

ASX Announcement | 8 April 2024
AdAlta Limited (ASX:1AD)

AdAlta and SYNthesis BioVentures partner for the development of next generation cell-based immunotherapies for solid cancers

Memorandum of Understanding (**MoU**) executed to investigate a jointly owned special purpose entity to bring Asian innovation to western patients

Investment highlights

- AdAlta and SYNthesis BioVentures Fund (SYNBV) have executed a Memorandum of Understanding (MoU) to investigate the formation of a new special purpose entity, AdCella, to provide innovative cellular immunotherapies originating in Asia with a pathway to western regulated markets and enhancement with AdAlta's i-body® technology
- Cellular immunotherapies, including CAR-T cells, are living drugs made from immune cells engineered or reprogrammed to fight cancer and are delivering transformational outcomes for patients with blood cancers
- AdAlta's i-body® technology is ideally suited to creating highly optimised, multi-functional cellular immunotherapies likely needed to deliver the same outcomes for patients with solid cancers
- The unique capabilities of the Asia Pacific region present an opportunity to create a unique pipeline of i-body® enabled assets destined for western regulated markets
- MoU formalises AdAlta and SYNBV's commitment to complete due diligence on an extensive in-licensing pipeline of potential near to clinic assets and establish AdCella, combining AdAlta's i-body immunotherapy and clinical capabilities with SYNBV's deep China expertise and access to alternative capital sources

Melbourne, Australia: AdAlta Limited (ASX:1AD) (AdAlta) and SYNthesis BioVentures Fund (SYNBV) are pleased to announce that they have executed a Memorandum of Understanding (**MoU**) to investigate the formation of a jointly owned entity, to be called AdCella, that, once established, will provide innovative cellular immunotherapies originating in Asia with a pathway to western regulated markets via Australian clinical trials and further enhancement with AdAlta's i-body® technology.

AdAlta and SYNBV join forces under an MoU to expand AdAlta's clinical stage pipeline and facilitate access to western regulated markets and i-body® technology for Asian cellular immunotherapy innovation

AdAlta and SYNBV have identified an opportunity to rapidly expand AdAlta's clinical stage pipeline in the field of cellular immunotherapy. Under the MoU executed today, AdAlta and SYNBV will investigate the formation of a jointly owned special purpose entity, provisionally named AdCella, to bring advanced cellular immunotherapy products from Asia to western regulated markets.

AdCella's objective, once formed, is to identify partners with technology platforms capable of developing multi-functional cellular immunotherapies addressing the challenges of trafficking, targeting and immune suppression in solid tumours. AdCella would then license or acquire global (outside Asia) commercialisation rights to these products in return for conducting initial clinical trials for western regulated markets in Australia and providing access to AdAlta's i-body® technology for integration into their future product pipeline. Many of the initial assets would be substantially de-risked because they will have already generated clinical data in their "home" markets.

With AdCella as their bridge to western regulated markets, partner companies will gain unique access to Australia's clinical and manufacturing ecosystem, AdAlta's capabilities to conduct clinical trials acceptable to US FDA, AdAlta's i-body® platform for the next generation of multi-functional cellular immunotherapy products in their pipeline and access to both public and private sources of capital. Australian patients may benefit from earlier access to these new therapies than would otherwise be possible without AdCella.

AdCella is the next step in AdAlta's stated strategy of building out its product development business by securing clinical stage assets that complement the i-body® platform. SYN BV's deep expertise in cross border transactions and access to alternative capital sources, especially with China, is highly complementary to AdAlta's operational and technology skills and enables AdAlta to accelerate execution of its strategy.

SYN BV Managing Director, Prof Andrew Wilks said: *"We are pleased to embark on this collaboration with AdAlta to make AdCella a reality. The opportunity to work with a quality management and clinical team while leveraging our extensive experience in China is an appealing prospect for the SYNthesis Group and for SYNthesis BioVentures in particular. We believe that this collaboration will further our fund's strategy of investing in promising early stage science by leveraging the inherent advantages of the Australian biotech ecosystem."*

AdAlta CEO and Managing Director, Tim Oldham said: *"As part of our stated strategy to expand our clinical stage pipeline with assets that work with our i-body® platform, we have identified a unique and exciting opportunity to bring highly innovative cellular immunotherapies to Australian patients. We are delighted to be working with the SYN BV team: their skills, experience and networks in drug development, capital raising and Asia complement ours and significantly strengthens AdCella's competitive position. We will be able to implement this exciting strategy much more rapidly and with greater capital efficiency and reduced risk as a result of this collaboration."*

Cellular immunotherapies are transforming cancer outcomes

Cancer is very effective at hiding from or inhibiting the effect of a patient's own immune system. Recent advances in understanding the immune system have resulted in new drugs capable of removing the brakes from, or stimulating the immune system, however better outcomes are still needed.

