3 June 2021

ASX Announcement

ADALTA PRESENTS AT SHARE CAFÉ HIDDEN GEMS AND BIO DIGITAL

MELBOURNE Australia, 3 June 2021: AdAlta Limited (ASX:1AD), the clinical stage biotechnology company developing novel therapeutic products from its i-body platform, is pleased to provide investors with a copy of its latest investor presentation, highlights from which are to be presented by CEO, Dr Tim Oldham at the upcoming Share Café Hidden Gems investor webinar and BIO Digital conference.

The Share Café Hidden Gems investor webinar will be held **tomorrow, Friday 4 June from 12:30pm AEST / 9:30am AWST** and is able to be viewed live via Zoom. To access further details of the event and to register (at no charge), please copy and paste the following link into your internet browser: https://us02web.zoom.us/webinar/register/5416151767246/WN_J9qXooSqQLW1evtXHQtTmg

The BIO Digital conference, one of the largest annual industry partnering conferences, will be held virtually on **10-11 and 14-18 June, 2021**. To access further details of the event, please copy and paste the following link into your internet browser: https://www.bio.org/events/bio-digital.The video of Dr Oldham's presentation will be made available on AdAlta's website.

AdAlta is pleased to be able to provide investors and shareholders these additional forums to learn about the Company's progress.

Authorised for lodgement by:

Tim Oldham
CEO and Managing Director
June 2021

Notes to Editors

About AdAlta

AdAlta Limited is a clinical stage drug development company headquartered in Melbourne, Australia. The Company is using its proprietary i-body technology platform to solve challenging drug targeting problems and generate a promising new class of single domain antibody protein therapeutics with the potential to treat some of today's most challenging medical conditions.

AdAlta is conducting Phase 1 clinical studies for its lead i-body candidate, AD-214. AD-214 is being developed for the treatment of Idiopathic Pulmonary Fibrosis (IPF) and other human fibrotic diseases, for which current therapies are sub-optimal and there is a high unmet medical need.

The Company is also entering collaborative partnerships to advance the development of its i-body platform. It has an agreement with GE Healthcare to discover i-bodies as

diagnostic imaging agents against Granzyme B, a biomarker of response to immuno-oncology drugs.

AdAlta's strategy is to maximise the products developed using its next generation i-body platform by internally discovering and developing selected i-body enabled product candidates against GPCRs implicated in fibrosis, inflammation and cancer and partnering with other biopharmaceutical companies to develop product candidates against other classes of receptor, in other indications, and in other product formats.

Further information can be found at: https://adalta.com.au

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AdAlta
next generation protein therapeutics

Corporate overview

June 2021

Disclaimer

Investment in AdAlta is subject to investment risk, including possible loss of income and capital invested. AdAlta does not guarantee any particular rate of return or performance, nor do they guarantee the repayment of capital.

This presentation is not an offer or invitation for subscription or purchase of or a recommendation of securities. It does not take into account the investment objectives, financial situation and particular needs of the investor. Before making any investment in AdAlta, the investor or prospective investor should consider whether such an investment is appropriate to their particular investment needs, objectives and financial circumstances and consult an investment advisor if necessary.

This presentation may contain forward-looking statements regarding the potential of the Company's projects and interests and the development and therapeutic potential of the company's research and development. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercialising drugs that are safe and effective for use as human therapeutics and the financing of such activities.

There is no guarantee that the Company's research and development projects and interests (where applicable) will receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this presentation. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning research and development programs referred to in this presentation.

AdAlta's purpose

To use our unique i-body technology to create multiple novel therapeutics for debilitating diseases that have proven difficult to drug with traditional antibodies

Idiopathic Pulmonary Fibrosis (IPF)

AdAlta's first target, already a $3b market, is a degenerative, fatal disease in dire need of improved treatment options



In IPF, scarring and stiffening of the lungs **progressively and irreversibly reduces lung function**

Despite being poorly tolerated and having difficult side effects, the two current therapies sell

$3b per year

3.8 years
median survival after diagnosis

>300,000
people living with IPF,
It is irreversible

40,000
people die from IPF every year

Burden of fibrotic lung disease following COVID-19 likely to be high.*

"Long COVID" is a developing issue – potentially further increasing the need for better anti-fibrotic drugs.

* PM George, et al, "Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy", Lancet published online May 15, 2020.

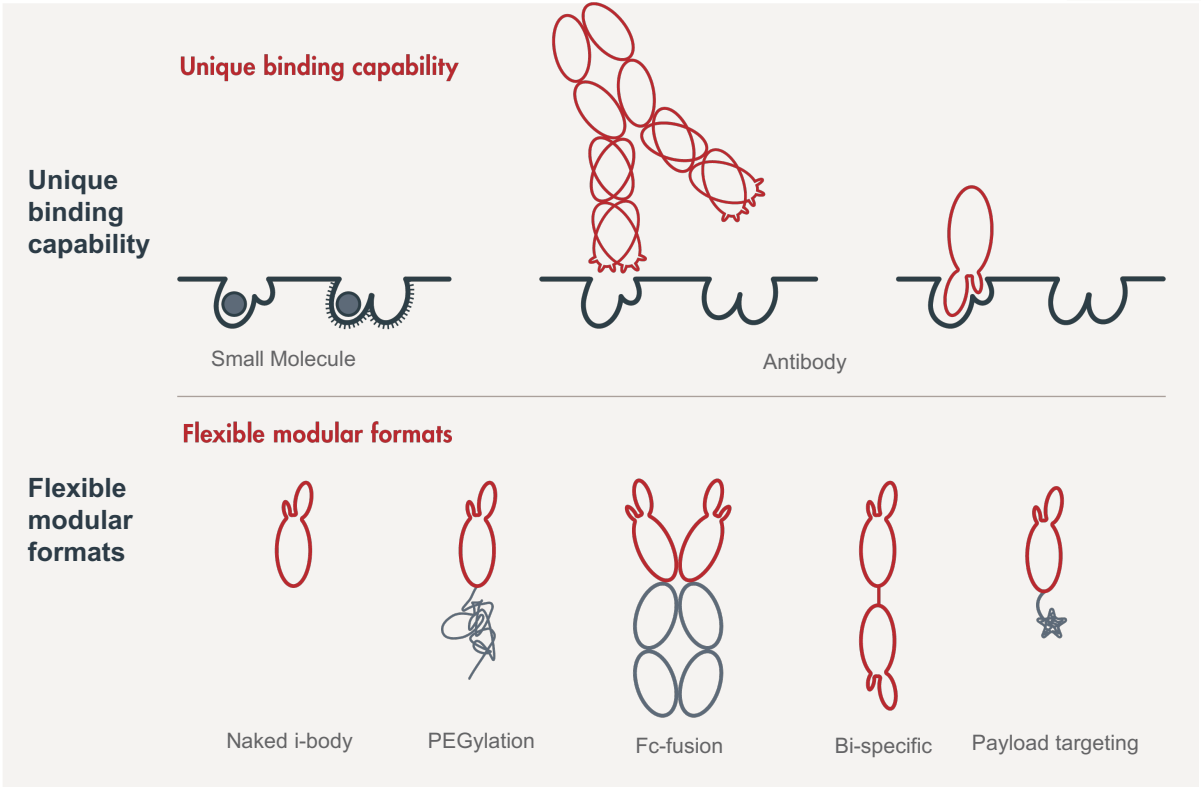
Why invest in AdAlta now?

