29 November 2021

ASX Announcement

AGM: CHAIR ADDRESS, CEO PRESENTATION AND FIRST i-CAR-T DATA

MELBOURNE Australia, 29 November 2021: AdAlta Limited (ASX:1AD), the clinical stage drug discovery company developing novel therapeutic products from its i-body platform is pleased to release presentations to be made its Annual General Meeting today by Chair, Dr Paul MacLeman and CEO and Managing Director, Dr Tim Oldham.

Highlights of the presentations include:

- Progress report against 2021 milestones set at the 2020 AGM
- Milestones for 2022 calendar year
- Proof of principle data showing i-bodies can be incorporated into Carina's CAR-T cells and achieve targeted cell killing.

AdAlta and Carina Biotech (Carina) announced a collaboration to develop precision engineered, i-body enabled chimeric antigen receptor T (CAR-T) cells as cancer therapeutics on 24 August 2021. Under the collaboration, AdAlta will discover i-bodies for up to five solid tumour targets (antigens) that Carina Biotech will then use with its proprietary CAR-T technologies to develop CAR-T cell therapy products. The i-body enabled CAR-T cell is expected to bring improved targeting, better penetration and treatment persistence when used to treat solid tumours.

In preliminary proof of principle studies, an AdAlta i-body binding to an undisclosed target was incorporated into three different CAR designs and successfully engineered into T cells using Carina technology to create three different CAR-T cells. The ability of these CAR-T cells to kill target cells expressing the target antigen were assessed.

Key findings of these proof of principle experiments were:

- 97% of T cells in culture incorporated the i-body CAR to become i-CAR-T cells which then expanded during manufacturing at the rates expected;
- i-body enabled CAR-T cells were capable of *in vitro* killing a cell line engineered to overexpress the i-body's target, but did not kill the original cells; and
- i-body enabled CAR-T cells were capable of *in vitro* killing of two colorectal cancer cell lines and (less effectively) a glioblastoma (brain) cancer cell line known to express the i-body's target. Illustrative data is shown in the attached presentation.

Managing Director and CEO, Dr Tim Oldham commented:
"We are very pleased to share the proof of principle data that so excited us about the potential of this collaboration. We look forward to first experimental results on agreed targets under the collaboration in the first half of next year."

The Company also notes the issuance of a first Singapore Patent 11201705583X and a second Australian Patent 2019203511 protecting the i-body sequence used in AdAlta's lead product, AD-214, sequences similar to this, and pharmaceutical compositions containing these i-body sequences and their uses in therapeutic and diagnostic applications, including Idiopathic Pulmonary Fibrosis (IPF), the lead indication for which

AD-214 is being developed. These patents expire on 8 January 2036. This adds to patent protection already obtained in Australia (2017), USA (2020 and 2021) and Japan (2021), with additional applications pending in Europe, China, India and other markets.

Authorised for lodgement by:

Tim Oldham
CEO and Managing Director
November 2021

Notes to editor

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 properties 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. A second target implicated in fibrosis is in discovery research.

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

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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CHAIR'S ADDRESS

Ladies and gentlemen,

I am pleased to welcome you to AdAlta's 2021 Annual General Meeting. This AGM is being conducted in a fully virtual environment to enable participation of all those around the world affected by the ongoing pandemic. Wherever you're joining us from today, I thank you for your participation.

Looking back, it is appropriate to characterise FY2021 as one of substantial progress for AdAlta – where we advanced our existing i-body enabled assets and expanded our pipeline.

Our lead asset, AD-214 which is being investigated for Idiopathic Pulmonary Fibrosis and Interstitial Lung Disease, completed a Phase I clinical trial, demonstrating that it was very well tolerated in single and multiple intravenous doses in healthy volunteers.

We also successfully developed a radio-labelled version of AD-214 for PET imaging, with pre-clinical studies demonstrating the value of this asset as a translational research tool. This showed that, although we could progress to Phase II with the current formulation of AD-214, this would not be the optimal formulation from a cost or patient convenience perspective. The time to availability of our next clinical batch of AD-214 affords us the opportunity to develop both inhaled and iv formulations. Importantly, we now have a clear pathway to clinical trials in Idiopathic Pulmonary Fibrosis (IPF) patients using an inhaled formulation of AD-214, which we think will be preferred by both patients and clinicians. Despite the pre-clinical imaging results not being exactly as expected, our pre-clinical efficacy data remains valid and we continue to be confident that AD-214 could offer an important new option for sufferers of debilitating fibrotic diseases.

Our commercial collaboration with GE Healthcare moved to the next phase, following the successful identification of multiple i-bodies to be advanced into pre-clinical development for use as a potential PET diagnostic imaging agent. GE Healthcare are leading pre-clinical development and AdAlta continue to earn revenue from this collaboration as we support pre-clinical and manufacturing development.

