ASX Announcement | 22 January 2024
AdAlta Limited (ASX:1AD)

JPMorgan Week and Advanced Therapies Week partnering progress and presentation; AD-214 Phase I extension study update

AdAlta has advanced its AD-214 and i-CAR cell therapy partnering programs during events associated with the JPMorgan Healthcare Conference (8-11 January 2024, San Francisco, USA) and Advanced Therapies Week (16-19 January 2024, Miami, USA) including an Innovation Stage presentation at Advanced Therapies Week highlighting the Company's capabilities to enable cell and gene therapies. The Company also reports that final participants have received their final dose in AD-214 Phase I extension study.

Investment highlights

- January partnering activity included Biotech Showcase™, BIOPartnering@JPM Week and Advanced Therapies Week
- 20 discussions relating to AD-214 licensing or asset financing, including a third top 20 pharma company requesting confidentiality agreement
- Final participants received final AD-214 dose in Phase I extension study; final results due end February to support partnering
- Significant interest in the potential of i-bodies to enable multifunctional advanced (cell and gene) therapies and the Company's i-CAR-T strategy
- Innovation Stage presentation at Advanced Therapies Week highlighting i-body® capability in cell and gene therapy

AdAlta Limited (ASX:1AD) ("AdAlta" or "the Company") is pleased to report positive progress on partnering initiatives at key January partnering conferences.

January partnering conferences important to advancing licensing and investment deals
AdAlta attended Biotech Showcase™ and BIOPartnering@JPM Week as part of JPMorgan Healthcare Week (8-11 January in San Francisco, USA), one of the most significant industry events for partnering and investment each year, followed by Advanced Therapies Week (16-19 January, Miami, USA) a key gathering of developers of, investors in and service providers to the cell and gene therapy industry.

The Company was advancing its three key partnering objectives:

1. Secure financing for Phase II clinical studies of its lead asset, AD-214, in Idiopathic Pulmonary Fibrosis by either out-licensing, or co-developing in a third party financed asset specific investment vehicle.
2. Establish new co-development collaborations to develop i-body-enabled i-CAR-T therapies

3. Secure access to clinic ready technology that is complementary to the i-body® platform

AdAlta CEO and Managing Director, Tim Oldham said: "*Our investors and shareholders are extremely interested in our partnering initiatives. While we cannot forecast the success or ultimate value of these, we continue to believe that they represent considerable upside potential for shareholders if successful. I am delighted with January's progress towards our AD-214 partnering goals and the positive reception our i-CAR-T cell therapy strategy is receiving.*"

New AD-214 partnering leads – three top 20 pharma companies under confidentiality agreement
Across the two weeks of partnering events, the Company participated in 20 meetings related to AD-214. With many partners already in AdAlta's out-licensing pipeline waiting for the results of the ongoing Phase I extension study, the Company was pleased to field several new licensing enquiries. Of particular note were:

- A new confidentiality agreement request from a top 20 global pharmaceutical, the third such company actively progressing detailed evaluation of AD-214.
- Approximately half the discussions were new interest from investors exploring co-developing/asset financing of Phase II clinical trials of AD-214.

AD-214 Phase I extension study on track
A key milestone for AD-214 several partnering discussions is completion of the Phase I extension study testing the safety and tolerability of AD-214 at planned Phase II doses. All participants have now successfully received all doses, with final results on track for delivery by end of February 2024.

Based on the favourable interim results reported previously,[1] the Company is working to assemble a shortlist of partners to advance discussions as rapidly as possible once final results are available.

AdAlta's role in next generation cell and gene therapies well received
AdAlta has identified the potential for the i-body® platform to become a key building block of advanced cell and gene therapy products, and particularly i-body® enabled Chimeric Antigen Receptor-T cell (i-CAR-T cell) therapies for solid tumours. Building on AdAlta's i-CAR-T collaboration with Carina Biotech, a clear opportunity is emerging to use the i-body® platform as the smallest available tool to help direct these transformational therapies specifically to cancer and/or to enhance their function when they arrive. During Advanced Therapies Week, the Company was able to further test this strategy with potential co-development partners, investors, and owners of clinic ready assets that AdAlta could potentially license.

The strategy and positioning were well received, increasing confidence in the potential to develop a robust and valuable clinical stage pipeline of assets after AD-214 and expanding the potential applications of i-bodies beyond CAR-T cell therapy to include gene and mRNA delivered therapies.

In an Innovation Stage presentation entitled "i-body next generation enabled advanced therapies" at 1:20am on Saturday 20 January AEST, CEO and Managing Director, Tim Oldham, summarized AdAlta's capabilities in this transformational new field and the unique advantages of working with AdAlta in Australia. A copy of the presentation, directed to a technical audience, is attached.

For a video summary of this release and opportunity to engage in virtual discussion see:
https://investorhub.adalta.com.au/link/GyVdgr

This ASX announcement has been authorised for release by the Board of AdAlta Limited (ASX:1AD).

For further information, please contact:

AdAlta Limited (ASX:1AD) **Media & Investor Enquiries**

[1] ASX Release 20 November 2023

Tim Oldham
CEO & Managing Director
P: +61 3 9479 5159
E: t.oldham@adalta.com.au

The Capital Network
Julia Maguire
P: +61 2 8999 3699
E: julia@thecapitalnetwork.com.au

About AdAlta Limited

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 enabled protein and cell 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 is extending 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. Preparation for Phase II clinical studies is also underway.