Very near-term catalysts across two programs, multiple expansion opportunities

ASSETS TODAY	**i-body platform to create products** Enables creation of therapeutics for **multi-billion dollar markets** underserved by traditional antibodies	**Lead asset AD-214: unique, needed and valuable** Unique mode of action **Phase I:** single doses well tolerated **US$3b market for IPF** IPF assets earn high, early milestones	**Asset 2 GZMB: early revenue, fully funded** PET imaging agent to identify responders to immunotherapy **Pre-clinical** **Fully funded** by GE Healthcare: **A$1.4m revenue to date** **US$6.4b PET imaging market**
NEAR TERM CATALYSTS	**Clear vision for growth** Poised to expand pipeline: 2 products today 5 by end 2021 ~10 by end 2023	**AD-214: grow and de-risk** Further Phase I data Further pre-clinical data supporting AD-214 use in multiple indications First partnering window in Q4 CY21	**Other assets: progress, diversify** GZMB asset progress to pre-clinical development Second co-development collaboration mid-2021 Two further internal programs in 2021

What is the i-body advantage?

All the selectivity and specificity of antibodies with greater versatility and tunability



Minimising off-target side effects

Unique binding capability potentially allows greater selectivity and specificity, tunable affinity

Multiple drug administration routes

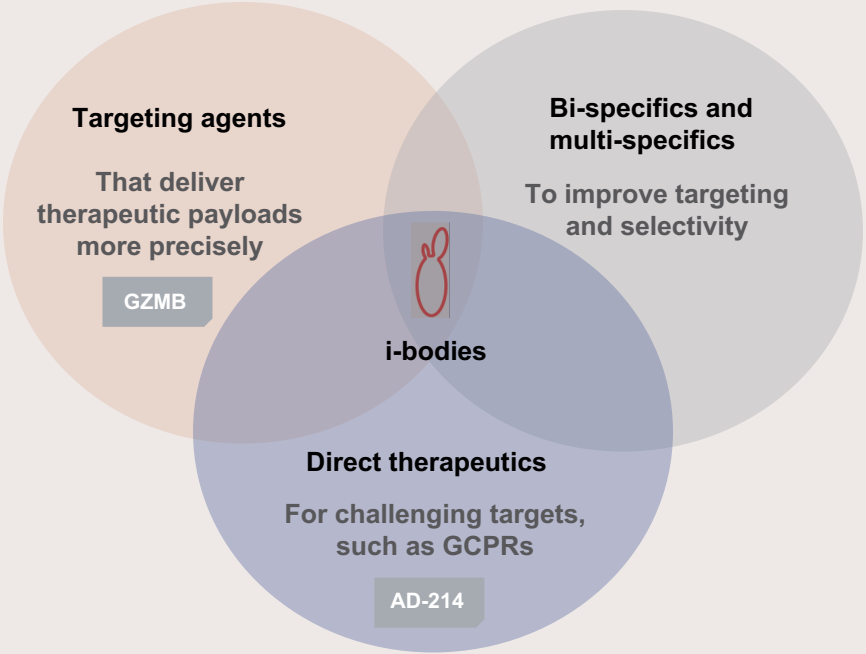
Amenable to multiple administration routes (e.g. injection, inhalation and topical)

Robust

Resilient to pH and temperature cycling

Diverse applications of i-bodies

i-body technology can enable a wide range of applications



AD-214: first in class treatment for fibrosis

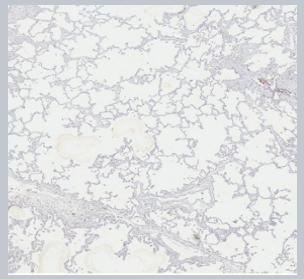
AD-214's initial focus is the US$3b IPF market

First-in-class (novel mode of action) treatment for fibrotic diseases, which can affect almost every organ

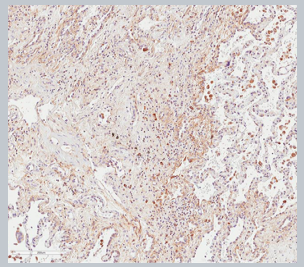
Targets a receptor called **CXCR4: a critical player in the development of fibrosis** in many organs and the progression of many cancers

Initial focus is **Idiopathic Pulmonary Fibrosis (IPF)**, one of a group of **Interstitial Lung Diseases (ILDs).** CXCR4 is highly expressed in IPF and other ILDs

Human Lung Tissue



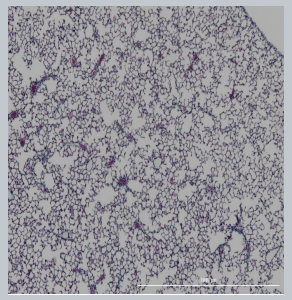
Normal



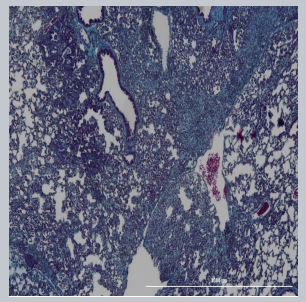
Diseased

Brown stain shows amount of CXCR4

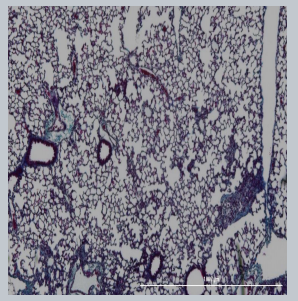
Mouse model of lung fibrosis



Normal mouse lung tissue



IPF mouse lung tissue (21 days after bleomycin [BLM])



IPF mouse lung tissue + AD-214 (21 days after BLM; AD-214 at 10mg/kg every 4 days from day 8)

Purple stain shows amount of collagen (fibrosis)

AD-214 Phase 1 clinical program

The Phase 1 program is evaluating safety and distribution of AD-214 in healthy volunteers and patients

Phase 1 protocol in healthy volunteers

Part A
(Completed)

Single dose, healthy volunteers (HV SAD)

42 patients in 7 cohorts

0.01-20 mg/kg dose

Part B
(Commenced Q2 2021)

Multiple ascending dose, healthy volunteers (HV MAD)

12 – 24 patients in 3 cohorts

5-15 mg/kg every 2 weeks

Objectives of Phase 1 Part A and B:

- Top-line safety data by end 2021
- Explore optimal dosing intervals
- Supports Phase II, FDA IND application in all CXCR4 indications

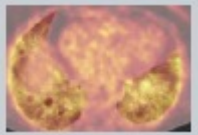
Phase 1b protocol in IPF and ILD (and other fibrotic disease) patients*

Arm 1

PET screening of fibrotic diseases

Open label with standard of care**

~12 patients (~6 IPF/ILD) + PET



Arm 2

Multi-dose in IPF/ILD

Open label with standard of care**

~6 patients, max 6 doses over 18 weeks +/- PET imaging

Objectives of Phase 1b:

- Safety in IPF/ILD in combination with standard of care**
- Effect of elevated lung CXCR4 on distribution and receptor engagement of AD-214 in IPF and ILD patients
- Explore change in CXCR4 expression over time as potential biomarker

* Supported by a Biomedical Translational Bridge grant from Medical Research Future Fund and MTPConnect.

** Includes pirfenidone, nintedanib or non-pharmacologic intervention.

AD-214 – Phase 1 trial: results to date

Single doses well tolerated, AD-214 clearly engages CXCR4 target for extended duration

Results from single dose studies (Part A)

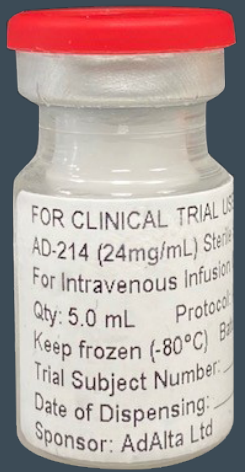
AD-214 has an excellent safety profile
- No dose limiting toxicities or adverse events of clinical concern
- No concerning clinical laboratory results
- No concerning immune responses or clinical symptoms
- Consistent with Non-Human Primate (NHP) toxicology studies

AD-214 engages the CXCR4 receptor
- Clear markers of target (CXCR4) engagement observed

Receptor occupancy sustained at high levels for extended periods
- Supportive of longer dosing interval than projected from NHP if replicated in patients



Lung
IPF/ILD



IPF late-stage clinical landscape: a narrow development field

AdAlta's novel mode of action expected to be attractive to partners as an alternative to, and in combination with other therapies