We also entered a collaboration with Carina Biotech Pty Ltd (Carina) to develop precision-engineered, i-body enabled, CAR-T cells with potential to make these breakthrough therapies available to a wider range of patients with solid cancers. Both the GE and Carina collaborations contribute to our strategy to expand our pipeline and provide commercial validation of our platform.

AdAlta is now in the middle - or expansion - phase of the growth strategy we outlined in 2020. Our near-term strategic priorities remain the following, which Tim Oldham will expand upon through his CEO's presentation.

Firstly, we will continue to progress AD-214 through clinical value inflection points following successful completion of Phase I clinical studies.

Secondly, we will continue to add additional assets to our internal pipeline.

Thirdly, we will progress multiple collaborations in our external pipeline. The PET imaging agents that GE Healthcare is developing could generate royalty revenue for AdAlta much earlier than AD-214 and in FY22 we also anticipate first experimental results from our new collaboration with Carina.

Fourthly, we will continue to invest in our drug discovery and development platform to continue to improve its efficiency and intellectual property protection.

I would like to acknowledge and thank you, our shareholders, who supported us last year with $8.1 million in new funds and for your continued support and encouragement of our strategy.

I'd like to express my gratitude to our management team and Board for all the significant effort deployed throughout FY21.

Finally, the COVID-19 pandemic has continued to disrupt individuals, companies and economies in unprecedented ways in 2021. AdAlta is in the fortunate position that our laboratories, collaborators and clinical trial sites have generally been able to remain open and our programs suffered only minor delays as a result, with the most significant impact being the previously announced extended lead time for our next AD-214clinical material.

Our thoughts are with all those less fortunate than us, and particularly with the survivors of COVID-19 infection who it would appear may be at greater risk of developing lung fibrosis. This highlights even more the importance of the work we are doing to bring AD-214 to the lung fibrosis patients who so desperately need new therapeutic options.

We will now progress to the formal business of the meeting, after which our CEO and Managing Director, Dr Tim Oldham to deliver his report and provide opportunities for questions.

AdAlta
next generation protein therapeutics

Building momentum, remaining agile

Tim Oldham PhD, CEO and Managing Director

Annual General Meeting, 29 November 2021

AdAlta today

AdAlta is building significant growth momentum while retaining agility to respond and adapt to data and opportunities

- **i-body platform**: can create therapeutics addressing targets underserved by traditional antibodies

- **Fibrosis/inflammation: lead asset AD-214** preparing for Phase II clinical trial
  - US$3b IPF market today,[1] multiple US$b indication potential
- **Second target in discovery**

- **Immuno-oncology: two co-development collaborations**
  - GZMB PET imaging agent with **GE Healthcare**: US$6.4b PET imaging agent market[2]
  - i-body enabled CAR-T with **Carina Biotech**: US$20b market by 2028[3]

- **Continuing to build out pipeline** with additional internal and external programs: targeting 10 by 2023

1. GlobalData, Idiopathic Pulmonary Fibrosis Opportunity Analysis and Forecasts to 2029, November 2020
2. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021
3. 2028 forecast by Grandview Research, “T-cell Therapy Market Size, Share & Trends Analysis” Feb 2021

AdAlta's purpose

To use our platform technology and development capabilities to create multiple novel therapeutics for debilitating diseases that have proven difficult to drug with traditional antibodies

Progress against calendar 2021 goals (per 2020 AGM)

2021 goals were achieved or modified in direct response to new data or emerging near term opportunities with greater value



AD-214 clinical

- ✓ Phase I single and multi-dose safety: successfully completed, AD-214 well tolerated with clear evidence of long duration CXCR4 engagement
- ✓ Safety studies in patients: replaced with health volunteers to generate safety data for Phase II more rapidly



AD-214 PET imaging

- ✓ Pre-clinical development of RL-AD-214 for PET imaging: successfully completed
- ✕ 1st images in patients: deferred based on pre-clinical studies until improved formulation available



Partnerships

- ✓ GE Healthcare commence pre-clinical development of GZMB i-body PET agent: AdAlta engagement extended; $1.5m revenue to date
- ✓ 2nd external collaboration: multi-target CAR-T collaboration with Carina Biotech – 1st target commencing discovery



Internal pipeline and platform development

- ✓ 2 new targets into discovery: 1st commenced; 2nd from Carina collaboration; nearer term formulation development
- • i-body2.0: program commenced, scope now expanded to include bi-specifics, manufacturing (GE collaboration) & formulation improvements