The Company is also entering collaborative partnerships to advance the development of its i-body® platform. It has a collaboration with Carina Biotech to codevelop 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.

For more information

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AdAlta

i-body® enabled next generation advanced therapies

AdAlta Limited (ASX:1AD)
Advanced Therapies Workshop
Miami
19 January 2024

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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 (ASX:1AD): Progressing multiple transaction opportunities

Purpose: i-body® targeting for next generation therapeutics

Going where antibodies can't to produce high-value, next generation protein and cell therapies for debilitating diseases

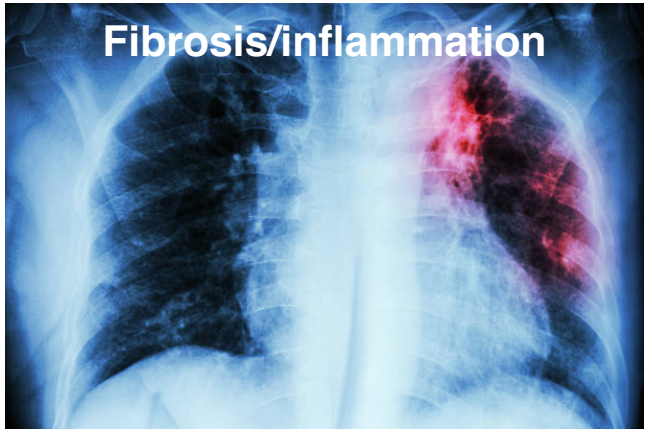
Discovery business

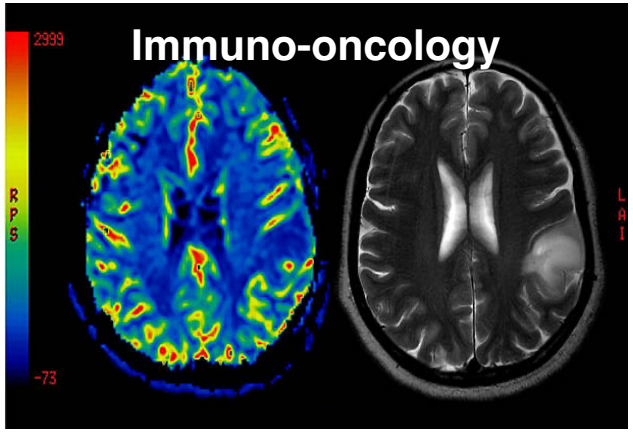
i-body® "inventory" of high value product candidates for development or licensing

i-body® platform + in-house discovery team

Product development business

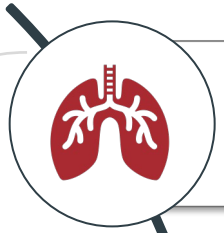
Product candidates progressing through value-adding development milestones for out-licensing or co-development





Experienced leaders, in-house protein engineering + cost effective Australian location

AdAlta's portfolio: High value therapeutics addressing challenging diseases in fibrosis and immuno-oncology and a platform grow further



Fibrosis: degenerative, progressive, fatal

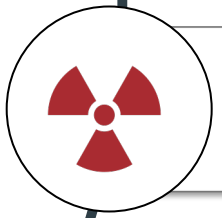
AdAlta's AD-214 could meet a desperate need for new approaches for debilitating diseases of the lung (US$4.3b), kidney (US$10b) and eye (US$15b) – Phase I complete

Comparator licensing transactions: >US$45m up front; US$320-1,000m milestones

CAR-T cell therapy providing new hope… for blood cancer patients so far

*AdAlta and Carina's i-CAR-T cells could offer the same hope for solid tumour patients (US$20b by end of decade) – discovery/*in vivo *PoC stage*