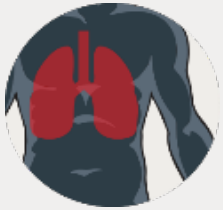
Company	Drug	Mode of action	Phase	Orphan Drug Designation
Roche	**PRM-151**	Endogenous human protein that directs the immune cells called macrophages to turn off and reverse fibrotic processes	Phase 3 (Mono or combination therapy)	YES
FibroGen	**Pamrevlumab**	Human monoclonal antibody (mAb) that inhibits the activity of connective tissue growth factor (CTGF) to inhibit myofibroblast activation, collagen deposition and other pro-fibrotic factors	Phase 3 (Monotherapy)	YES
United Therapeutics CORPORATION	**Inhaled Treprostinil**	Small molecule analogue of prostacyclin that reduces pulmonary artery pressure through direct vasodilation of the pulmonary and systemic arterial vascular beds	Phase 3 (Supportive care/ symptom reduction)	YES
AdAlta	***AD-214***	*i-body-Fc fusion protein blocking CXCR4 to inhibit inflammatory cell migration, epithelial to mesenchymal transition and fibrotic growth factor production, and deposition of collagen*	*Phase I*	*YES*

AD-214: multiple indication extension options

Each additional indication could address multiple markets with U$ billion potential

Data in tissue and animal models show that AD-214 can improve fibrosis across a range of fibrotic diseases and may improve cancer –
multiple indication extension potential

- **LUNG (lead indication):** Idiopathic Pulmonary Fibrosis with natural extension to Interstitial Lung Disease
- **EYE:** Wet-Age Related Macular Degeneration
- **CANCER**: 23 different cancers, enhancement of I/O drugs
- **KIDNEY**: Chronic kidney disease
- **LIVER:** NASH
- **SKIN**: Hypertrophic scars



Lung
IPF/ILD
>US$3b



Eye
Wet-AMD
>$15b



Cancer
23 different cancers, I/O
>$1b ea



Kidney
RENAL FIBROSIS
>US$10b



Liver
NASH & CIRRHOSIS



Skin
SCLERODERMA

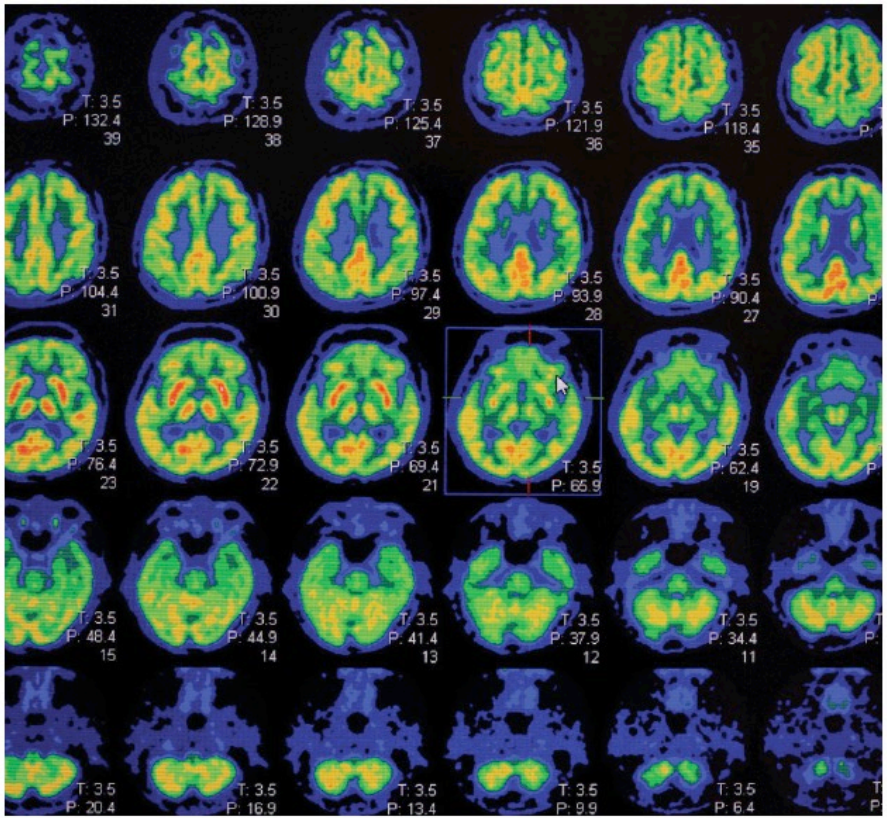
IPF partnering: valuable early options

IPF assets have recently yielded attractive deal terms at early stages of development

Feb-21: License by Graviton up to US$517.5m - Phase I	Jul-19 license by Boehringer Ingelheim €45m + €1.1b – Phase I
Nov-20: Galapagos collaboration + license €320m - Phase 2 ready	Nov-19 acquired by Roche $390m + $1b – Phase II Aug-15 BMS option to buy $150m + $1.25b milestones
Aug-20: License by AstraZeneca US$17m + US$360m – Preclinical	Jan-20 platform license by Boehringer Ingelheim upfront undisclosed + $1b milestones – Preclinical

Immuno-oncology (I/O) imaging

I/O drugs revolutionising cancer treatment, but only work in 20-40% of patients. PET imaging identifies them faster



Immuno-oncology (I/O) drugs **reactivate the patient's own immune system** to fight cancer

US$95 billion

I/O market[1]

PET imaging biomarkers of an activated immune system can help identify responders early: **reduces cost, improves choice of therapy, accelerates drug development**

Only **20-40%** of patients respond to I/O drugs[2]

PET imaging agents have

substantially

shorter development time than therapeutics

US$6.4 billion

PET imaging agent market[3] (largest products >US$400m[4])

1. 2026 forecast by ResearchandMarkets.com, Immuno-Oncology - Market Analysis, Trends, Opportunities and Unmet Needs - Thematic Research, March 2021
2. P Sharma, et al, Cell 168(4) 707 (2017)
3. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021
4. AD Nunn, J Nucl Med (2007) 169

GZMB i-body asset: GE Healthcare co-development collaboration

Second asset poised to enter pre-clinical development; and could generate royalty revenue sooner than a therapeutic

AdAlta and GE Healthcare are co-developing a PET imaging agent against granzyme B (GZMB)

AdAlta GE Healthcare

Granzyme B can be used as a **biomarker to show whether cancer immunotherapies,** such as checkpoint inhibitors, **are working effectively**

This would significantly improve therapy selection/patient outcomes and reduce cost

GE Healthcare funded discovery at AdAlta, and will now progress GZMB i-bodies through pre-clinical and clinical development and commercialisation

Total development time substantially shorter than therapeutics

May 2021 status

- Panel of GZMB i-bodies identified, now progressing to pre-clinical development
- A$1.4 million revenue earned to date (milestones and research fees). AdAlta will generate additional research fees assisting with pre-clinical and manufacturing development
- Further milestones and royalties to be earned on development and commercialisation success: pipeline asset added at no financial cost to AdAlta

Business model

Two key commercialisation pathways for platform

GE Healthcare

External assets

Collaborations with pharma and biotech to further leverage the i-body platform
GE Healthcare deal: Granzyme B

One new collaboration forecast in 2021

AdAlta
next generation protein therapeutics

Internal assets

In-house pipeline of drug candidates:
license to pharma for major upfronts, milestones and royalties
Lead candidate: AD-214