Other achievements

- • Orphan Drug Designation for AD-214
- • Four new patents granted covering AD-214 (Japan, Singapore and second US and Australian patents)
- • $4m Vic Government RDTI low interest loan facility & $0.7m BTB Grant amendment to support inhalation development

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

Achievements in 2021 have laid the foundation for acceleration of our growth

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)

Now here

Via…

- Laying the foundations for growth
- AD-214 progressing through clinical and commercial development
- Building internal and external pipeline
- Continuous platform improvement

C Accelerate (from ~mid-2021)

Preparing for acceleration

Towards 2023…

- Multi-product, multi-partner platform company
- AD-214 partnering, new indications
- ~5 internal GPCR programs
- 3-5 co-development partnerships
- Fully leveraging our platform, discovery, preclinical and clinical capabilities

AdAlta assets and business model

AdAlta's pipeline is expanding to plan. The i-body platform is creating wholly owned or co-developed assets. Our team is building skills in fibrosis/inflammation and immuno-oncology.

Co-developed assets

GE Healthcare

Granzyme B i-body enabled **PET imaging** agents for use in immuno-oncology

Pre-clinical

carina biotech

Precision engineered, i-body enabled **CAR-T** cells potentially providing new hope for patients with cancer

Discovery

Immuno-oncology theme

One more target to be added in early 2022

Wholly owned assets

AdAlta next generation protein therapeutics

Lead candidate: AD-214
First in class anti-fibrotic targeting CXCR4

Phase I
Orphan Drug Designation for IPF

AdAlta next generation protein therapeutics

Undisclosed target: GPCR for fibrotic disease
Discovery

Fibrosis and inflammation theme

Platform



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

Four needs AdAlta is addressing today

AdAlta's platform and pipeline is already offering the potential to address four major opportunities in our industry

Antibodies cannot do everything!
AdAlta's i-bodies are a new drug discovery platforms for challenging targets

Idiopathic pulmonary fibrosis: degenerative, fatal
AdAlta's AD-214 could meet a desperate need for new approaches for a debilitating disease

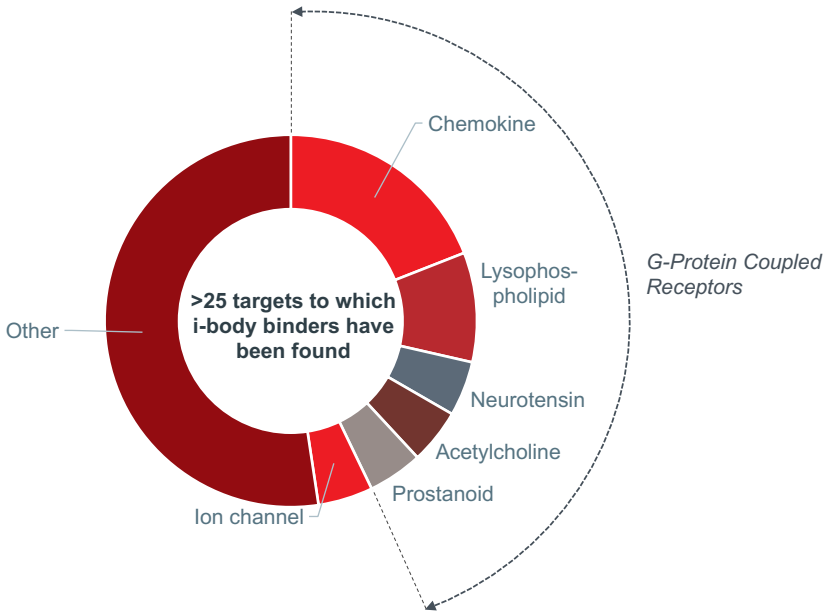
Immuno-oncology drugs revolutionising cancer treatment … for some
AdAlta and GE Healthcare's GZMB PET imaging could identify responders early

CAR-T cell therapy providing new hope for blood cancer patients
AdAlta and Carina's i-body CAR-T cells could offer same hope for patients with solid tumours