Comparator licensing transactions: >US$10m up front; >US$300m milestones



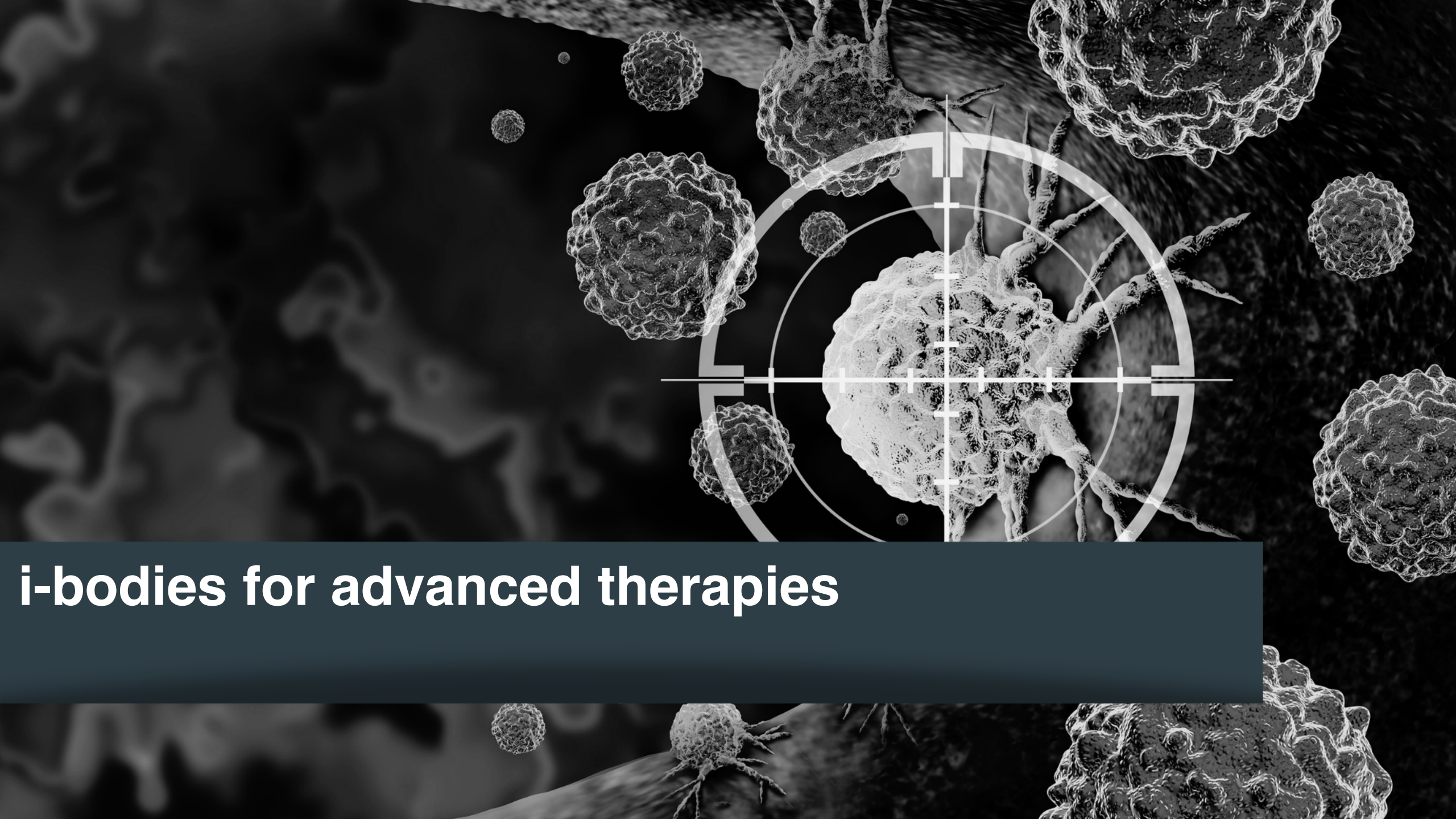
Immuno-oncology drugs revolutionising cancer treatment… for some

AdAlta and GE Healthcare's GZMB i-PET imaging agent could identify responders early (US$6b) – in vivo *PoC*

Comparator product revenue potential: >US$400m pa

Traditional antibodies can't do everything!

AdAlta's i-bodies are a differentiated drug discovery platform partners can leverage for difficult diseases – building inventory

