

#### 1 June 2022

#### **ASX Announcement**

## AdAlta to present at BIO International Convention

**MELBOURNE Australia, 1 June 2022:** AdAlta Limited (ASX:1AD), the clinical stage biotechnology company developing novel therapeutic products from its i-body platform, is pleased to advise that CEO and Managing Director, Dr Tim Oldham, has been selected to present at the Bio International Convention in San Diego, California on Monday 13 June, US time.

BIO is the world's largest advocacy association representing member companies, state biotechnology groups, academic and research institutions, and related organizations across the United States and in 30+ countries. The BIO International Convention is the world's largest gathering of the biotechnology industry. It attracts more than 15,000 biotechnology and pharma leaders for one week of intensive networking to discover new opportunities and promising partnerships.

#### Presentation details

Date and time: 13 June at 12:30pm (PST)

Conference: BIO International Convention

Room: Live in Theatre 1

A copy of Dr Oldham's presentation is attached, and a video version is available via this link: <a href="https://adalta.com.au/investors/presentations">https://adalta.com.au/investors/presentations</a>. The presentation highlights the multiple indication and route of delivery potential for lead asset, AD-214, in fibrotic diseases and the exciting potential of AdAlta's immuno-oncology collaborations with Carina Biotech (i-CAR-T) and GE Healthcare (i-PET imaging).

One-on-one meetings are also being scheduled via the BIO partnering system or by contacting AdAlta directly (details below).

Authorised for lodgement by:

Tim Oldham CEO and Managing Director June 2022



#### **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.

The i-body technology mimics the shape and stability of a unique and versatile antigen binding domain that was discovered initially in sharks and then developed as a human protein. The result is a range of unique proteins capable of interacting with high selectivity, specificity and affinity with previously difficult to access targets such as G-protein coupled receptors (GPCRs) that are implicated in many serious diseases. i-bodies are the first fully human single domain antibody scaffold and the first based on the shark motif to reach clinical trials.

AdAlta has completed Phase I clinical studies for its lead i-body candidate, AD-214, that 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. AdAlta has a second target in discovery research, also in the field of fibrosis and inflammation.

The Company is also entering collaborative partnerships to advance the development of its i-body platform. It has a collaboration with Carina Biotech to co-develop precision engineered, i-body enabled CAR-T cell therapies (i-CAR-T) to bring new hope to patients with cancer. It has an agreement with GE Healthcare to co-develop i-bodies as diagnostic imaging agents (i-PET imaging) against Granzyme B, a biomarker of response to immuno-oncology drugs, a program now in preclinical development.

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

For more information, please contact: Investors

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# Developing high value drugs for challenging diseases

Tim Oldham PhD, CEO and Managing Director BIO2022



# Disclaimer

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This presentation may contain forwardlooking 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 at a glance



### **Building out pipeline**

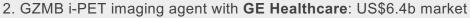
Targeting 10 programs by end 2023

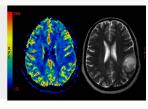


GE Healthcare

# Immuno-oncology: two co-development collaborations









# Fibrosis/inflammation: wholly owned pipeline

- 1. AD-214 first in class anti-fibrotic preparing for Phase II clinical trials
- 2. Second target in discovery





#### i-body platform

Powerful drug discovery tool for creating drugs against diseases underserved by traditional antibodies



# Four human health needs AdAlta is addressing today



#### Antibodies cannot do everything!

AdAlta's i-bodies are a differentiated drug discovery platform for difficult diseases



#### Idiopathic Pulmonary Fibrosis: degenerative, fatal

AdAlta's AD-214 could meet a desperate need for new approaches for a debilitating disease



#### CAR-T cell therapy providing new hope ... for blood cancer patients

AdAlta and Carina's iCAR-T cells could offer same hope for patients with solid tumours



Immuno-oncology drugs revolutionising cancer treatment ... for some

AdAlta and GE Healthcare's GZMB iPET imaging agent could identify responders early



Platform: i-bodies



# i-bodies: sdAB-like molecules with engineered binding loops conferring unique binding properties



AdAlta i-bodies are combination of a human protein with unique long loop binding sites that mimic the structural features of the shark single domain antibody system







Human protein scaffold Engineered target specific binding loops



AdAlta i-body library contains 10<sup>10</sup> unique i-bodies. Each unique i-body has different binding loops



12-15kDa protein 90% smaller than MAb 50% smaller than scFv



# i-bodies allow for high affinity, high specificity binding to targets that are intractable for traditional antibodies

# **Small Antibodies** i-bodies Flexible, modular formats **Molecules** CAR cell therapy ADC/ radiotherapeutic Bi-specific Fc-fusion i-bodies are ~10% the i-bodies have high The i-body CDR specificity, size of human structure confers

i-bodies have high specificity, avoiding off-target issues of small molecules i-bodies are ~10% the size of human antibodies, capable of engaging sterically hindered cell membrane receptors The i-body CDR structure confers unique binding capabilities, enabling unique epitope engagement and tunable pharmacology

PEGylation



Naked i-body



Lead program: AD-214



# About | Idiopathic Pulmonary Fibrosis (IPF)

Scaring and stiffening of the lungs progressively and irreversibly reduces lung function

>300,000 people living with IPF; 40,000 people die from IPF every year

Only 3.8 years median survival after diagnosis

Two current therapies sell for \$3b per year ...