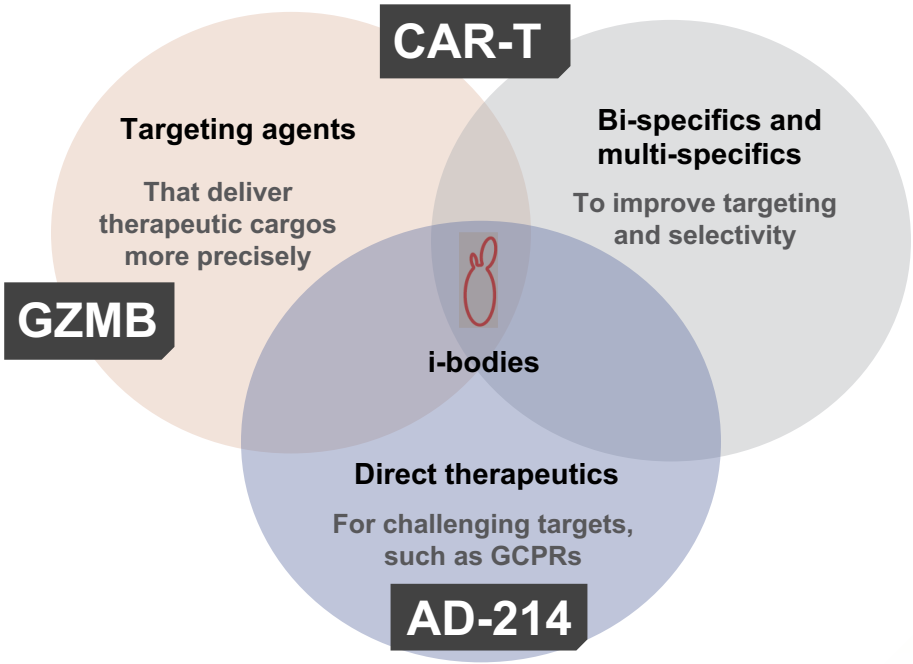
An immensely powerful drug discovery platform

i-body technology can enable a wide range of therapeutic and diagnostic products

Wide range of target classes



Wide range of product formats



Phase I clinical and PET imaging inform Phase II dosing and route of administration

Intravenous AD-214 is well tolerated in Phase I studies; PET imaging with radiolabelled AD-214 supports early transition to inhaled route of administration

Phase I clinical study successfully completed[1]
- Intravenous AD-214 is well tolerated in single and multiple doses
- Target (CXCR4) binding observed with extended duration

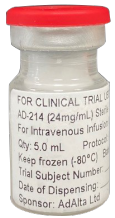
Resupply of AD-214 clinical material secured[2]
- Defines timeline for Ph II clinical study

Pre-clinical intravenous studies inform optimal administration[3]
- PET imaging shows rapid liver distribution (reduced bioavailability)
- Preclinical animal data supports potential iv safety, efficacy profile