Two more targets to be added in 2021

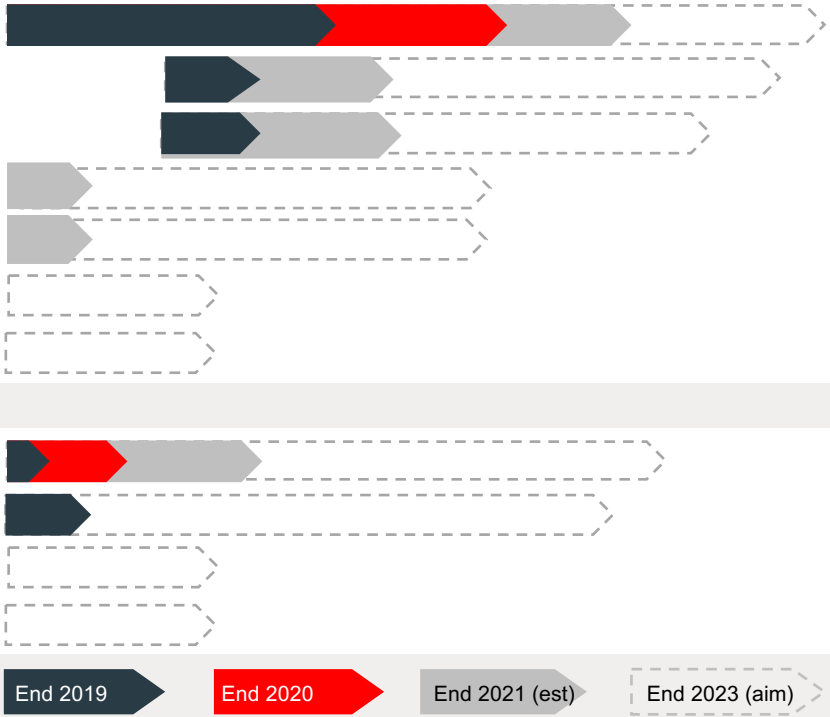


Platform

Patented, diverse i-body discovery platform:
20 billion different i-bodies for drugging undruggable targets.

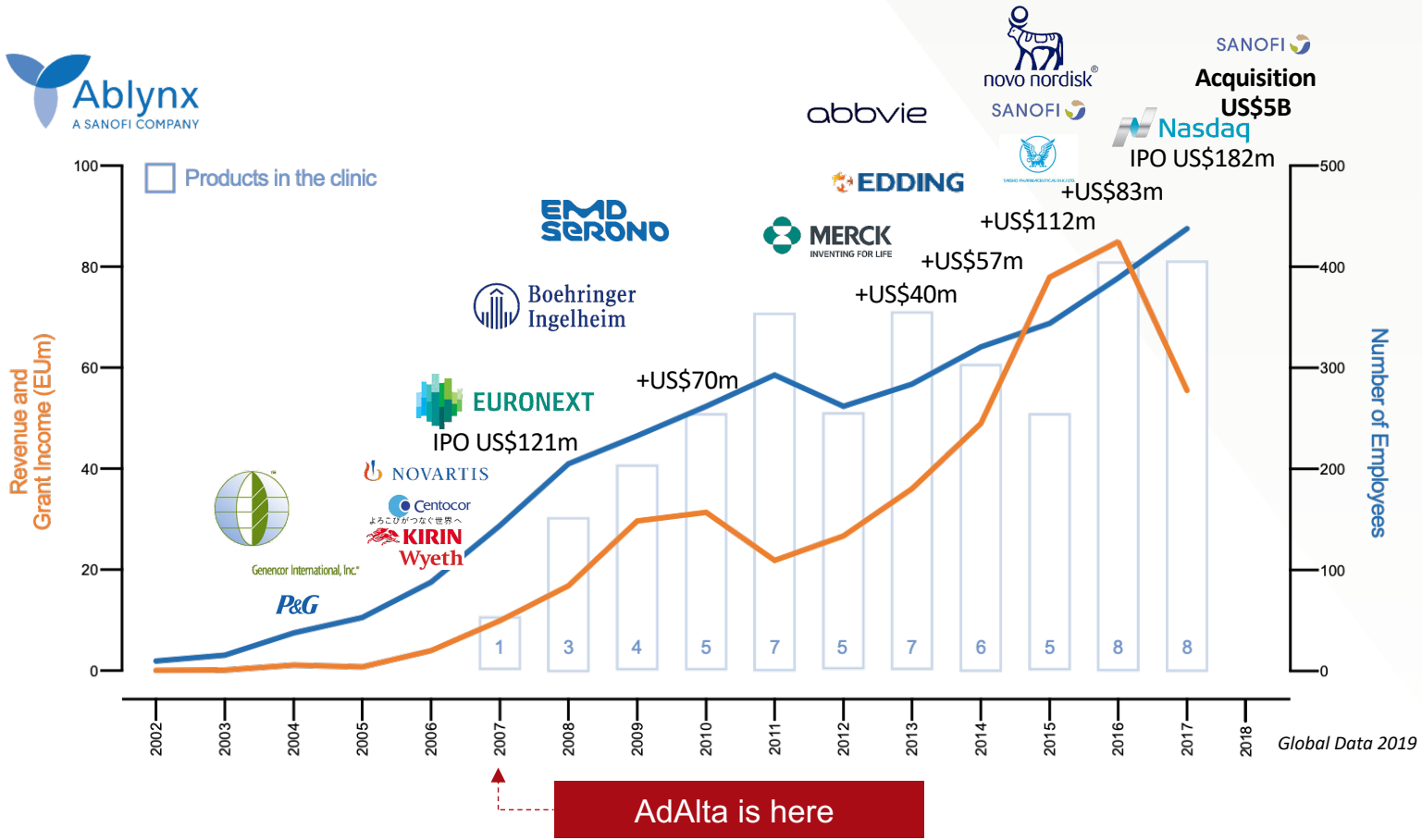
An expanding pipeline of i-body enabled products

	TARGET	PARTNER	PRODUCT/ INDICATION	DISCOVERY	PRECLINICAL, PRODUCT DEV	IND ENABLING STUDIES	PHASE I	PHASE II
INTERNAL PIPELINE	CXCR4	AdAlta	**AD-214:** Idiopathic Pulmonary Fibrosis					
			AD-214: Indication 2					
			AD-214: Indication 3					
	Target 2	AdAlta	Not disclosed					
	Target 3	AdAlta	Not disclosed					
	Target 4	AdAlta	*TBC*					
	Target 5	AdAlta	*TBC*					
EXTERNAL PIPELINE	GZMB	GE Healthcare	PET imaging I/O					
	TBC	Partner #2						
	TBC	Partner #3						
	TBC	Partner #4						



The potential of our strategy: Ablynx case study

Multiple internal and external assets drive value, attract partners



Corporate landscape: leveraging platforms

Creating multiple internal and partnered assets drives value creation for platform companies

AdAlta value

=

AD-214 value

+

External partnerships

+

Platform value

Micro-antibody platforms	GPCR platforms
argenx April-16 license by Abbvie $40m upfront + $645m milestones & royalties	HEPTARES therapeutics Feb-15 acquired by Sosei $400m Phase Ib asset + 7 pre-clinical leads
pieris Feb-18 collaboration with Seattle Genetics (3 targets) $30m upfront + $1.2b milestones & royalties	receptos Jul-15 acquired by Celgene $7.8b Ph III, Ph II and GPCR platform
Ablynx A SANOFI COMPANY Feb-18 acquired by Sanofi €3.9b	Ablynx A SANOFI COMPANY April-16 license with Boehringer €8m + €125m milestones Phase I GPCR nanobody

Milestones for remainder of 2021

News-flow rich period for remainder of CY2021

	AD-214	Other Assets
H1 2021	✓ Orphan Drug Designation for AD-214 in IP ✓ Results of Phase I single dose studies in healthy volunteers ✓ Phase I multi-dose studies in healthy volunteers commence • PET tracer pre-clinical development results	✓ Progression of the GEHC collaboration from discovery to pre-clinical development • Entering a second collaboration agreement
H2 2021	• Phase 1b commences: First studies in IPF patients, generating safety data in patients and in combination with standard of care. • First PET images to visualise distribution of AD-214 in the lungs of IPF patients • 1st partnering window opens • Top line results of multi-dose studies in healthy volunteers • Additional indications pre-clinical data	• Commencing development of two new i-body enabled internal pipeline assets • New i-body 2.0 IP filed

