5 April 2022

ASX Announcement

INHALED AD-214 PRECLINICAL PROGRAM PROGRESSING

Key points:

- **Comprehensive package of *in vivo* and *in vitro* studies underway for AD-214 in an inhaled format**
- **Aiming to confirm AD-214 can be delivered to the far airways of the lungs; be retained in fibrotic tissues; and modulate the progression of fibrosis**
- **Results expected across next two quarters**
- **Program on track to be completed in the September quarter of 2022, despite the data readout from an initial study being delayed due to technical difficulties**
- **Expert team of inhalation therapeutic advisers and contractors assisting**

MELBOURNE Australia, 5 April 2022: AdAlta Limited (ASX:1AD) the clinical stage biotechnology company developing novel therapeutic products from its i-body platform, has finalised the preclinical development program to develop an inhaled version of AD-214, its lead asset. AD-214 is being developed as a first in class therapeutic for fibrotic diseases including Idiopathic Pulmonary Fibrosis (IPF) and other Interstitial Lung Diseases (ILDs).

In July 2021, AdAlta announced the successful completion of a Phase I clinical trial assessing the safety and tolerability of AD-214 in healthy volunteers, the securing of production slots to deliver the next batch of clinical grade AD-214 in mid-2023 and that it would use the intervening period to develop a more patient convenient, lower cost inhaled formulation of AD-214.

AdAlta has now finished mapping out the preclinical development plan for the inhaled formulation of AD-214.

Dr Tim Oldham, CEO and Managing Director, commented:

"*Our team, working with world experts in various fields of inhalation drug delivery, have designed a comprehensive package of preclinical studies to demonstrate that AD-214 can be delivered to the lower airways of the lungs, distributes to fibrotic tissue and can affect the course of fibrosis once there. These are complex studies and our team's approach is to develop a rich body of evidence supporting the potential of inhaled AD-214 that does not critically depend on the results of any individual study. As the data becomes available progressively over the next two quarters, inhaled AD-214 will be further de-risked, enabling additional partnering discussions*."

The development plan addresses three questions:

1. Delivery: can nebulised AD-214 reach the lower airways of the lungs intact?
2. Distribution and retention: can AD-214, once in the lower airways of the lungs, reach and be retained in fibrotic tissue?
3. Efficacy: can AD-214 moderate fibrotic disease progression when delivered directly to fibrotic lung tissue?

The ongoing and planned experiments to address these questions are anticipated to produce a steady flow of data between now and completion in the September quarter.

Delivery, distribution and retention will be studied using PET imaging and pathology studies in both animal and *in vitro* cultured tissue models.

In vivo efficacy studies include the gold standard bleomycin mouse model of IPF. Data from this study has been delayed due to technical difficulties establishing a fibrosis baseline in the first attempt. This is not an uncommon issue for studies of this kind. This study will be repeated without affecting overall timelines.

In vivo efficacy studies will be supported by *in vitro* studies in human lung airway cells and in cultured human lung tissue. They will be further complemented by results from studies of AD-214 in animal models of other fibrotic diseases (kidney and eye).

Work to optimise a formulation of AD-214 for nebulisation and inhalation is expected to be completed in parallel with the preclinical studies, enabling large animal toxicology studies to be initiated in the March quarter of 2023. Assuming success, these will in turn enable the next clinical studies to commence in the second half of 2023 as previously announced.

Next clinical studies are anticipated to comprise an initial healthy volunteer bridging safety study which will be combined with IPF patient imaging studies using the already developed radiolabelled (for PET imaging) version of AD-214 ahead of efficacy studies in IPF patients.

The flow of results anticipated over the next three quarters is set out in the table below.

June quarter • Binding of AD-214 to CXCR4 and anti-fibrotic effects *in vitro* in cultured human lung tissue
Mid-2022 • Anti-fibrotic effects of AD-214 in cultured human lung airway cells • Distribution and retention of inhaled, nebulised AD-214 in sheep (PET imaging and pathology studies) • Manufacture of AD-214 for toxicology studies
September quarter • Efficacy of inhaled AD-214 in bleomycin mouse model of IPF • Selection of lead AD-214 inhalation formulation
December quarter • Preparation for AD-214 inhalation toxicology studies • Initiate cGMP manufacturing of AD-214 for Phase II clinical trials (booked Jul'21)

In delivering this program, AdAlta is leveraging significant global expertise in inhaled drug delivery:

- Arrangements are being finalised to conduct imaging studies of AD-214 distribution and retention with Allergenix Pty Ltd (Australia), a preclinical contract research organisation (CRO) specialising in sheep models of pulmonary drug delivery and pulmonary disease including asthma, COPD and fibrosis. Sheep lungs are structurally very similar to human lungs.

- Dr Louise Organ, who developed the sheep IPF model and has extensive experience using cultured human lung tissue to model the activity of anti-fibrotic agents, has recently joined the AdAlta team and will lead these studies.
- Prof Antje Prasse, a world recognised IPF researcher at the Fraunhofer Institute (Germany), has previously shown that AD-114, the i-body incorporated into AD-214, can inhibit the growth of spheroids from cells collected from the lining of the airways in IPF patients, and is now repeating these studies using AD-214.
- Contracts are being finalised with a new contract research organisation to overcome the technical difficulties associated with establishing fibrosis in the bleomycin mouse model of IPF to further explore distribution, retention and anti-fibrotic effect of AD-214 directly delivered to the lungs.
- Specialist inhalation contract manufacturing firm, Vectura Ltd (UK), has been contracted to optimise a formulation of AD-214 for nebulisation and inhalation.
- ITR Laboratories Canada Inc (Canada) has been contracted for inhaled toxicology studies.

AdAlta acknowledges the support of MTPConnect and the Medical Research Future Fund to this work via a Biomedical Translational Bridge Program Grant (announced December 2019 and October 2021, total funding $0.98 million).

Authorised for lodgement by:

Tim Oldham

CEO and Managing Director

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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 an agreement with GE Healthcare to co-develop i-bodies as diagnostic imaging agents against Granzyme B, a biomarker of response to immunooncology 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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