Direct lung delivery (inhalation) of AD-214: a superior format for IPF

Improved intravenous formulation for other indications, derisks IPF

Phase II studies in IPF scheduled for 2H 2023 with superior formulation

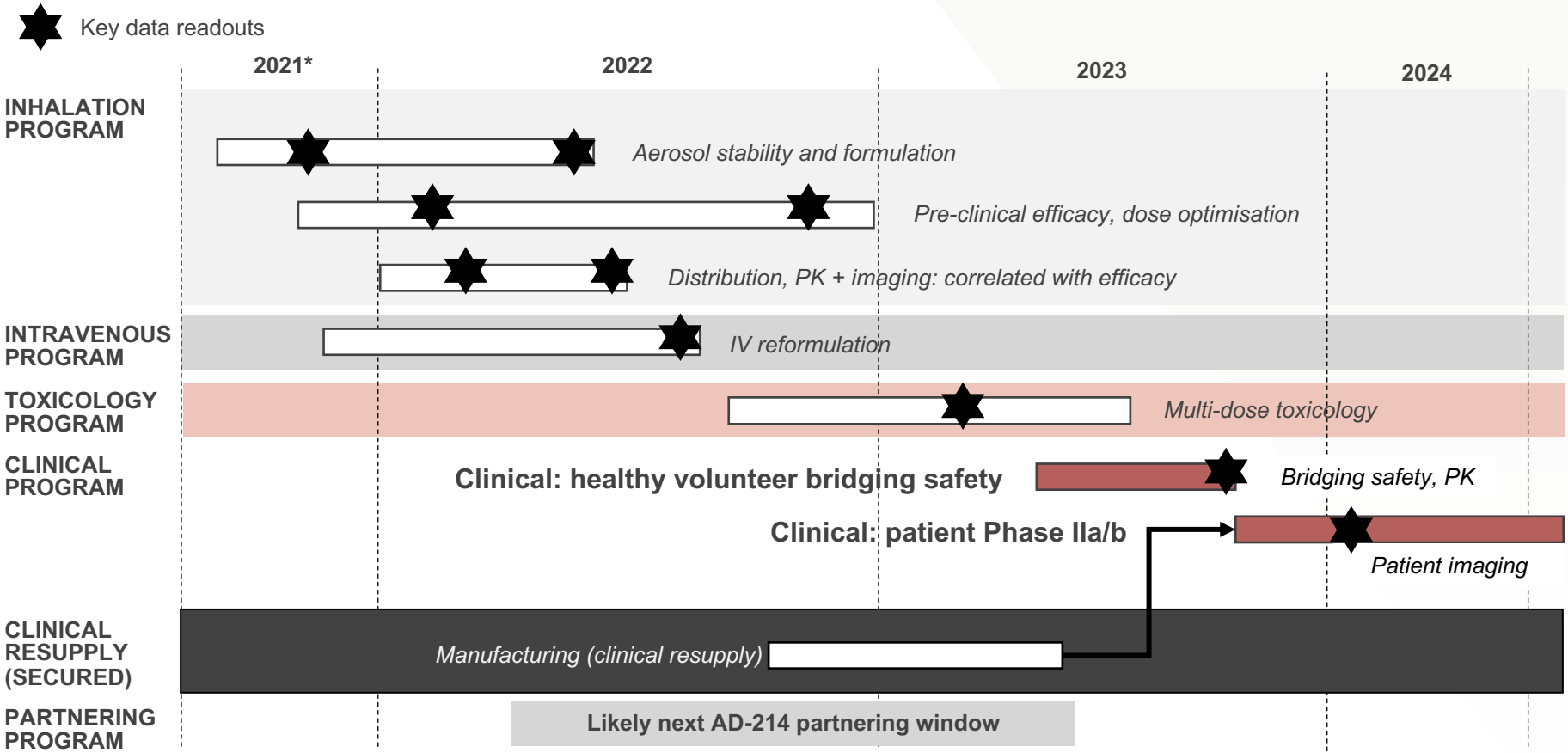




1. ASX Releases 10 Mar 2021 and 19 Jul 2021
2. ASX Release 1 July 2021
3. ASX Release 19 July 2021

Key milestones progressively de-risk AD-214 development: IPF Phase II 2023

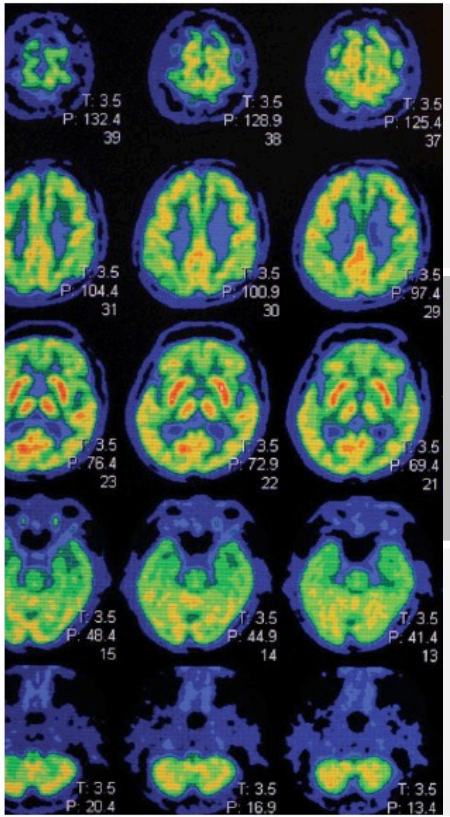
Quarterly milestones to de-risk formulation; extensive use of pre-clinical imaging; AD-214 partnering window from late 2022



* Calendar years

Immuno-oncology (I/O) PET imaging

US$6.4b PET imaging market: could help identify the 20-40% of patients who will respond to revolutionary I/O drugs faster



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

US$95 billion I/O market[1]

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

Granzyme B (GZMB) is produced by immune cells to kill cancer

Potential biomarker of immune system activated by I/O drugs

PET imaging GZMB can help
identify responders early

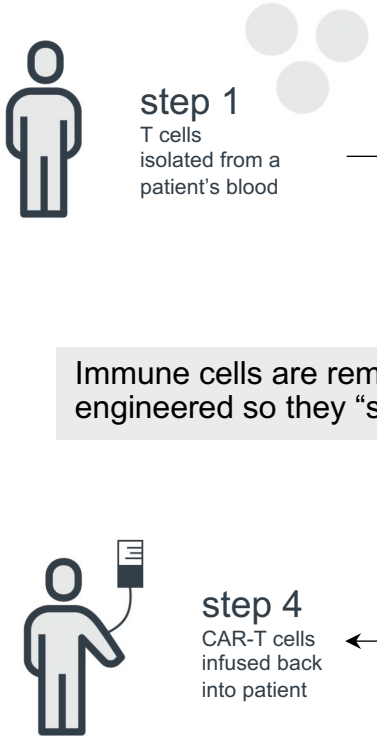
PET imaging agents have
short development time

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

CAR-T therapies are revolutionising cancer treatment

Reprogramming a patient's own immune system to fight cancer is a fast-growing market at the cutting edge of medicine



Immune cells are removed from blood and re-engineered so they "see" cancer as a pathogen

US$20.3b

revenue forecast for 2028[1]

50%

solid tumour share of revenues by 2030[2]