Industry experienced leadership and advisors

Team with experience from discovery through manufacturing, clinical and commercialisation

Board



Dr Paul MacLeman
Chair



Liddy McCall
(alt: Dr James Williams) Director



Tim Oldham, PhD
CEO & Managing Director



Dr Robert Peach
Independent Director



Dr David Fuller
Independent Director

Executive



Tim Oldham, PhD
CEO & Managing Director



Mick Foley, PhD
Chief Scientific Officer



Dallas Hartman, PhD
Chief Operating Officer



Claudia Gregorio-King, PhD *VP Clinical Product Development*



Michael Rasmussen
Consultant Medical Expert

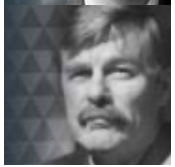
Scientific Advisory Board



Brian Richardson
Drug discovery and development expert



Steve Felstead
Clinical development



John Westwick
Pulmonary drug discovery and development

Corporate snapshot

Key financial details (21 May)

ASX code 1AD	1AD
Market capitalisation	**A$31.87m**
Share price (12 month range)	A$0.135 ($0.069 - 0.265)
Ordinary Shares (daily volume)	245,175,853 (629,809)
Listed Options	23,348,803
Unlisted Options	7,514,067
Cash (31 Mar 2021)	**A$6.05m**

Major shareholders (19 Apr) %

Yuuwa Capital LP	22.0
Platinum Asset Management	11.6
Meurs Holdings Pty Ltd	7.3
Radiata Super Pty Ltd	2.4
Sacavic Pty Ltd	1.8
Other (1,399 total holders)	*54.9*
Total	**100%**

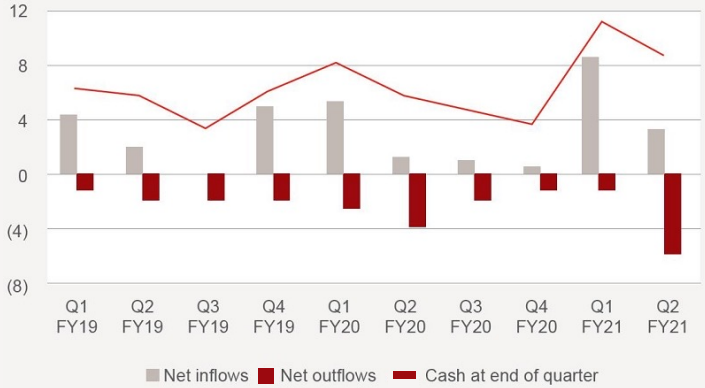
Analyst Coverage

Edison
Pitt Street Research
Securities Vault
BioShares

Share price performance (last 12 months)



Quarterly cash flows (A$ million)



Investment proposition



Platform to create value

Patented, validated i-body platform for asset creation: designed for “difficult” targets



Lead asset has multiple indications

AD-214: first-in-class asset for multiple fibrotic indications and cancer

>$3b market potential in first indication



GZMB asset: GEHC partnership

Solving the challenge of identifying I/O drug responders

PET imaging agent market worth US$6.4b



Clear vision for growth

Build on existing clinical and commercial validation of platform to add internal programs, expand collaborations



Leading expertise

Experienced drug development team in place



Several near-term growth catalysts

AdAlta substantially undervalued relative to peers, with near term and mid-term value drivers.

AdAlta
next generation protein therapeutics

Contact:

Tim Oldham, CEO and Managing Director
enquiries@adalta.com.au
www.adalta.com.au

AdAlta
next generation protein therapeutics

Appendix: Strategy

AdAlta has successfully transitioned to the expansion phase of our growth plan

A Maximise catalysts from current funded base (2020)

From…

- i-body platform in clinic for difficult drug targets
- Clinical and commercial validation: AD-214 Phase I trial and GE partnership

B Expand (~mid 2020 to late 2021)

Via…

- Laying the foundations for growth
- Progress AD-214
- Build internal and external pipeline
- Continuous platform improvement

C Accelerate (from ~mid-2021)

Towards 2023…

- Multi-product, multi-partner platform company
- AD-214 partnering, new indications
- ~5 internal GPCR programs
- 3-5 co-development partnerships

Our strategy

i-body technology platform and library
Proof of Principle against > 25 targets

A

In-house pipeline of drug candidates
Usually GPCRs in fibrosis, inflammation, oncology
Invest to value inflection (typically Phase I or II)

Licence to pharma
Major upfronts + milestones and royalties

B

Pharma, biotech partnerships
Partner-led target selection and development
Partner-enabled complex formats eg bivalent drugs

Co-develop with pharma, biotech
Research fees + milestones and royalties



Select novel, challenging drug targets where the i-body structure is most advantaged

Multiple i-body drugs and diagnostics
New drug class
Potential in multiple disease indications

GE Healthcare

AdAlta
next generation protein therapeutics

Appendix: AD-214

AD-214: road to the clinic

Validated target

- CXCR4
- Player in inflammatory, fibrotic processes
- Biomarker, prognostic indicator

Novel mode of action, IP

- Patented CXCR4 i-body antagonist
- CXCR4 expressed on diverse cell types
- Inhibition of fibrotic cell migration

GMP manufacturing

- Fc-fusion format
- CDMO: KBI Biopharma
- IND-ready CMC package

NHP GLP toxicology

- Very clean tox profile
- Half-life supports weekly dosing
- Sustained receptor occupancy

