ASX Announcement | 19 December 2023
AdAlta Limited (ASX:1AD)

i-body®-ENABLED BREAKTHROUGH IN MALARIA TREATMENT

In collaboration with La Trobe University, AdAlta has discovered an i-body® believed to be the first ever antibody-like molecule capable of high potency inhibition of malaria parasite invasion of red blood cells and liver cells across multiple strains of the parasite. This discovery demonstrates the versatility of the i-body® platform and potentially opening new avenues to malaria treatment.

Key highlights

- **Research collaboration with La Trobe University leads to breakthrough discovery of new i-bodies which protect cells from invasion by malaria and related parasites**
- **Lead i-body® for first time achieves both binding across multiple strains of malaria and related parasites, and high potency inhibition of invasion**
- **Lead i-body® also inhibits malaria invasion of both red blood cells and liver cells, potentially breaking the malaria lifecycle at multiple stages**
- **Patent application filed and pre-print manuscript describing results published**
- **AdAlta and La Trobe are now evaluating grant funding opportunities to further explore the potential of this discovery**

AdAlta Limited (ASX:1AD) ("AdAlta" or "the Company") is pleased to announce a breakthrough from a collaboration with La Trobe University. The research has led to the discovery of a new family of i-bodies capable of inhibiting the invasion of red blood cells and liver cells by multiple strains of the malaria parasite. This is a world-first outcome[1], representing the first high potency antibody-like molecule capable of such pan-strain (multi-strain) efficacy.

La Trobe University's Prof Mick Foley, who is also AdAlta's Founding Chief Scientist, commented:

"*We believe we have delivered a world first here. Until now, no antibody-like molecule has combined the ability to bind strongly to multiple strains of malaria parasite with high potency killing. This variability between strains has plagued all previous attempts to produce a single antibody that can inhibit parasite invasion. When combined with protecting cells from invasion at two different life cycle stages of the parasite, the new i-body confers the real possibility we may be able to bring forward a new approach to treating malaria.*"

[1] Based on AdAlta's screen of publicly available information

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

"*These results are further evidence of the value of our long-standing collaboration with La Trobe University. We congratulate Prof Foley and graduate student Dimuthu Angage on these results*.

"*These outcomes once again demonstrate the versatility and power of the i-body platform to address drug targets and diseases that challenge traditional antibody approaches. This breakthrough finding in malaria is in quite a different target class and therapeutic area from our other programs, adding further value to our intellectual property portfolio and another asset with commercial potential.*"

Strain variation creates challenges for malaria treatment

AMA1 is a malaria protein that is critical to enabling invasion of malaria parasites (primarily *Plasmodium falciparum*) into red blood cells and, at a different stage of their lifecycle, liver cells. AMA1 is a major vaccine candidate and a target of immunotherapy. A key challenge in developing therapeutics or vaccines against AMA1 is the high degree of variability of parts of the AMA1 protein from strain to strain and over time. To date there has been no AMA1 antibody developed that both recognises all strains of *Plasmodium* and is a strong inhibitor of invasion.

Collaborative research with La Trobe University has delivered breakthrough outcomes

AdAlta has now overcome the challenge described above. Through a long-term collaboration with Professor Mick Foley's laboratory at La Trobe University, AdAlta has discovered i-bodies that bind with high affinity to a region of AMA1 that is conserved or constant across all *Plasmodium* strains. In *in vitro* studies, multiple *Plasmodium* strains have been shown to bind the lead i-body equally or more tightly than the natural receptor of AMA1. Further, the lead i-body was shown to inhibit multiple strains from invading human red blood cells (merozoite stage) and liver cells (sporozoite stage), interrupting the parasite life-cycle at two different stages.

The results have been published in pre-print form pending peer review at the journal Nature Communications. A copy can be accessed here: https://www.researchsquare.com/article/rs-3671797/v1. AdAlta has filed new intellectual property protecting this invention and is now seeking collaborators and grants to further develop it.

Malaria disease burden is significant, territory is expanding

The World Health Organisation's latest World Malaria Report notes that there were 247 million cases of malaria in 2021 and 619,000 deaths. Malaria continues to challenge not just developing countries where it is endemic, but also travellers, aid personnel and military personnel visiting these regions. In 2023, the US reported the first locally acquired malaria cases in 20 years and Johns Hopkins University noted that conditions are becoming more favourable for malaria transmission.[2] Locally acquired cases have been reported in EU since 2021.[3]

For a video summary of this release and opportunity to engage in virtual discussion see: https://investorhub.adalta.com.au/link/mepz1P

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

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[2] https://publichealth.jhu.edu/2023/malarias-comeback-in-the-us
[3] https://blogs.biomedcentral.com/bugbitten/2023/08/25/locally-acquired-malaria-in-europe-and-the-us/

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® enabled 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.

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