... despite having limited effectiveness and serious side effects

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

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

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



# AD-214 | Completed Phase I, preparing superior inhalation format for Phase II

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

- i-body-Fc fusion targeting CXCR4
- Pre-clinical efficacy in lung, kidney, eye fibrosis

# Phase I intravenous (iv) clinical study successfully completed<sup>1</sup>

- · AD-214 (iv) is well tolerated, binds CXCR4 tightly
- Preclinical animal data supports potential iv efficacy

# Drug substance manufacturing secured for next clinical studies in 2021<sup>2</sup>

- Delivery mid 2023
- Next clinical studies to commence second half of 2023



# Direct lung delivery (inhalation) potentially a superior format for IPF<sup>3</sup>

- PET imaging shows rapid liver distribution<sup>4</sup>
- Direct lung delivery could reduce dose, costs
- At home inhalation more flexible, convenient than iv
- Differentiated routes of administration enable partnering by indication



Preclinical development of inhaled formulation well advanced

Route of administration, indication priorities for clinical program to be finalized in 2H 2022

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# Inhaled AD-214 | Milestones and opportunities in 2022

# June 2022 quarter

 Antifibrotic effects in cultured human lung tissue

#### **Through mid CY 2022**

- Antifibrotic effects in cultured human lung tissue
- Imaging distribution, retention in sheep
- Manufacturing AD-214 for toxicology studies

#### September 2022 quarter

- Efficacy in bleomycin mouse model\*
- Inhaled AD-214 formulation selected

#### **December 2022 quarter**

- Preparation for inhalation toxicology studies
- cGMP manufacturing commences for Phase lb/II clinical trials

#### Aim of pre-clinical studies

- 1. Demonstrate nebulised AD-214 can reach lower airways of sheep lungs (similar to human)
- 2. Demonstrate that AD-214 reaching the lower airways is retained in fibrotic tissue (bleomycin mice, sheep, cultured lung tissue)
- 3. Demonstrate AD-214 delivered to fibrotic tissue can moderate disease progression (bleomycin mice, cultured lung tissues and cells)

Pre-clinical success anticipated to accelerate existing partnering discussions



# AD-214 | Valuable IPF partnering options as early as Phase I

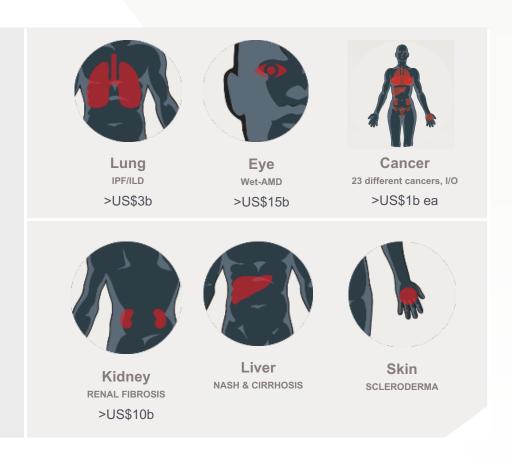
Date	Licensee	Licensor	Transaction Terms	Clinical Phase
Nov-21	BLADE OTHER A PEUTIOS	BIOTECH ACQUISITION COMPANY	US\$254m Upfront	2 (Ready)
Nov-21	OncoArendi Therapeutics	<b>Galápa</b> gos	€320m Milestones	2 (Ready)
Sep-21	Syndax 🥕	Incyte	US\$152m Upfront +US\$602m Milestones	2 (Ready)
Nov-19	Promedior	Roche	US\$390m Upfront +US\$1b Milestones	2
Feb-21	東德制药 TIDE PHARMACEUTICAL	GRAVIT N NOTITICE CONTINUES	US\$517.5m Milestones	1
Jul-19	bridgebio	Boehringer Ingelheim	€45m Upfront +€1.1b Milestones	1

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# AD-214 | Multiple indication extension options in other forms of fibrosis

- Preclinical tissue and animal models show that AD-214 may improve fibrosis across a range of fibrotic diseases and cancer
- Unique formulations for different indications enable multiple potential partnering deals

 Each additional indication could address multiple markets with US\$ billion potential



<sup>\*</sup> Subject to development of a satisfactory, improved intravenous formulation.