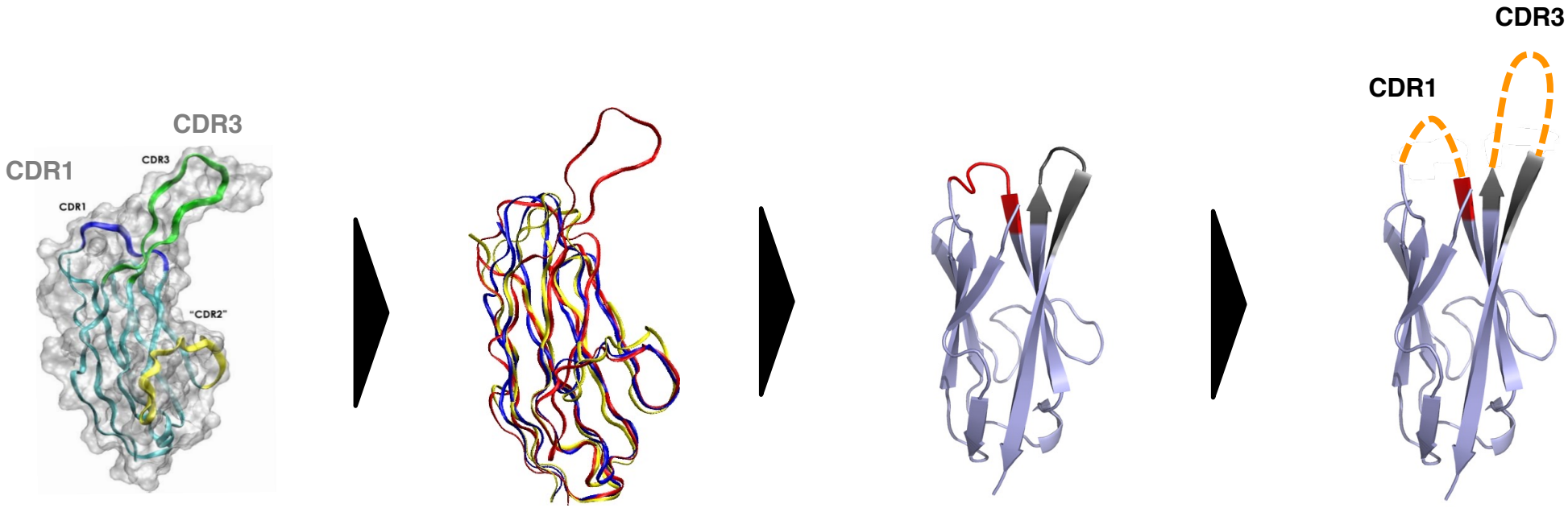


i-bodies for advanced therapies

Invention of i-body® technology: first fully human domain antibody system

hNCAM domain 1 scaffold + randomized synthetic shark VNAR-like binding loops

- **10% the size of Mab; 50% the size of scFv; CDR3 up to 24 AA**
- **Capable of engaging unique receptor epitopes and inducing unique pharmacology**



Shark VNAR

Basic research on unique shark immune system …

Ribbon overlay*

… led to discovery that the i-set family of human proteins have the same scaffold structure …

hNCAM Domain 1

… leading to the choice of human NCAM domain 1 for the current scaffold …

i-body® library

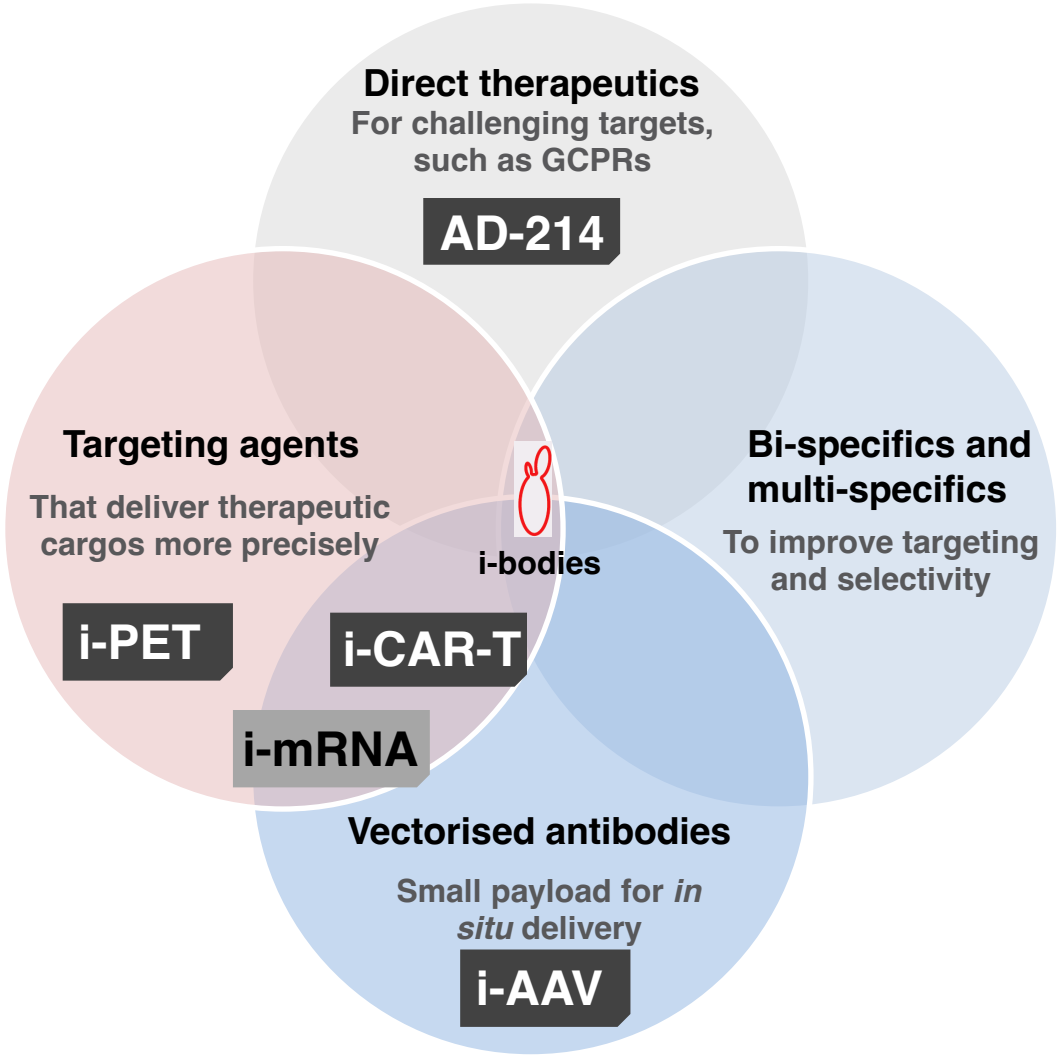
… and invention and patenting of i-bodies by adding randomized synthetic VNAR-like binding loops to NCAM-1

* Shark VNAR (red); human i-set immunoglobulins (yellow and blue)

An immensely powerful drug discovery platform applicable to multiple therapeutic formats