Cellular immunotherapies are living drugs made from a patient or donor immune cells that have been primed, engineered or reprogrammed to fight cancer. A specific example is Chimeric Antigen Receptor (CAR) cell therapies which involve modification of a patient's immune cells (T cells, NK cells, macrophages, etc) so that they produce a CAR on the cell surface that enables the patient's immune system to recognise and kill diseased cells such as cancer.

CAR-T cell therapies are revolutionising treatment of blood cell cancers. Six USA FDA approved CAR-T cell therapies¹ have been successfully used to treat patients who have failed multiple rounds of traditional therapy, with some patients experiencing more than ten years of life extension after a single CAR-T cell infusion. Building on these successes, the market for CAR cell therapies is projected to grow from US\$1 billion in 2020 to more than US\$20.3 billion by 2028,² with more than 50% of revenues to be derived from CAR-cell therapies against solid tumours by 2030.³

AdAlta's i-body® platform is ideally suited to developing next generation cellular immunotherapies for solid cancers

To deliver the same outcomes for patients with solid cancers as has been achieved for blood cancers requires cellular immunotherapies that are better at migrating or trafficking to a solid tumour, while also able to differentiate cancerous cells from healthy cells and attack cancer cells that may not all look the same (have the same antigens or targets on their surface), and overcome the immune suppressive shield raised by the tumour.

¹ <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products>

² Grandview Research, "T-cell Therapy Market Size, Share & Trends Analysis" Feb 2021

³ Polaris Market Research, "CAR-T Cell Therapy Market Share, Size Trends, Industry Analysis Report", June 2021

This requires that cellular immunotherapies for solid cancer have more features and functions engineered from the start. Since the amount of genetic material that can be inserted into a cell at once is finite, the building blocks of these functions are required to be as small as possible.

AdAlta's i-body® technology brings unique properties to the field of CAR cell therapy. Until now, fragments of monoclonal antibodies called scFv's have been used to target CAR cells to tumours. The smaller size of i-bodies makes them suitable for the creation of combination CARs capable of targeting of multiple tumour antigens. Their unique targeting capabilities enable them to target novel and difficult to access tumour antigens. Further, they are small enough to be made and secreted by immune cells to help overcome immune system suppression induced by tumours. These are significant advantages over scFv fragments, making i-bodies potentially part of the solution to extending these therapies to solid tumours. These advantages underpin AdAlta's CAR-T collaboration with Carina Biotech Pty Ltd.⁴

The unique capabilities of the Asia Pacific region present an opportunity to build a unique pipeline of i-body® enabled assets and provide them with a pathway to western regulated markets

More than half of all cellular immunotherapy clinical trials globally are conducted in China.⁵ Chinese (and Korean) companies are able to quickly and cost effectively design and optimize novel cellular immunotherapy products, including generating early clinical efficacy data. Many are already developing extensive pipelines of sophisticated, multi-functional CAR-cell therapies against novel cancer targets for use in solid tumours and have early clinical efficacy data. Equally, many of these companies lack the resources, networks and know how to translate this innovation into western regulated markets, and many are using traditional scFv technology, limiting the pace and efficiency of their pipeline growth.

Australia has world class cellular immunotherapy research, manufacturing and clinical trials capability that is compliant with, and recognized by, US Food and Drug Administration (US FDA) and European Medicines Agency (EMA) and Australian cell therapy trials remain lower cost than the US.

Combining Asia Pacific cellular therapy innovation with Australia's established cellular therapy ecosystem and AdAlta and SYN BV's skills and networks provides a pathway for these innovative products to reach a western regulated market as quickly, safely and efficiently as possible.

MoU formalises SYN BV and AdAlta's commitment to work together to pursue this opportunity

Under the MoU, AdAlta and SYN BV will work together over a period of six months (with potential to extend this collaboration for a further six months) to complete due diligence and negotiate final binding agreements and initial asset selection from a pipeline of more than ten assets and partners currently identified as suitable candidates for AdCella. Assuming success in identifying and securing suitable assets, AdAlta will own 75% of AdCella and SYN BV 25% prior to AdCella's next financing. The parties will then have the first option to participate in any future financing and will work together to secure third party financing where necessary. The costs of completing the activities contemplated by the first six months of the MoU are not expected to materially alter AdAlta's underlying operating cash requirements (after excluding costs of the recently completed Phase I extension clinical study).

Further details on the key terms of the MoU can be found in the Appendix.

