Nominees Pty Ltd	3.08
Meurs Holdings Pty Ltd	3.05
Other shareholders	47.45
Total	100%

Share price performance (last 12 months)



Financial results: funded into Phase I

AUD million

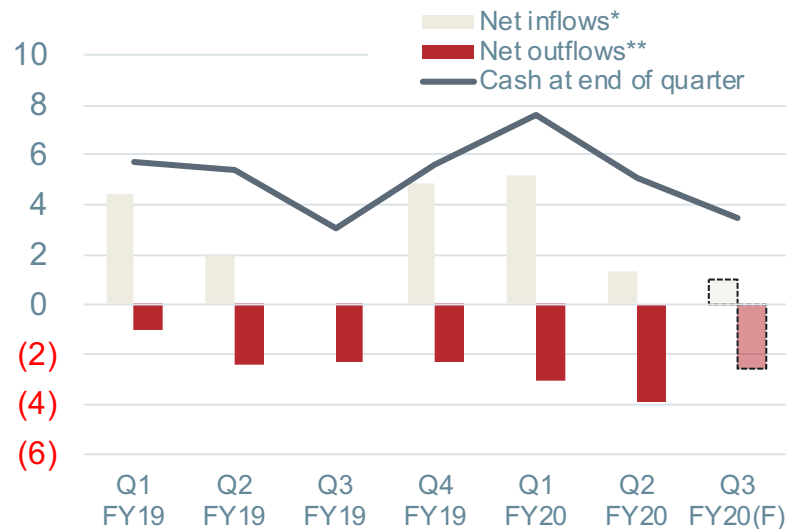
Financial year cash flows

Cash	FY18 (AUD million)	FY19 (AUD million)	FY20 H1 (AUD million)
Operating inflows	1.86	2.11	3.88
Operating/investing outflows	(5.79)	(8.10)	(7.00)
Financing cash flows	0.01	9.24	2.59
Starting cash	6.22	2.31	5.56
Ending cash	2.31	5.56	5.03

Key drivers

- Capital raising Q1FY19 (\$4.3m) and mid-2019 (\$7.0m)
- R&D Tax refund Q2FY19 (\$2.0m) and Q1FY20 (\$3.5m)
- Platform partnering revenues and R&D Tax loan facility H1 FY20
- Key drivers of outflows: GMP manufacturing, NHP toxicology study; clinical trial costs are lower burn rate

Quarterly cash flows



Outlook

- **Cash balance plus cash management strategies fund the Company to complete healthy volunteer Phase 1 clinical studies**

Market benchmarks

Breaking: Jan-20 Boehringer Ingelheim and Enleofen ink \$1 Billion+ fibrosis deal

Fibrosis lead AD-214



Sep-15 acquired by Roche
\$105m + \$475m milestones
phase I



Jul-19 license by Boehringer
Ingelheim €45m + €1.1b
phase I



**Nov-19 acquired by Roche
\$390m + \$1b – Phase II**

Aug-15 BMS option to buy
\$150m + \$1.25b milestones

Micro-antibodies



April-16 license by Abbvie
\$40m upfront + \$645m
milestones & royalties



Feb-18 collaboration with
Seattle Genetics (3 targets)
\$30m upfront + \$1.2b
milestones & royalties



Feb-18 acquired by Sanofi
€3.9b

GPCRs



Feb-15 acquired by Sosei
\$400m Phase Ib asset + 7 pre-
clinical leads



Jul-15 acquired by Celgene
\$7.8b Ph III, Ph II and GPCR
platform



April-16 license with
Boehringer
€8m + €125m milestones
PhI GPCR nanobody

Significant 2019 achievements

AD-214

- ✓ Successfully completed AD-214 cell-line and manufacturing process development; completed manufacturing of clinical AD-214 bulk drug substance
- ✓ Completed Phase I-enabling non-human primate toxicity (safety) studies (pharmacology data pending)

i-body platform partnerships

- ✓ Entered partnership with GE Healthcare to develop pre-clinical targets for diagnostic imaging – received first ever partnering revenue