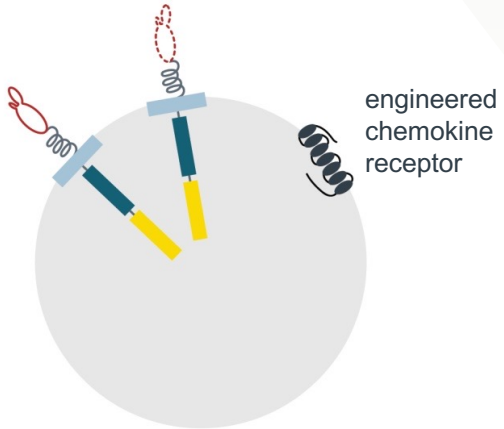
1. Grandview Research, "T-cell Therapy Market Size, Share & Trends Analysis" Feb 2021
2. Polaris Market Research, "CAR-T Cell Therapy Market Share, Size Trends, Industry Analysis Report", June 2021

Advantages of i-body enabled CAR-T

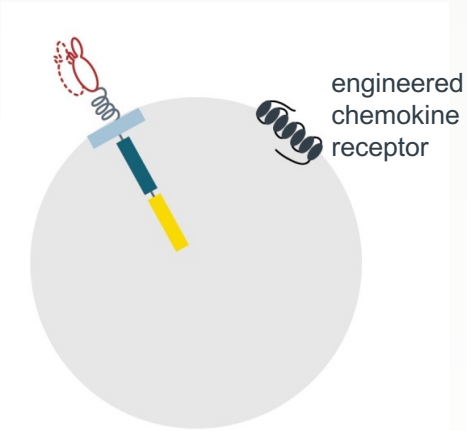
i-body enabled CAR-T cells may demonstrate improved precision, performance and persistence, particularly in bi-specific and dual CAR-T cells[1]

- **Specifically designed for antigens considered difficult or intractable for traditional approaches**
- **Half the size of the traditional CAR binding domain**
  - Enables greater flexibility in CAR design
- **Ideally suited to dual and bispecific CARs**
  - Target 2 antigens on cancer cells
  - Less likely for tumour cells to be missed
  - Reduces chance of damaging healthy tissue
- ***In vitro* proof of principle established**

i-body enabled mono / dual CAR



i-body enabled bi-specific CAR

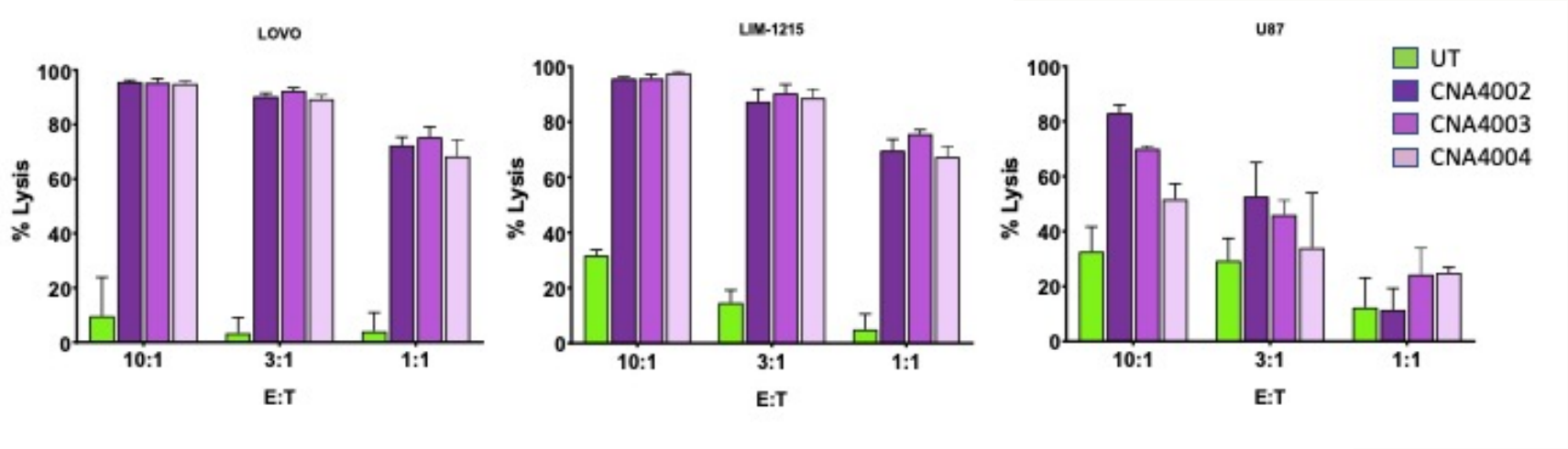




1. ASX Release 24 Aug 2021

Building the first i-CAR-T cell therapy: proof of principle results

i-body enabled CAR-T cells have been successfully generated by Carina and demonstrate *in vitro* cell killing (lysis)[1]