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

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

⁴ <https://investorhub.adalta.com.au/announcements/4008558>

⁵ GlobalData, Pharma Intelligence Center, (accessed 24 May 2023)

For further information, please contact:

AdAlta Limited (ASX:1AD)

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

Media & Investor Enquiries

The Capital Network
Russell Katz
P: +61 2 8999 3699
E: russell@thecapitalnetwork.com.au

SYNthesis BioVentures Pty Ltd

Fabio Turatti
Managing Director
P: +61 455 365 059
E: fabio.turatti@synbv.com

About SYNthesis BioVentures

SYNthesis BioVentures is venture capital fund focused on early stage therapeutics, investing in projects from discovery through preclinical proof of concept, IND enabling studies and early clinical development. It invests in small molecule therapeutics, biologics, and cell and gene therapies for indications with significant unmet need.

SYNthesis BioVentures was founded by serial entrepreneur, Professor Andrew Wilks who has been founder or co-founder of more than nine biotechnology companies including Cytopia, where he was an inventor of momelotinib (acquired by GSK for \$1.9B) that recently became one of the few Australian derived ethical drugs to achieve FDA approval, and SYNthesis med chem, a medicinal chemistry contract research organisation based in China and successfully exited in 2020. The leadership team includes Fabio Turatti PhD, who has 20 years' experience in pharma with extensive experience in licensing and partnering transactions, start-up funding, investment and capital models and operational experience in all aspects of drug development and commercial management, and Amir Zalcenstein PhD who has 17 years' experience in healthcare and biotech capital markets, venture capital and has been CEO or co-founder of five biotechnology start-ups.

To learn more about SYNthesis BioVentures, please click here: <https://synthesisbioventures.com/>

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 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. The Company is advancing partnering discussions to finance Phase II clinical studies, preparation for which is underway.

The Company is also entering collaborative partnerships to advance the development of its i-body® platform and expand its clinical stage pipeline. 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. It has entered a Memorandum of Understanding with SYNthesis BioVentures to investigate the formation of a jointly owned entity, to be called AdCella, that, once established, will provide innovative cellular immunotherapies originating in Asia with a pathway to western regulated markets via Australian clinical trials and further enhancement with AdAlta's i-body® technology.

AdAlta's strategy is to maximise the products developed using its next generation i-body® platform by 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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Appendix

Key terms of the AdAlta-SYNBV MoU

SYNBV and AdAlta have agreed work together for a minimum of 6 months to agree on and document the establishment of AdCella and to investigate the following objectives (the **Collaboration Purpose**):

1. Complete the establishment of AdCella including initial working capital financing to complete the remainder of the Collaboration Purpose.
2. Expand and complete due diligence on a pipeline of potential assets for AdCella in the field of cellular immunotherapies for solid cancers or non-cancer indications, originating primarily in Asia and which are ready to advance to clinical studies in Australia.
3. Agree the funding required to complete a Phase I clinical trial for each asset in Australia.
4. Develop term sheets and definitive licensing agreements to secure the first of these assets.
5. Raise sufficient capital to complete first western regulated clinical proof of concept studies in Australia in relation to those assets. SYNBV and AdAlta have the right to each invest \$7.5m and a first right of refusal to contribute additional capital in equal amounts or as otherwise agreed as required by AdCella.

The 6-month term of the MoU between SYNBV and AdAlta may be extended for a further 6 months by mutual agreement (the **Term**).

The parties will use commercially reasonable endeavours to complete the Collaboration Purpose contemplated by this MoU during the Term, and will use commercially reasonable endeavours to agree and execute any transaction documents necessary to give effect to the Collaboration Purpose.

AdAlta and SYNBV intend to own 75% and 25% respectively of AdCella prior to financing the initial assets. AdCella would have an option to license AdAlta's i-body® technology and other cellular immunotherapy assets and AdAlta would provide management services to AdCella.

While the parties agree that in their view there is a reasonable probability that the pre-requisites for the establishment of AdCella (being identifying and securing assets and capital) can be achieved within the Term:

1. No party is obliged to incur any further specific costs in relation to the Collaboration Purpose or MoU;
2. Either party may, at the completion of the Term, decide not to proceed to invest in or execute AdCella transaction documents;
3. Both parties may, at the completion of the Term, by mutual agreement decide that the Collaboration Purpose cannot be achieved; and
4. Neither party shall be obligated to invest any minimum quantity of financial or other resources,

In consideration for each party incurring costs associated with negotiating the transaction documents contemplated under the MoU, from the date of the MoU each party has agreed that neither it nor its officers, employees, consultants, advisers and agents may solicit or engage in discussions to participate in any research partnerships or other investments in relation to assets evaluated as part of the Collaboration Purpose, for the Term of this MOU and for 6 months after the termination of the MoU, unless the other party otherwise agrees.