Current examples

Future examples



Manufacturing and delivery

- Delivery and expression *ex vivo* and *in vivo* using viral vectors or DNA/RNA
- Efficient i-body® expression in bacterial fermentation systems
- Mammalian fermentation systems for more complex formats eg i-body-Fc-fusions
- Post synthesis chemical conjugation

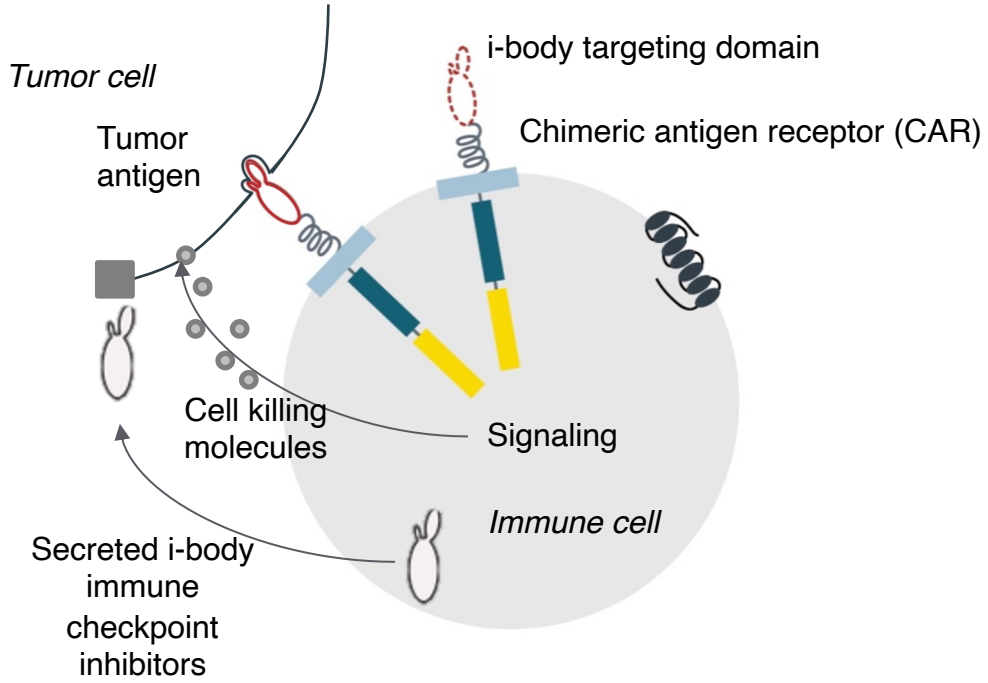
i-bodies enable optimized, multifunctional advanced therapy products when combined with partner platforms

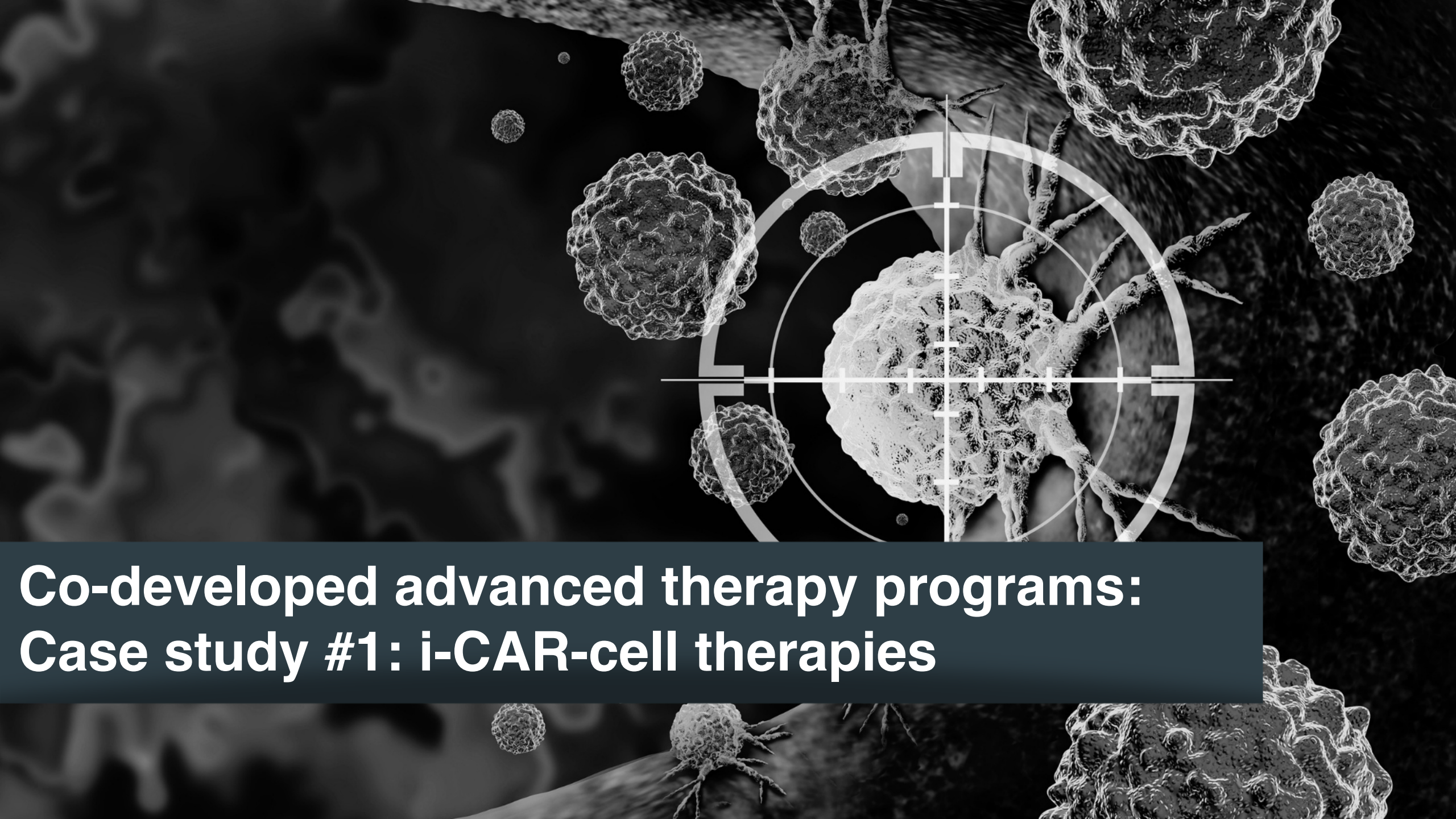
TINY i-body® needs LESS room in inserted gene, enabling MORE engineered function