Co-developed immuno-oncology assets

# About | CAR-T therapies

CAR-T therapies are providing new hope for patients with cancer who have failed all other options

Therapy involves removing immune cells from blood and re-engineering them so they "see" cancer as a pathogen

Already 6 FDA-approved CAR-T therapies ... but so far only for blood cancers

>\$US1 billion earned by CAR-T therapy products in 2020

\$US20.3 billion<sup>1</sup> revenue forecast for 2028 as more products are commercialised, science evolves

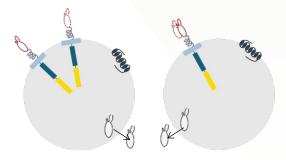
Solid tumours to account for >50% of CAR-T revenues by 20302

# i-bodies enable optimized CAR constructs (i-CARs)

Feature	Benefit		
Small size	Increased CAR gene cassette/vector capacity, efficient multi-functional CAR cell creation		
Long CDR3 binding domain	Access to unique tumor antigens/epitopes and TME modulating proteins in cancer tissue		
Tunable binding	Control of immune synapse (length + strength)		
Robust conformation	<ul> <li>Natural stability delivers robust CAR binding domain and stable secreted molecules</li> </ul>		

### **Superior i-CAR products**

- CARs against novel tumor antigens
- Dual and bi-specific CARs for enhanced specificity, reduced tumor escape and logic gated CARs
- · Secreted antibodies to modulate TME





# i-CAR-T assets | Carina co-development collaboration

AdAlta and Carina are combining i-bodies and a world class CAR-T platform to create iCAR-Ts that could offer improved precision, performance and persistence

#### Further expands AdAlta's pipeline in an attractive deal space

- Collaborating on up to five tumour targets
- Sharing costs to pre-clinical proof of concept (in mice)
- Jointly own resulting products: ready for partnering or further development

#### **Current status**

- i-body enabled CAR-T (i-CAR-T) cells have been successfully generated by Carina and demonstrate in vitro cell killing (lysis)<sup>1</sup>
- First target A selected, i-CAR-T cells incorporating i-bodies against Target A being built



immuno-oncology asset

# About | Immuno-oncology (I/O) PET imaging

Immuno-oncology (I/O) drug market is worth US\$95 billion¹...

... but only 20-40% of patients respond<sup>2</sup> to therapy

Granzyme B (GZMB) is produced by immune cells to kill cancer: potential biomarker of I/O drug activation of the immune system

PET imaging GZMB could help identify early who will – and won't – respond to I/O drugs

The PET imaging agent market is valued at US\$6.4billion<sup>3</sup>

Largest products >US\$400m<sup>4</sup>

<sup>1. 2026</sup> 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-PET imaging asset | GE Healthcare co-development collaboration

AdAlta and GE are co-developing a GZMB i-body PET imaging (iPET) asset to evaluate the effectiveness of immuno-oncology drugs

#### Revenue generative pipeline asset

- AdAlta earns research fees, development and sales milestone payments and royalties on product sales
- A\$2.27 million revenue\* earned to December 2021
- GZMB iPET asset could generate royalty revenue sooner than a therapeutic due to shorter diagnostic development timelines

#### **Current status**

- Panel of GZMB specific i-bodies identified
- · Pre-clinical proof of concept studies underway
- Manufacturing development underway







Co-developed iPET imaging immuno-oncology asset.



# I/O assets | Milestones and opportunities in 2022





Through mid CY 2022

GZMB iPET imaging agent

of concept

preclinical proof

Through mid CY 2022

 Initial in vitro cancer cell killing screening assays completed for iCAR-T target A September 2022 quarter

 iCAR-T targets B and C selected December 2022 quarter

iCAR-T Target A

- in vitro cancer cell killing assays complete
- in vivo proof of concept studies commenced



# Corporate snapshot

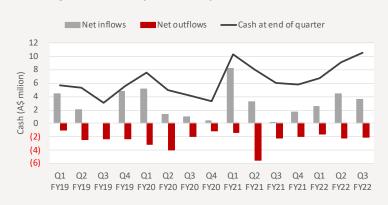
Key financial details (31 March 2022)				
ASX code	1AD			
Market capitalisation	A\$22.94m			
Share price (12 month closing range)	A\$0.073 (\$0.071 - 0.183)			
12 month return	(52)%			
Ordinary Shares (daily volume)	314,184,746 (308,506)			
Unlisted Options	14,184,060			
Cash (31 Mar 2022)	A\$10.54m			

<b>Major shareholders</b> (31 March 2022)	%
Yuuwa Capital LP	17.2
Platinum Asset Management	15.7
Meurs Holdings Pty Ltd	6.4
Radiata Super Pty Ltd	3.5
Sacavic Pty Ltd	3.1
Other (1,567 total holders)	54.1
Total	100%

Analyst Coverage				
Pitt Street Research				
Lodge Partners (pending)				









# Investment proposition



i-body platform to create value



Fibrosis/inflammation
Lead asset advancing to Phase II
>\$3b market potential in first indication<sup>1</sup>

Discovery initiated on 2<sup>nd</sup> target



Immuno-oncology
2 x co-development collaborations to leverage platform

✓ GE Healthcare: \$6b PET market<sup>2</sup>

✓ Carina Biotech: \$20b CAR-T market³



Leading expertise



Clear vision for growth through pipeline expansion



Regular near-term news flow



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