Pipeline research

- ✓ Key data published in *mABs* peer reviewed scientific journal, i-body half-life customisation
- ✓ Entered partnership with Excellerate Biosciences to accelerate characterization of GPCR binders

Organisation

- ✓ Board skills expanded with appointment of Dr Ros Wilson
- ✓ Appointment of new CEO & Managing Director, Dr Tim Oldham

FY20 news flow

► H2 2019

- ✓ Partnership announcement – GE partnership September 2019
- ✓ Publication of key i-body data in well recognised, peer reviewed scientific journal, mAbs
- ✓ 4-week NHP toxicology study – completed October 2019 (plus GMP production of AD214 bulk for Phase I study)
- ✓ Cash runway extension strategies – *Radium RDTI loan facility, BTB Grant Dec 2019*

► H1 2020

- ✓ Patent granted covering AD-214 granted in the US
- Publication of further key i-body/fibrosis data – *estimated February 2020*
- Additional pre-clinical PK/PD results for AD-214
- AdAlta strategy update (AD-214 clinical development and i-body platform growth)
- Ethics committee approval for Phase I human clinical studies
- **Phase I human clinical studies with AD-214 commence mid-year**

Management focused on milestone delivery



Tim Oldham, PhD
CEO & Managing Director

Appointed October 2019, Tim brings >20 years of life sciences business development, alliance management, portfolio and product development, and commercialisation experience in Europe, Asia and Australia, with a particular focus on biologics, cell and gene therapies and pharmaceutical products. He has significant ASX listed company experience, is currently a Non-executive Director at Acrux Ltd (ASX:ACR) and serves as Director of BioMelbourne Network Inc.



Mick Foley, PhD
Chief Scientific Officer

Founding scientist of AdAlta and a key inventor of lead i-body candidate, AD-214. Recognized expert in phage display. NIH, NHMRC, ARC, Gates funding and over 70 scientific publications.



Dallas Hartman, PhD
Chief Operating Officer

Prior to joining AdAlta, Dallas was Vice President of Product Development at the NASDAQ listed biotechnology company Nexvet. Undertook postdoctoral research at the University of Texas Southwestern and the University of Melbourne where his work was supported by fellowships from the Howard Hughes Medical Institute. Over 14 years experience at CSL with analytical focus on biologics.

International Board, Scientific Advisory Board

Extensive track record of drug, antibody development, capital raising and exits

Board



Dr Paul MacLeman
Chair



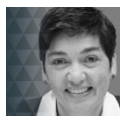
Liddy McCall
Director



Dr Robert Peach
Independent Director



Dr James Williams
Director



Dr Ros Wilson MBBS
Independent Director



Scientific Advisory Board



Dr Mick Foley
AdAlta CSO
Expert in phage display



Brian Richardson
Drug discovery and
development expert



Steve Felstead
Clinical development



John Westwick
Pulmonary drug discovery
and development



AdAlta Limited (ASX:1AD) Summary

- ▶ **i-body platform technology for multiple products against “difficult” targets**
- ▶ **First in class lead internal program AD-214 to commence Phase I clinical trial mid-2020**
 - Has significant pre-clinical validation demonstrating broad anti-fibrotic and anti-inflammatory effects as well as safety in multiple fibrotic diseases
 - Initial focus on treating Idiopathic Pulmonary Fibrosis (IPF): orphan drug designation obtained; market history of early commercialisation transactions in fibrosis
 - Key manufacturing and toxicology milestones achieved
- ▶ **Partnering providing additional opportunities to expand pipeline**
 - Recent licensing deal with global medical technology firm, GE Healthcare, to develop i-bodies for diagnostic imaging: first licensing revenue received
- ▶ **Experienced leadership driving strategic focus on pipeline expansion (internal and partnered)**
- ▶ **Cash balance and cash management strategies sufficient to fund healthy volunteer Phase 1 clinical studies for AD-214**



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