Results in superior, multifunctional advanced therapy products

- **Targeting**
  - Novel (tumor) antigens;
  - Dual and bi-specific CARs
- **Persistence and performance**
  - Overcome immune suppression “checkpoints”: armored CARs
  - Enhanced trafficking, reduced exhaustion
- **Payload**
  - Higher payload for vectorized antibody therapeutics (mRNA, etc)

i-CAR-T example





Co-developed advanced therapy programs: Case study #1: i-CAR-cell therapies

The solution: Co-developed multi-specific i-CAR-T products in development with Carina Biotech (repeatable partnering model)

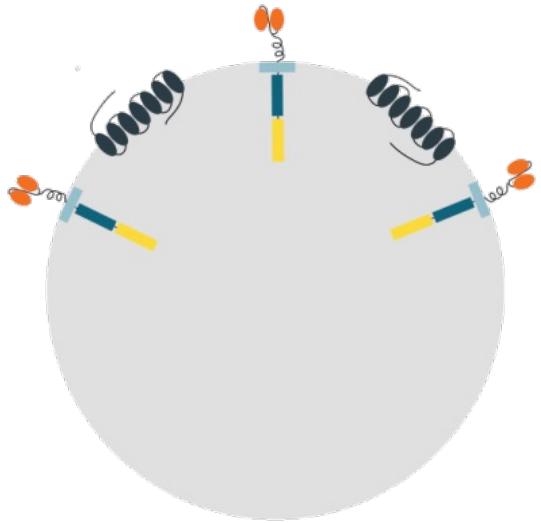
AdAlta
next generation protein therapeutics

i-body® platform

carina biotech

cell therapy platform

i-CAR-Ts for solid tumor patients



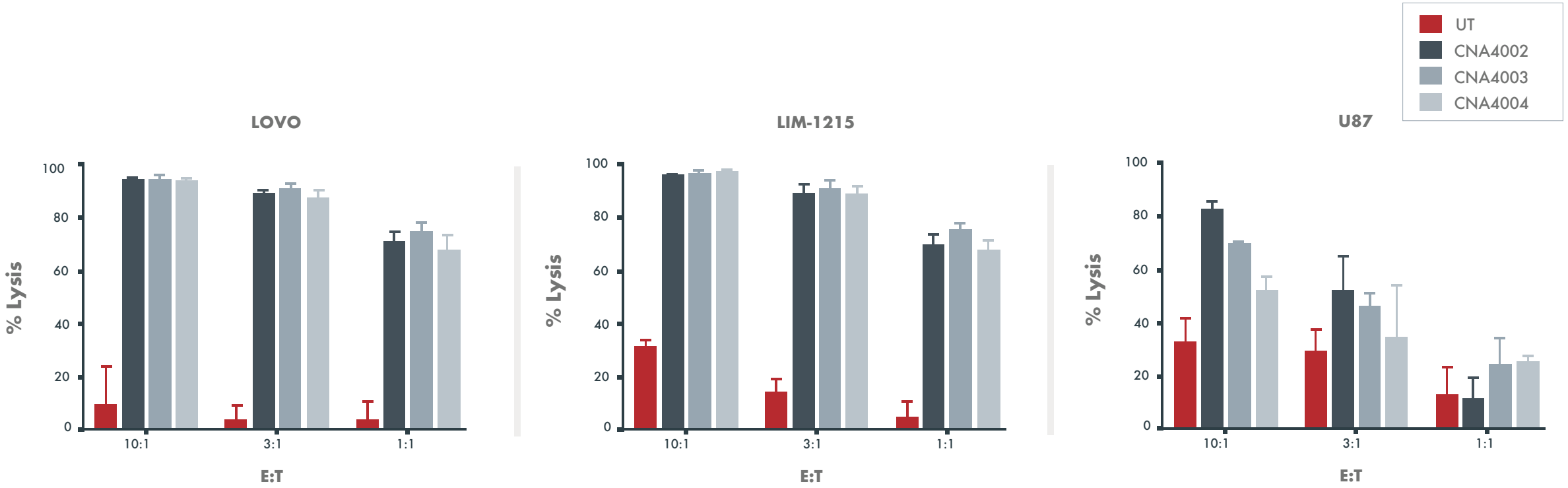
Collaboration overview

- AdAlta discovers and supplies i-bodies against solid tumor associated antigens (targets)
- Carina engineer into i-CAR-T cells and demonstrate *in vitro* cytotoxicity (cell killing)
- Joint funding of *in vivo* proof of concept studies in relevant tumor models
- Joint (50:50) ownership of resulting i-CAR-T products

