4 July 2022

ASX Announcement

AD-214 program modified to maximise partnering options, extends cash runway

Key messages

- **Development of inhaled version of AD-214 for IPF progressing**
- **Results of pre-clinical efficacy studies of AD-214 in eye fibrosis imminent**
- **Pre-clinical data demonstrating protective effect of AD-214 in a mouse model of kidney fibrosis published in peer reviewed journal**
- **Partnering discussions confirm interest in all three indications**
- **Manufacturing campaigns and toxicology studies deferred to optimally align with partner preferences and the different needs of each indication**
- **Cash runway extended via AD-214 program modification**

MELBOURNE Australia, 4 July 2022: AdAlta Limited (ASX:1AD), the clinical stage biotechnology company developing novel therapeutic products from its i-body platform, has modified the sequencing of AD-214 manufacturing campaigns and toxicology studies to better align these key programs with the emerging priorities of potential partners, and the results of pre-clinical studies due in the September quarter 2022. The Company has been able to secure a six-month deferral of pre-booked manufacturing campaigns and toxicology studies, which also ensures that AdAlta can delay financial commitments to these studies, extending its existing cash runway.

AdAlta's CEO and Managing Director, Dr Tim Oldham said:

"We are highly encouraged by the range of potential partners for AD-214, including new and confirmed existing interest generated at the BIO2022 conference held in San Diego last month and several who have signed confidentiality agreements to access additional data. Meeting their varied interests could require different manufacturing and toxicology campaigns with different associated costs to those we originally had planned. By the end of the September quarter 2022 we also anticipate having significant new pre-clinical data in multiple indications and routes of administration for AD-214.

While we have been focussed on speed to clinical trials, it is now prudent that we make final decisions about incurring the significant costs of manufacturing and toxicology with the fullest possible data and partnering information in hand, and to that end have negotiated a deferral of the commencement of these campaigns with our suppliers."

Adapting manufacturing and toxicology programs to optimise AD-214 value

The optimal volume of AD-214 to be manufactured for future toxicology and clinical studies, the final formulation step in manufacturing, and the optimal design of toxicology studies vary according to the indication to be studied in future clinical trials. The different disease area and geographic interests of different potential partners and the data that will become available through the September quarter 2022 will help shape AdAlta's formulation and partnering strategy.

To ensure that its manufacturing campaigns and toxicology studies are designed to maximise

the development options for, and hence value of, AD-214, the Company has negotiated a 6-month deferral of AD-214 production and toxicology campaigns to maximise decision-making flexibility and ensure that these significant cash commitments are made with the benefit of the maximum amount of pre-clinical data and confirmed partner indication priorities. Clinical timelines are expected be delayed by a lesser amount.

Financial impact

AdAlta will now not need to commit cash to the next round of manufacturing and toxicology costs until the end of 2022. The changes to the program as outlined above have accordingly extended the company's cash runway.

Further details about AD-214 pre-clinical programs, partnering discussions and manufacturing campaigns can be found in the Appendix below.

Authorised for lodgement by:

Tim Oldham
CEO and Managing Director
July 2022

APPENDIX

Lung fibrosis (IPF)

The current lead indication for AD-214 is idiopathic pulmonary fibrosis (IPF), for which AdAlta is developing an inhaled formulation. Successfully developing an inhaled formulation of AD-214 would improve patient convenience and cost and would also enable AD-214 to be partnered for IPF separately to kidney fibrosis.

Pre-clinical studies are progressing which demonstrate that AD-214 can be delivered to the smallest airways (alveoli) of the lungs; that it can bind to its target, CXCR4 there, and that it can block the development of fibrosis. *Ex vivo* efficacy studies in human lung tissue have commenced in our own laboratories with initial results imminent. Studies in sheep investigating how AD-214 distributes through the airways (Allergenix, Melbourne) and *in vivo* efficacy studies in the gold standard bleomycin mouse model of efficacy (LabCorp, UK) are scheduled to commence in early July 2022 with results expected by quarter end.

Eye fibrosis

Leakage of retinal blood vessels and resulting fibrosis is a major cause of blindness in diseases such as Age-related Macular Degeneration (AMD). AdAlta has previously demonstrated[1] that AD-114, the anti-CXCR4 i-body AD-114 that forms the functional part of AD-214, can reduce the size, leakiness and subretinal fibrosis in laser induced lesions in the eyes of mice.

Similar studies are now being conducted with AD-214 in both the laser induced lesion model and a second mouse model that develops leaky blood vessels spontaneously and is therefore more representative of progressive diseases such as AMD.

Analysis of tissue samples from these studies is now underway, with analysis of results

[1] See for example: XA Wang, M Foley, G Venables, E Fletcher, Inhibition of the chemokine receptor CXCR4 reduces pathology in a laser induced mouse model of choroidal neovascularisation, ARVO Annual Meeting 2017, poster 2259-B0213

expected in the next quarter. Preliminary results confirm that AD-214 is detectable in the eye for at least 30 days following intravitreal injection, supporting potential dosing schedules in line with current therapies for AMD.

Kidney fibrosis

A leading peer reviewed journal, *JCI Insights*, recently published the results of two mouse models of kidney fibrosis demonstrating that AD-114 and AD-214 play a role in protecting kidneys from fibrosis.[2] The paper was selected as an "Editors' Choice". The studies, conducted in collaboration with the laboratory of Professor Carol Pollock, University of Sydney, treated mice with folic acid or ureteral obstruction to induce kidney fibrosis. They showed that AD-114 and AD-214 normalised or reduced a variety of fibrosis responses including collagen accumulation, macrophage (immune cell) infiltration, inflammatory response and fibroblast activation in mice. *In vitro* studies showed that AD-114 blocked key fibrosis signalling pathways.

Insights from partnering discussions

AdAlta has an ongoing program to engage with potential partners for the further development and commercialisation of AD-214, including via presentation and attendance at the BIO International Convention 2022 in San Diego, USA in June. Several of these discussions have progressed to evaluation of confidential information. Significantly the interest in AD-214 extends to multiple fibrotic indications. Potential partners have different preferences for the lead indication, and hence different requirements for toxicology study design and clinical AD-214 supply should a partnering deal be achieved prior to next clinical studies.

Manufacturing and toxicology campaigns

AdAlta is aiming to develop disease specific formulations to enable multiple partnerships for AD-214. AdAlta has demonstrated that the intravenous formulation of AD-214 used in Phase I clinical studies can be nebulised for inhalation.[3] In collaboration with Vectura (UK), AdAlta is exploring whether further improvements can be made to optimise the formulation for inhalation. These studies are expected to reach a key decision point in September 2022 that will determine the formulation to be progressed into inhalation clinical studies. The Company is also engaged in continuous improvement initiatives for the manufacturing of AD-214 and of its intravenous formulation.

To support further rapid progress to IPF clinical trials, in July 2021, the Company booked manufacturing slots to enable commencement of trials in the second half of 2023.[4] Manufacturing of toxicology material and toxicology studies were scheduled accordingly. These are significant costs and they become irrevocably committed well before commencement of the campaigns.

[2] Qinghua Cao, Chunling Huang, Hao Yi, Anthony J. Gill, Angela Chou, Michael Foley, Chris Hosking, Kevin Lim, Cristina Triffon, Ying Shi, Xin-Ming Chen and Carol A. Pollock, *A single domain i-body (AD-114) attenuates renal fibrosis through blockade of CXCR4*, JCI Insight. 2022. https://doi.org/10.1172/jci.insight.143018
[3] ASX Release 9 December 2021
[4] ASX Release 1 July 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.

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 pre-clinical 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

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