9 December 2021

ASX Announcement

INHALED AD-214 PASSES FIRST DEVELOPMENT MILESTONE

Key points:

- **AD-214 successfully nebulised, achieving important milestone on inhaled development pathway for AdAlta's lead fibrosis drug candidate**
- **AD-214 retains ability to bind to its target following pre-clinical nebulisation**
- **17-46% of an AD-214 dose delivered from commercial nebulisers could be deposited in the smallest human lung airways – exceeding AdAlta's pre-study expectations of 10%**
- **Pre-clinical efficacy studies of inhaled AD-214 have commenced**

MELBOURNE Australia, 9 December 2021: AdAlta Limited (ASX:1AD), the clinical stage drug discovery company developing novel therapeutic products from its i-body platform, is pleased to announce that initial testing of AD-214 in nebulisation devices has exceeded expectations.

AdAlta is developing a patient-preferred and lower cost inhaled formulation of AD-214 for future clinical studies in Idiopathic Pulmonary Fibrosis (IPF). An important early step in development is to ensure that AD-214 can be successfully converted to fine droplets or aerosols for penetration to the smaller airways of the lungs, a process called nebulisation. Two studies have now been conducted.

AdAlta's CEO, Dr Tim Oldham commented,
"The results of these studies support AD-214 being delivered by inhalation without losing its ability to bind to CXCR4 and at particle sizes with potential to travel to the furthest reaches of the lungs that are most affected by IPF. Simulations of the dose deposited in these regions exceeded our initial expectations. These results give us even greater confidence that we can deliver an inhaled formulation in time for scheduled future clinical studies."

In the first study, undertaken by AdAlta, AD-214 was passed through a microspray device commonly used to administer bleomycin to the lungs of mice (bleomycin is used to induce fibrosis in mice). Administering AD-214 by the same method is intended to deliver AD-214 to the regions of bleomycin induced fibrosis. AD-214 was shown to bind to its target, CXCR4, after passing through the microsprayer without signs of aggregation or degradation. Efficacy studies of AD-214 delivered by microsprayer in a bleomycin mouse model of IPF have now commenced at PharmaLegacy Laboratories (Shanghai) Co Ltd, with initial results expected early in 2022.

In the second study, AD-214 was nebulised in two commercially available nebulisers suitable for human use. The aerosol particle size and fine particle fraction (fraction of particles less than 5 μm in diameter) were measured and the fraction of the dose that would be deposited in different regions of the lung was simulated using the independent International Commission of Radiological Protection (ICRP) model. AdAlta's objective was to ensure nebulisers produced greater than 50% fine particle fraction and greater than 10% deposition in alveolar or small airway, region of the lungs which is important for IPF therapy. The study was conducted by specialist inhalation contract development and manufacturing organisation, Vectura Ltd (UK). Results significantly exceeded expectations:

Parameter	Nebuliser A	Nebuliser B
Fine particle fraction	55%	60%
Fraction of delivered dose deposited in lungs*	69%	38%
Fraction of delivered dose deposited in alveolar region of lungs*	46%	17%

* As modelled using the ICRP model

As previously announced (July 2021), AD-214 has successfully completed Phase I safety studies by intravenous administration and clinical supplies of drug substance for the next clinical trials are scheduled to be available in mid-2023. Pre-clinical PET imaging studies supported development of an inhaled formulation for those trials to improve bioavailability, improve patient convenience and reduce cost (by reducing dose).

Authorised for lodgement by:

Tim Oldham
CEO and Managing Director
December 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 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 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 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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