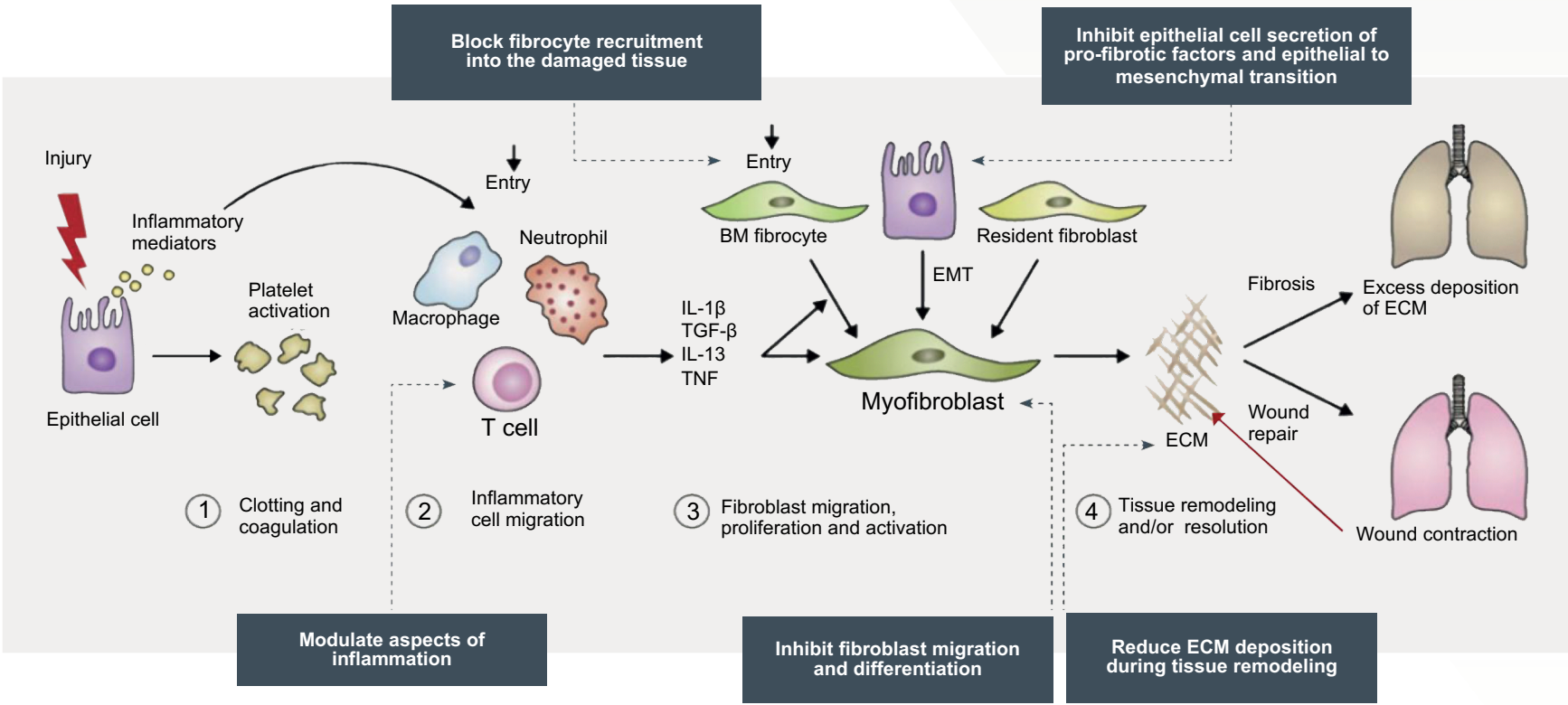
NHP GLP toxicology

- Bleomycin mouse model of IPF
- Ashcroft Score, gene expression, collagen
- Eye, kidney, liver cancer PoC

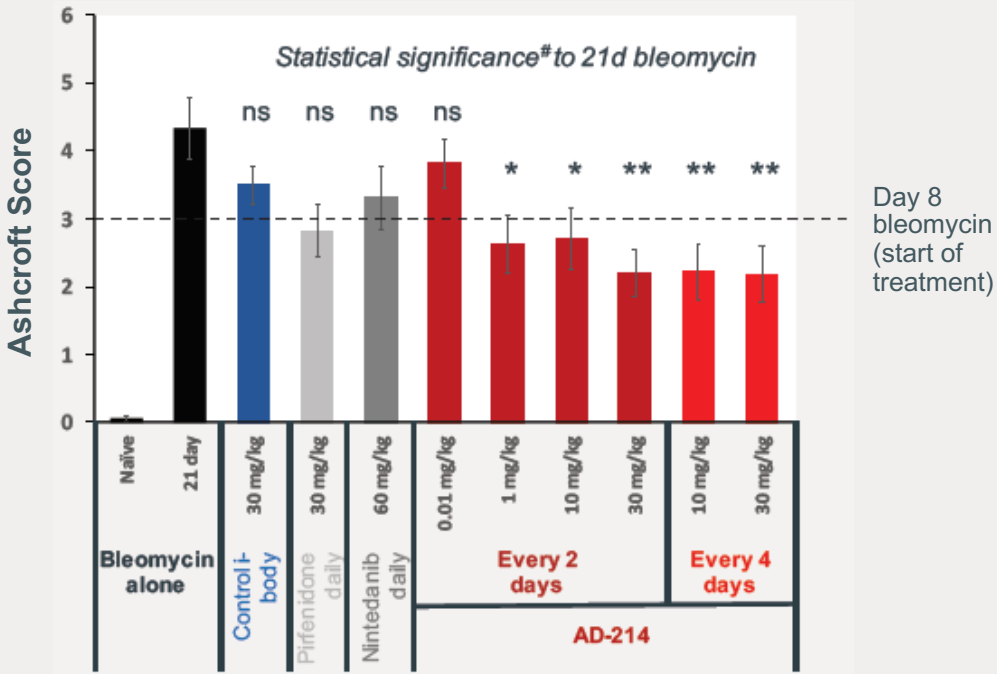
Pre-IND meeting

Panel of pre-clinical studies "generally sufficient" to support an Investigational New Drug application
The Phase I trial design is "reasonable"
Specific guidance readily incorporated into Phase I protocol and ongoing development plans

AD-214 inhibits key features of the fibrogenic pathway with novel MOA



AD-214 induced reduction in progression of fibrosis in mouse bleomycin model



AD-214 reduced Ashcroft Score with statistical significance compared to bleomycin treated mice at:

- 1-30mg/kg every second day
- 10-30mg/kg every fourth day

Wide range of dosing regimens can be used to test efficacy

- 10mg/kg every second day exhibited effectiveness by most study parameters
- Human equivalent dose: 1mg/kg (estimated)

AD-214 efficacy demonstrated in gold standard IPF disease model

Supportive of potential human therapeutic window beginning as low as 1mg/kg

NHP GLP toxicology: AD-214 safe

3 non-human primate studies completed
Good Laboratory Practice (GLP) study to evaluate safety and toxicology

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:

- body weight
- ophthalmoscopy
- blood pressure
- electrocardiography
- respiratory function
- neurological function
- coagulation
- urinalysis
- organ weight
- macroscopic and microscopic findings

Minor, transient, completely reversible increase in total white cell and circulating CD34+ cells

Small, transient, completely reversible decrease in serum total protein and albumin at highest dose only (100 mg/kg)

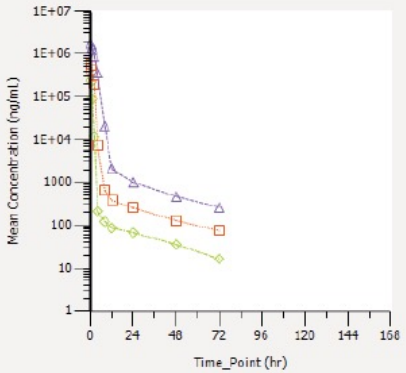
Tox study results were in line with expectations and in keeping with previous studies

No major organ toxicity has been observed on repeat dosing at high doses
No suggestion of off-target toxicities

Non-human primate GLP toxicology: Phase I dose justification

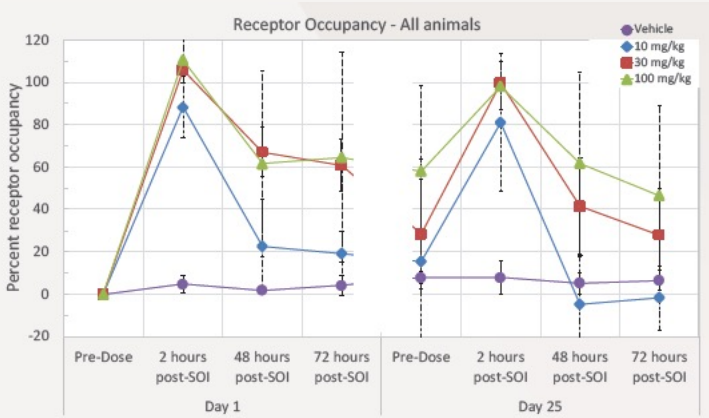
Pharmacokinetics

- Elimination half-life 22-29h
- Human equivalent: ~71h (estimate)
- AD-214vailable for >3 days



Pharmacodynamics

- >60% receptor occupancy* for 72h at >30mg/kg
- Human equivalent: ~10mg/kg (estimate)
- High receptor binding for >3 days

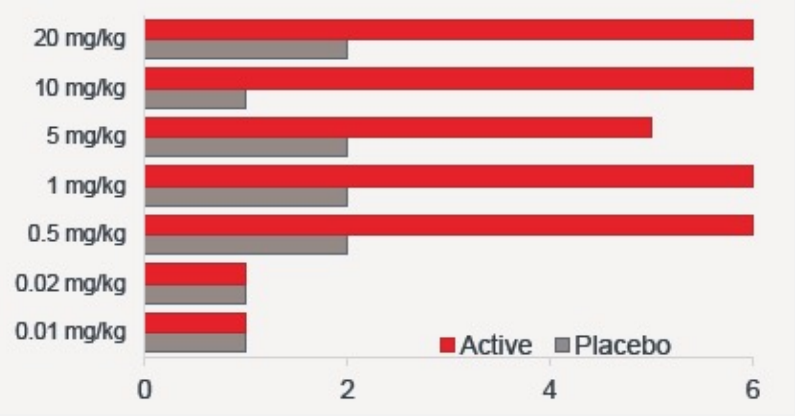


Supportive of human therapeutic dose window including 10mg/kg intravenously, weekly or every second week