Collaboration progress

- ✓ i-body® enabled CAR-T (i-CAR-T) cells have successfully demonstrated *in vitro* cancer cell line killing (lysis)
- ✓ 3 programs under way
  - Target A: progressed to *in vivo* proof of concept
  - Targets B and C in i-body® discovery

i-body enabled CAR-T (i-CAR-T) cells demonstrate *in vitro* cell killing[1]

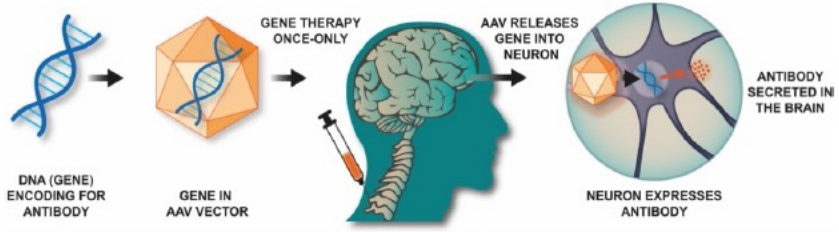


- Cell lines: colorectal cancer (LOVO and LIM1215); glioblastoma (U87)
- CAR-T constructs: CNA4002/CNA4003/CNA4004 incorporate an i-body against target “X” and variable linker lengths
- Control: unmodified T cell (UT) that does not result in significant killing (lysis) of these cell lines
- i-CAR-T cells 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]ASX Release 29 November 2021.

Co-developed advanced therapy programs: Case study #2: i-AAV *in vivo* production

AdAlta VNARs delivered to brains of mice with functional effect using AAV-5 (DegenRx owned product)



DegenRx

DOI: 10.1002/alz.040920

DRUG DEVELOPMENT

PODIUM PRESENTATIONS

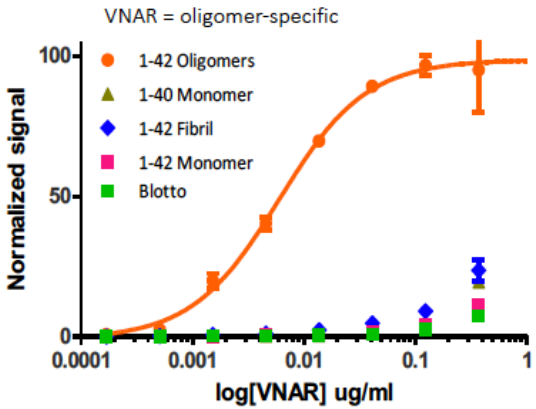
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Nonhuman: Preclinical immunotherapeutic studies

AAV mediated gene therapy as local treatment modality directed against amyloid beta oligomers in the brain using a high affinity, high specificity antibody

Bas Blits[1] | Yvonne Gouwenberg[2] | Titia Gebuis[2] | Rolinka van der Loo[2] | Ronald E. van Kesteren[2] | August B. Smit[2] | Hans Preusting[1] | **Guus Scheefhals**[1]

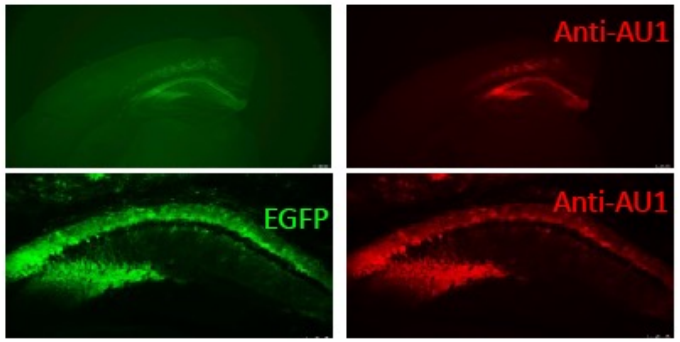
AdAlta discovered VNAR-DX001 is highly specific to ab-oligomers



VNAR-DX001 detected in CA1 region following direct hippocampal or ICV injection of AAV-5 vector

IHC on tissue section

AAV-GFP-AU-1 into CA1 (1 ul $1^{E}13$ gc/mL)



DegenRx

Improved cognition in rat AZD model (water maze test)