Experimental details

- LOVO and LIM1215 are colorectal cancer cell lines; U87 is a glioblastoma cell line
- 3 different Carina CAR-T constructs incorporating i-body against a single target “X” (CNA4002/CNA4003/CNA4004)
- UT is an unmodified T-cell that does not result in significant killing (lysis) of these cell lines
- i-CAR-T cells manufactured with 97% transduction (i-body CAR insertion) efficiency
- i-CAR-T cells included 60-70% CD4+ (helper) and 20-30% CD8+ (cytotoxic – killer) T cells

1. 210921 Carina iBody Datapack SB (2021) – previously unpublished data

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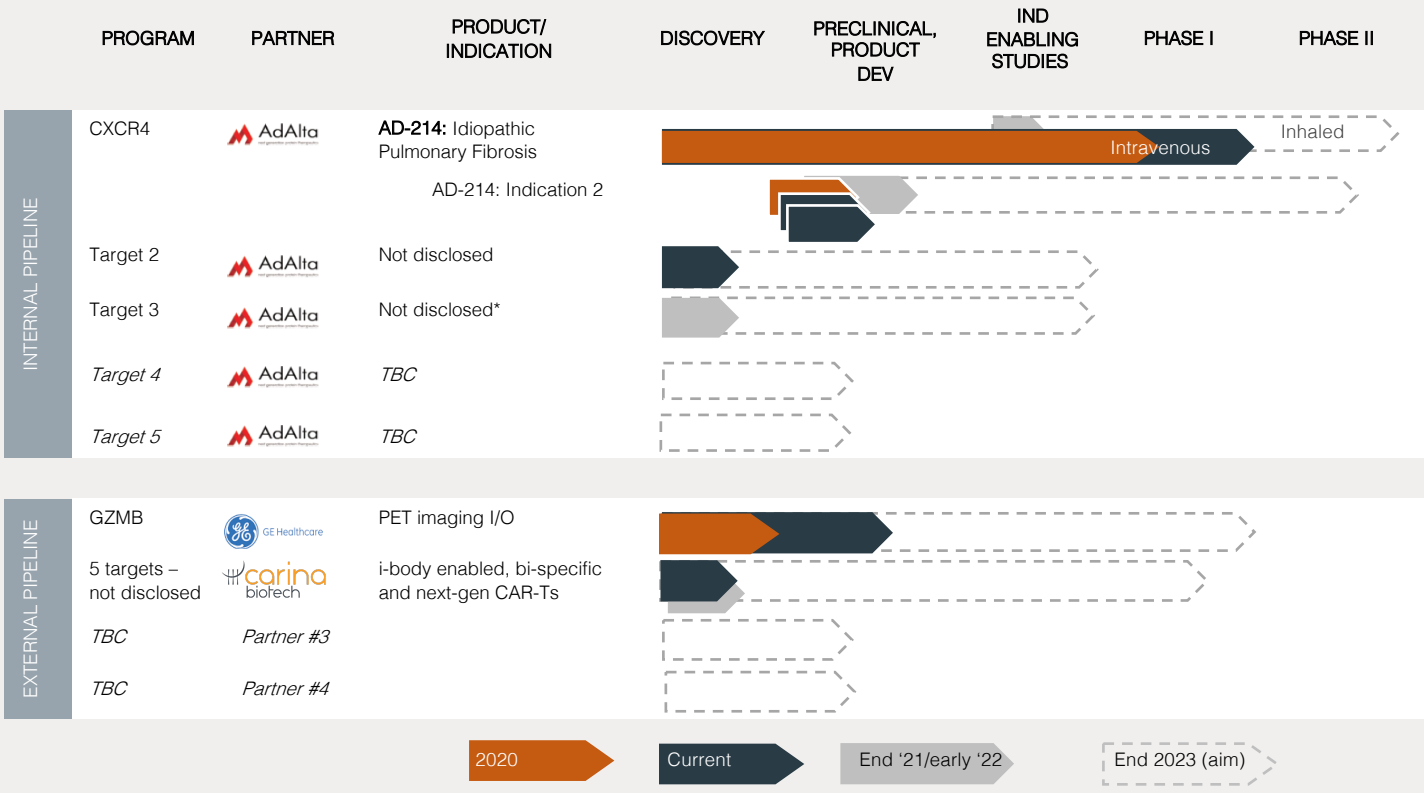
Current approved CAR-T products

Five FDA approved CAR-T products for blood cancers generate strong revenues and are in high demand