AD-214 Phase I Part A design detail*

Protocol: A Phase I dose-escalating study of the safety, tolerability, PK and PD of single and repeat doses of AD-214 in healthy volunteers (HVs) and patients with interstitial lung disease (ILD)

Part A: Single ascending dose in healthy volunteers
Patient numbers by cohort
Total n=42 (31 active, 11 placebo, blinded)



CMAX CLINICAL RESEARCH
scientia CLINICAL RESEARCH
360biolabs
CNS Intelligent Development

Primary

- Safety, tolerability of AD-214
  - adverse events, physical examinations, vital signs, ECG
  - clinical laboratory tests (hematology, chemistry, coagulation, cytokines)

Secondary

- PK, RO of AD-214
- Immunogenicity of AD-214

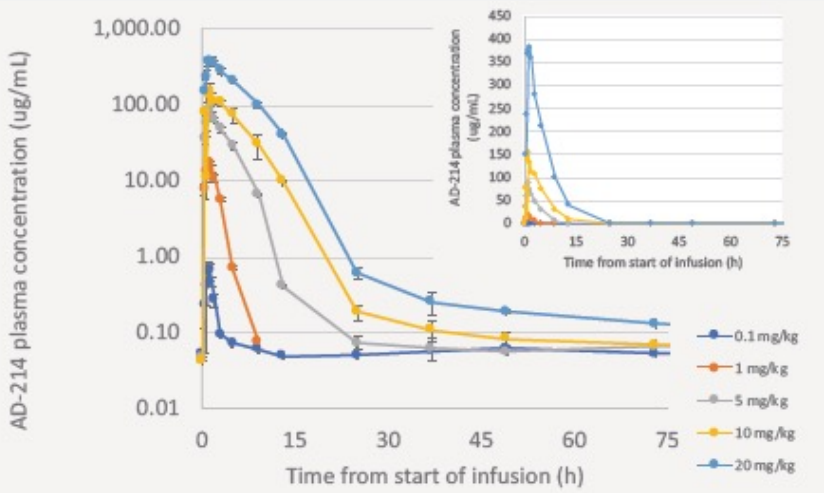
Exploratory

- PD markers (SDF-1, CD34+)

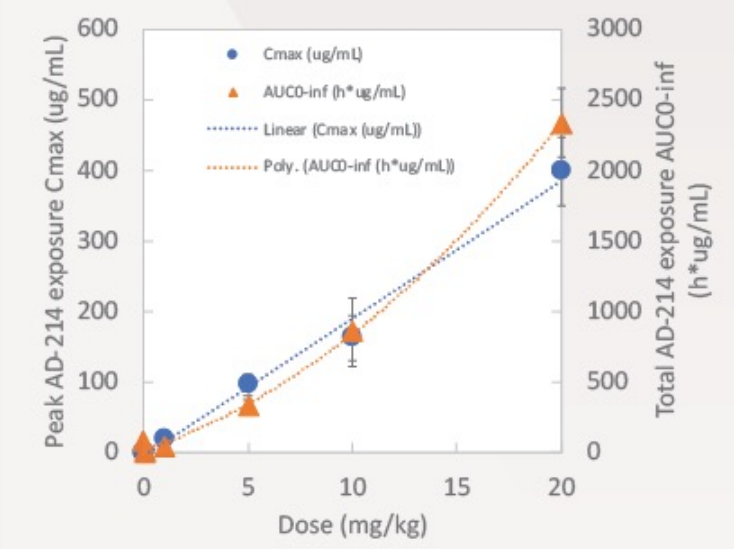
AD-214 pharmacokinetics increase proportionally with dose (single doses)

- **Maximum exposure, Cmax, increases in a dose proportional manner**
- **Total exposure, AUC0-inf, increases in a more than dose proportional manner**
- **Elimination half-life t1/2 ~40h**

AD-214 plasma concentrations (log and linear scale)



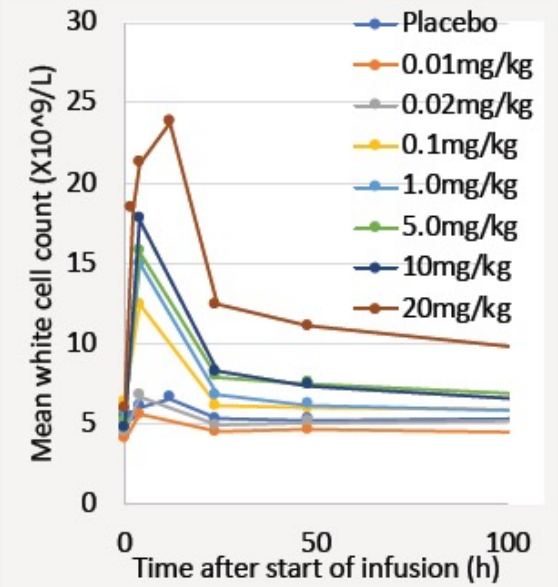
Maximum and total plasma exposure



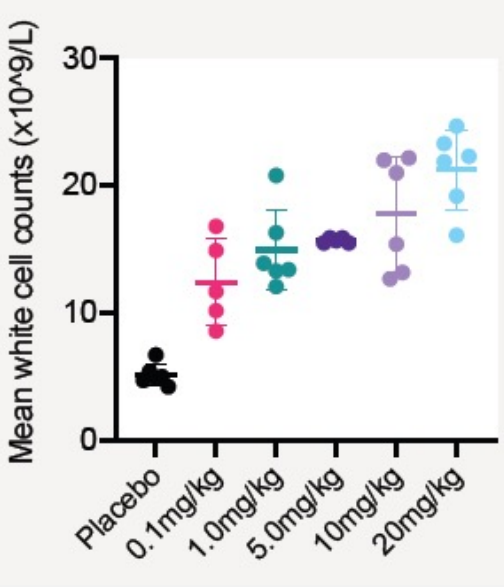
Transient white blood cell and blood stem cell increases indicate CXCR4 engagement

Observed in Phase I HV SAD*
Transient, dose dependent, increase in WCC and CD34+ counts at 4-12 hours consistent with CXCR4 blockade