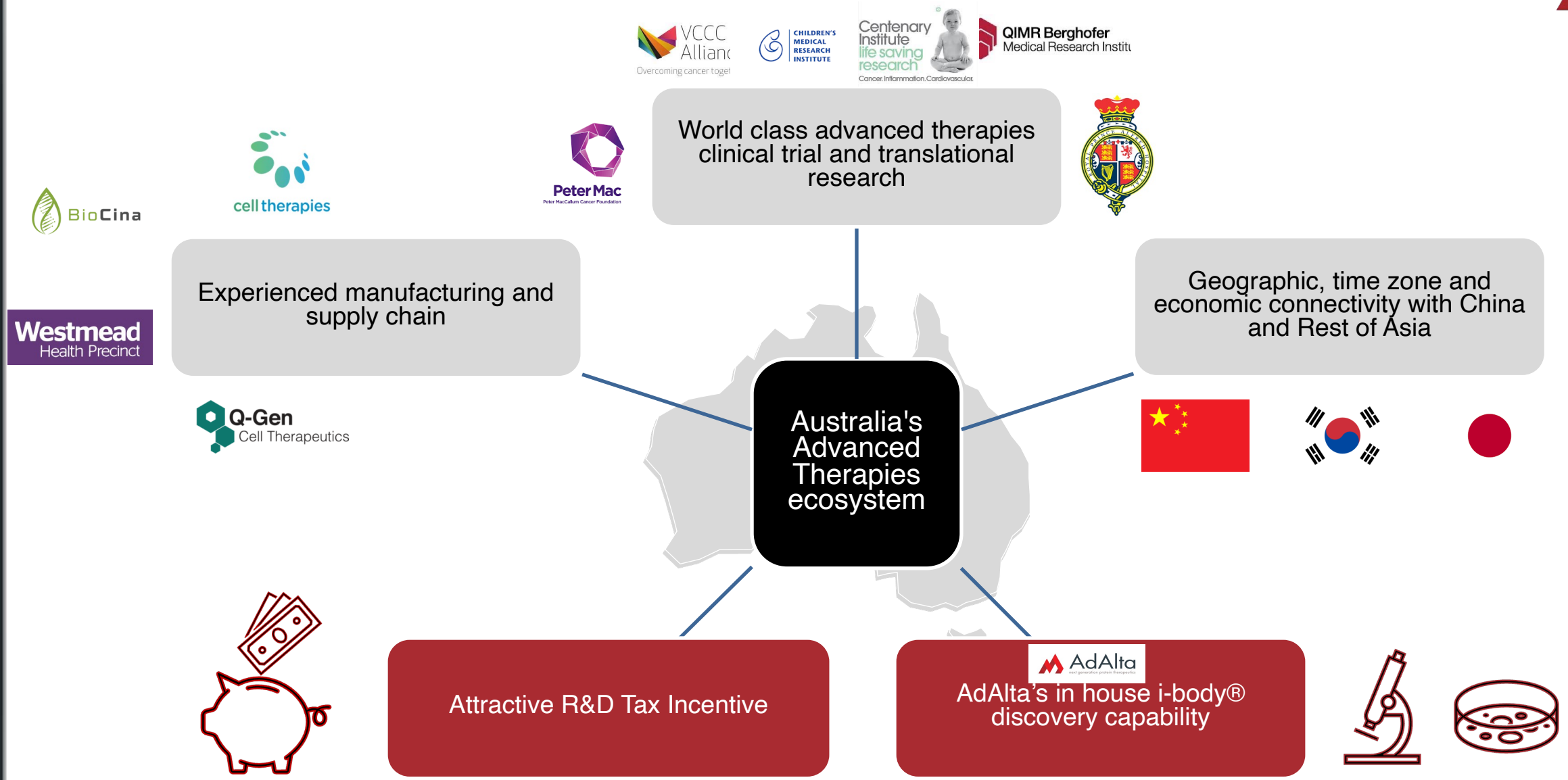
Collaboration overview

- AdAlta discovered VNAR-DX001 with high selectivity for ab-oligomers only
- VNAR-DX001 assigned to CrossBeta Biosciences and DegenRx for development

Source: Blits et al, AAV mediated gene therapy as local treatment modality directed against amyloid beta oligomers in the brain using a high affinity, high specificity antibody, *Alzheimer's Dement*, 2020 16(9) DOI: 10.1002/alz.040920; WO 2018/084712A1; DegenRx

Partnering with AdAlta for Advanced Therapies

Partnering with AdAlta brings Australian ecosystem advantages into play



Advanced therapies are key for AdAlta's growth strategy

AdAlta's three core strategies

1. Realise the value of lead asset AD-214

Near term partnering opportunities

- Out-licensing; or
- Co-development/asset financing

Advanced therapies partnering opportunities

2. Progress i-CAR and i-PET programs

- Co-development collaborations in core i-body® application areas

3. Invest in i-body® platform and pipeline

- Sponsored research collaborations in non-core i-body® application areas
- Complimentary IND ready technology and product in-licensing

AdAlta

A modern targeting system for next generation drugs

AdAlta Ltd (ASX:1AD)
Presentation to Advanced Therapies Workshop
January 2024

For more information please contact:

Tim Oldham
CEO & Managing Director
+61 403 446 665
t.oldham@adalta.com.au

Investor Relations
The Capital Network
Julia Maguire
+61 2 8999 3699
julia@thecapitalnetwork.com.au

www.adalta.com.au