Manufacturer	NOVARTIS	Kite A GILEAD Company	Kite A GILEAD Company	Bristol Myers Squibb	Bristol Myers Squibb
Product	KYMRIAH® (tisagenlecleucel) Suspension for IV infusion 	YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion 	TECARTUS® (brexucabtagene autoleucel) Suspension for IV infusion 	Breyanzi® (lisocabtagene maraleucel) 	Abecma® (idecabtagene vicleucel) 
Notable CAR-T transactions	UPenn and Novartis Alliance Aug 2012[2]	Gilead acquired Kite Aug 2017 US$11.9b[1]	Gilead acquired Kite Aug 2017 US$11.9b[1]	Celgene acquired Juno Jan 2018 US$9b; BMS acquired Celgene Jan 2019 US$74b[3]	Celgene acquired Juno Jan 2018 US$9b; BMS acquired Celgene Jan 2019 US$74b[3]
FDA approval	**August 2017** (acute lymphoblastic leukemia, large B cell lymphoma)	**October 2017** (large B cell lymphoma)	**July 2020** (mantle cell lymphoma)	**February 2021** (large B cell lymphoma)	**March 2021** (multiple myeloma)
Revenue 2020[4]	**US$474m**	**US$563m**	**US$44m**	**N/A**	**N/A**

1. https://www.businesswire.com/news/home/20210204006011/en/Gilead-Sciences-Announces-Fourth-Quarter-and-Full-Year-2020-Financial-Results
2. https://www.novartis.com/
3. https://www.celgene.com/newsroom/cellular-immunotherapies/celgene-corporation-to-acquire-juno-therapeutics-inc/
4. businesswire.com/news/home/20210204006011/en/Gilead-Sciences-Announces-Fourth-Quarter-and-Full-Year-2020-Financial-Results, novartis.com, celgene.com/newsroom/cellular-immunotherapies/celgene-corporation-to-acquire-juno-therapeutics-inc/

An expanding pipeline of i-body enabled products



* Target #3 may be replaced by second Carina target, delivering shorter time to proof of concept

Calendar 2022 goals

Significant progress anticipated on both existing core programs and further pipeline expansion



AD-214 – first in class anti-fibrotic

- Inhaled formulation development: nebulisation feasibility, efficacy in animal model of IPF (Q1); lung distribution imaging in healthy and disease model animals (Q1); dose finding and clinical formulation (Q2)
- Intravenous formulation development (Q3)
- GLP toxicology with inhaled formulation (commences 2H22)
- Continuning partnering discussions (Q1); selection of next indication



GE Healthcare – GZMB PET imaging

- Pre-clinical proof of concept – milestone payment (mid-22)



Carina Biotech – i-body enabled CAR-T cells

- 1st experimental results on Target #1
- Commence i-body discovery on Target #2



Internal pipeline and platform development

- Initial functional data on i-body binders against internal Target #2 (2H22)
- i-body2.0: new intellectual property filed (end'22)
- 7 programs in pipeline (end'22)
- Additional patent filings, grants on individual i-body enabled products

Industry experienced leadership and advisors

Team with experience from discovery through manufacturing, clinical and commercialisation

Board



Dr Paul MacLeman
Chair



Liddy McCall
Director (alt: Dr James Williams)



Tim Oldham, PhD
CEO & Managing Director



Dr Robert Peach
Independent Director



Dr David Fuller
Independent Director

Executive



Tim Oldham, PhD
CEO & Managing Director



Dallas Hartman, PhD
Chief Operating Officer



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



Mick Foley, PhD
Founding Chief Scientist



Michael Rasmussen
Consultant Medical Expert

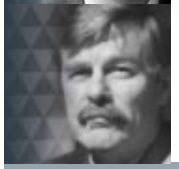
Scientific Advisory Board



Brian Richardson
Drug discovery and development expert



Steve Felstead
Clinical development



John Westwick
Pulmonary drug discovery and development

Development team

10 staff (9 PhD's)

Skills in protein chemistry, i-body discovery, product development, pre-clinical development, clinical development

Investment proposition



i-body platform to create value



Fibrosis/inflammation
Lead asset advancing to Phase II
>$3b market potential in first indication[1]

Discovery initiated on 2nd target



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

- ✓ GE Healthcare: $6b PET market[2]
- ✓ Carina Biotech: $20b CAR-T market[3]



Clear vision for growth



Leading expertise



Regular near-term news flow

1. GlobalData, Idiopathic Pulmonary Fibrosis Opportunity Analysis and Forecasts to 2029, November 2020
2. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021
3. 2028 forecast by Grandview Research, “T-cell Therapy Market Size, Share & Trends Analysis” Feb 2021

AdAlta
next generation protein therapeutics

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