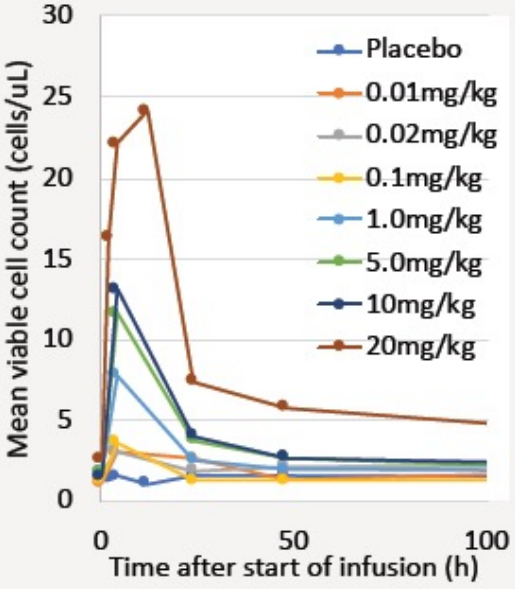
WCC counts



WCC counts at 4h

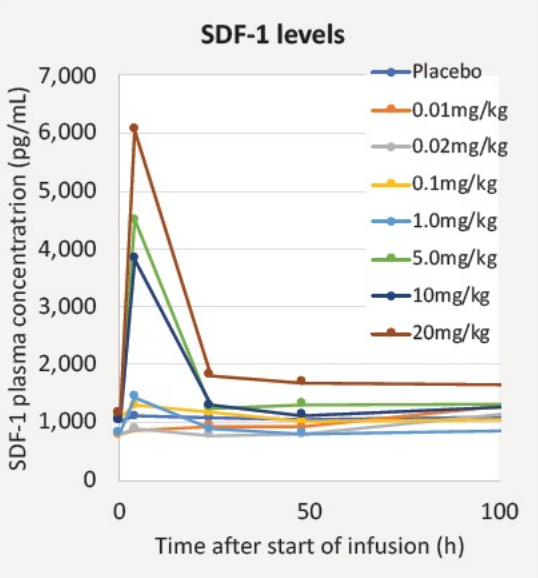


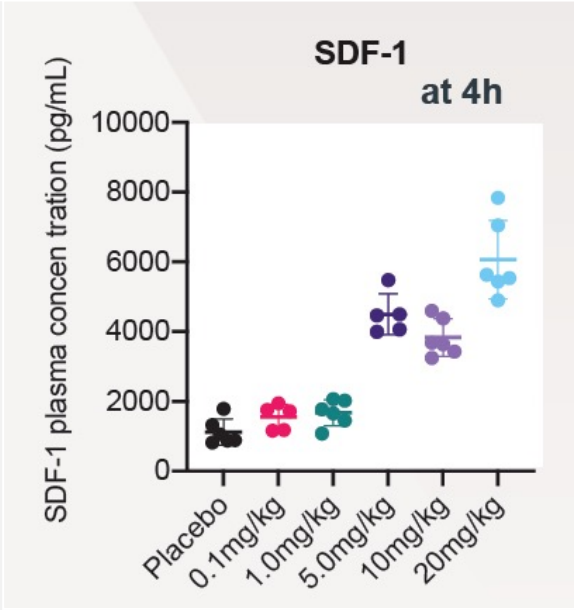
CD34+ cell counts



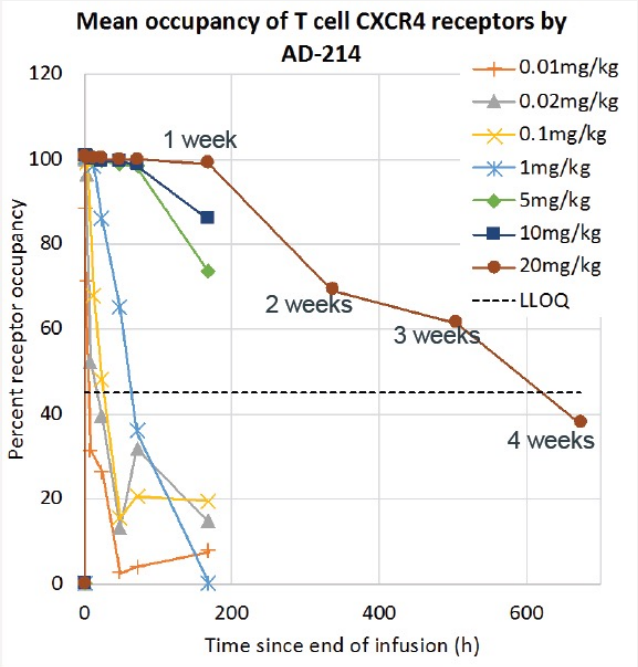
Transient increase in SDF-1 (natural ligand of CXCR4) consistent with CXCR4 engagement

Transient increases in SDF-1 levels at 4 hours in some participants, returning to baseline at 24h consistent with CXCR4 blockade





Sustained high levels of CXCR4 receptor occupancy on T cells



White blood cells naturally express CXCR4 in healthy individuals, providing an accessible surrogate for AD-214 target engagement or receptor occupancy (RO)

Understanding duration of RO is critical to inform dosing

Primary

- >70% CXCR4 RO at 7 days after 5-10 mg/kg infusion
- >60% CXCR4 RO at 21 days after 20 mg/kg infusion*
- ***Duration of RO is considerably longer than PK profile***

If replicated on CXCR4 receptors in fibrotic tissues, result supports extended dosing intervals despite relatively rapid clearance from circulation

* Receptor occupancy was monitored for one week at all dose levels except 20 mg/kg (4 weeks)

A clinician's perspective on AD-214 results so far

- **Un-met need in IPF/ILD remains – need to progress new therapies**
- Research at The Alfred suggests **if targeting CXCR4 works in IPF it may work in other ILD's**
- **AD-214 is well tolerated and ready to move forward into multi-dose studies in healthy volunteers and patients**
- The **data is supportive of extending dosing interval to two weekly at least**
- **AdAlta approach is methodical and appropriate**
  - PET imaging strategy is particularly important as an innovative way to explore target engagement and mode of action in diseased tissue
- **Key insights anticipated from multidose and early patient studies (in addition to safety):**
  - CXCR4 receptor engagement in tissue
  - Nature of the anti-drug antibodies that are expected with a biologic
  - Further characterisation of biomarker responses: CD34+, white cells, SDF-1a



Prof Glen Westall
leading respiratory and lung fibrosis specialist

AdAlta Investor Briefing
10 March 2021

AdAlta
next generation protein therapeutics

Appendix: i-bodies

i-bodies: next generation antibodies

i-bodies are human proteins that belong to the class of next-generation antibodies

Generation of the i-body

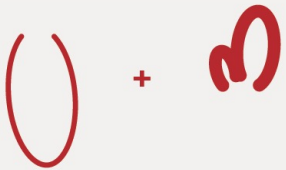
1



Shark antibody binding domain with unique long loop

2

Two long loops are engineered onto the human protein. These enable tight binding to the drug target and have a therapeutic effect



A **human** protein that is the same shape as the shark antibody is the backbone or scaffold protein of the i-body

3



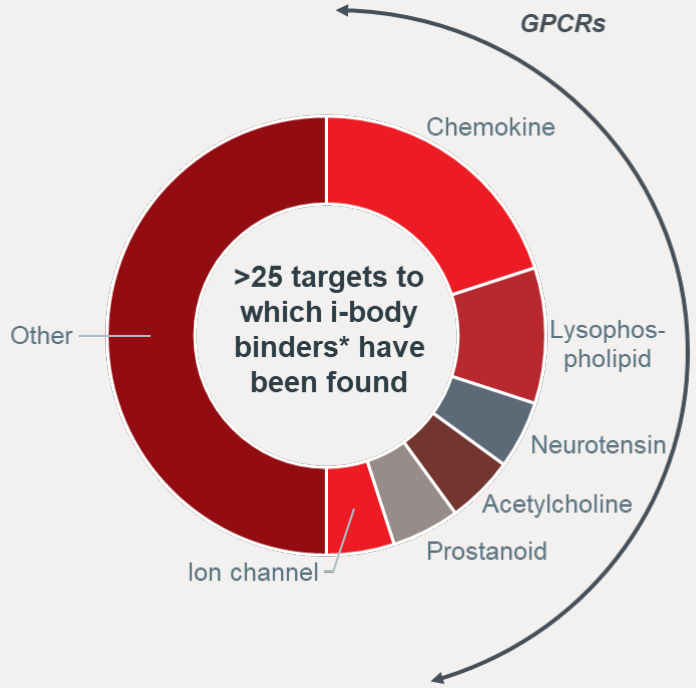
Each unique i-body has different binding loops. The i-body library has 20 billion unique i-bodies

AdAlta **i-body** is the combination of a human protein that mimics the shape of the shark antibody with unique long loop binding sites

The long loops of the i-body have exceptional targeting and binding properties, providing therapeutic access to drug targets that have evaded traditional monoclonal antibodies

Drug targets include G-protein-coupled receptors (GPCRs), currently the most heavily investigated class of drug targets in the body, and CXCR4 which is present in IPF

An immensely powerful drug development platform



i-body platform capability

- G-protein coupled receptors (GPCRs)
- Fibrosis, inflammation, oncology
- Diagnostics (PET tracers; cancer imaging)

GPCRs are the most heavily investigated class of drug today and 80% of GPCR targets are yet to be effectively exploited

*Includes both i-body and VNAR/IgNAR formats