ASX Announcement

24 February 2022

Long COVID-19 strategic collaboration with US Experts

- World first study* to assess up to 7,000 plasma proteins in Long COVID-19 patients
- Collaboration with a global leader in the clinical research of neurological aspects of Long COVID-19
- Study to look for blood disease markers to assess if amenable to treatment including with ATL1102
- Retained blood samples from patients to be tested in the US by leading proteomics group
- First results from testing anticipated in mid-2022

Antisense Therapeutics Limited [ASX: ANP | US OTC: ATHJY | FSE: AWY] (the Company) today announced the signing of an agreement and the start of a collaboration to study the neurological aspects of Long COVID-19 (Long Neuro COVID-19) with US based researchers led by Dr Igor Koralnik at the Northwestern Medicine Neuro-COVID clinic in Chicago, USA. Dr Koralnik is a global leader in the field, having treated over 1,000 patients with Long COVID-19 and having published on the subject matter in peer review journals[1,2]. The collaboration is not of a fixed term and will continue through the analysis and reporting of the research results.

Under the collaboration, Dr Koralnik will provide existing blood samples, collected from previously studied Long COVID-19 patients including those with neurological symptoms where blood immune cell changes were observed[1], to generate new data on up to 7,000 protein changes in these blood samples utilising a large-scale protein analysis known as proteomics.

The cost to Antisense of the agreement is not considered financially material in the context of its annual budgeted R&D expenditure and is to be funded from existing cash reserves, however, the nature of the arrangement is considered market sensitive. Project data and results will constitute the confidential information of ANP, and will be shared in confidence with North Western University (NWU) before ANP alone files for any patent applications. There are no conditions precedent, and the agreement is effective immediately to allow the transfer of NWU patient samples to undertake the planned analysis to generate the project data. The agreement is subject to usual industry termination provisions.

Of the first 80 million people in the US diagnosed as infected and surviving COVID-19[3], approximately 30% of hospitalized patients[4] and 45% of non-hospitalized patients[5] have developed some manifestation of Long COVID-19 syndrome which suggests more than 24 million people, to some extent, afflicted by the condition. According to the US Centre for Disease Control and Prevention "Post-COVID conditions are associated with a spectrum of physical, social, and psychological consequences, as well as functional limitations that can present substantial challenges to patient wellness and quality of life"[6].

Long Neuro COVID-19 is hypothesized to follow SARS-CoV-2 virus specific pathophysiological changes, with aberrant inflammatory disease and immune responses post-acute infection, similar to that reported with other viral infections including Epstein-Barr Virus (EBV) and associated Chronic Fatigue Syndrome[2]. Notably patients who had COVID-19 while also infected with EBV were at an increased risk of memory loss[7] and EBV infection increases the risk of autoimmune diseases such as Multiple Sclerosis (MS)[8] and associated adverse neurological manifestations. ANP's immunomodulatory drug ATL1102 has previously demonstrated biologic activity in MS patients[9].

The retained blood samples will be shipped to an industry leading proteomics group Somalogic in Boulder Colorado USA to be tested using their SomaScan® assay.[10] The data will then be analyzed to identify any proteins significantly affected in the blood of convalescent Long COVID-19 patients with no persistent symptoms and Long Neuro COVID-19 patients compared to healthy subjects in order to identify the proteins that are modulated in Long Neuro COVID-19 disease pathology and to assess if it is potentially amenable to treatment, including with ATL1102. Being able to access these existing clinical samples and test using the SomaScan® assay avoids the time and costs of undertaking a

prospective experimental study to collect such samples and enables ANP to be the first to generate the broadest search of plasma proteins conducted in this disease* and do so in a most cost effective manner.

The effects of ATL1102 were assessed by the SomaScan® assay of blood samples from the Phase II study in non-ambulant patients with DMD, where positive modulation of blood proteins were observed (data presented at the 2021 World Muscle Society conference – refer 24 September 2021 ASX announcement). ANP will now look to leverage this proteomics experience in this study focusing on patients with Long Neuro COVID-19.

Dr Koralnik said, "I am pleased to be collaborating with Antisense Therapeutics in the research field of Long COVID-19. COVID-19 is causing significant long term cognitive and fatigue complications in sufferers in hospitalized and non-hospitalized patients and also in people infected after vaccination. Cognitive assessment of non-hospitalized patients with Long COVID-19 showed significantly lower scores than the normal population on processing speed, attention and working memory. This proteomics study collaboration represents an important step forward towards the goal of understanding Long Neuro COVID-19 and potential for interventional treatment."

Dr George Tachas Director of Drug Discovery at Antisense Therapeutics said, "The Company is looking to capitalise on its deep understanding and experience in inflammatory and immune disease and the power of Somalogic's large scale proteomics platform testing to help shed light on Long Neuro COVID-19. Our goal is to identify new ways to better treat a disease that is negatively impacting the lives of millions of people around the world. This will be the first study of its kind in the world in characterizing 7,000 blood plasma changes in Long Neuro COVID-19 patients* and so we look forward to working with Professor Koralnik and his team to generate this novel data to identify opportunities for the diagnosis, prognosis and treatment of Long Neuro COVID-19 and for the new intellectual property that we anticipate to emerge from this exciting collaboration."

The first results from the testing of Long Neuro COVID-19 patient samples are anticipated in mid-2022.

This announcement has been authorised for release by the Board.

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* ANP is the first Company to utilize Somalogics proprietary SomaScan® assay for the analysis of plasma proteins in Long COVID-19 patients. The SomaScan® assay is 'the first and only platform that can simultaneously measure 7,000 proteins across a wide range of concentrations'.
https://somalogic.com/

About Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], is an Australian publicly listed biotechnology company, developing and commercializing antisense pharmaceuticals for large unmet markets in rare diseases. The products are in-licensed from Ionis Pharmaceuticals Inc. (NASDAQ: IONS), an established leader in antisense drug development. The Company is developing ATL1102, an antisense inhibitor of the CD49d receptor, for Duchenne muscular dystrophy (DMD) patients and recently reported highly promising Phase II trial results. ATL1102 has also successfully completed a Phase II efficacy and safety trial, significantly reducing the number of brain lesions in patients with relapsing-remitting multiple sclerosis (RRMS).

About ATL1102 ATL1102 is an antisense inhibitor of CD49d, a subunit of VLA-4 (Very Late Antigen-4). Antisense inhibition of VLA-4 expression has demonstrated activity in a number of animal models of inflammatory disease. ATL1102 has also shown to be very effective in reducing inflammatory brain lesions in patients with MS (Limmroth, V. et al Neurology, 2014; 83(20): 1780-1788) and recently delivered highly promising clinical results in patients with Duchenne muscular dystrophy (DMD) a rare and fatal muscle wasting disease where inflammation in the muscle leads to fibrosis and death of muscle tissue.

About Long COVID-19 In the US of the first 80 million people diagnosed as infected and surviving COVID-19[3], approximately 30% of hospitalized patients[4] and 45% of non-hospitalized patients[5] have developed some manifestation of Long COVID-19 syndrome (i.e more than 24 million people). According to the US Centre for Disease Control and Prevention "Post-COVID conditions are associated with a spectrum of physical, social, and psychological consequences, as well as functional limitations that can present substantial challenges to patient wellness and quality of life".[6] Confirmed infections numbers which increases daily can be followed on these links below[3]. Long COVID-19 cases in Australia before the Omicron wave were estimated at 20,000[11]. A body of published evidence now demonstrates that the SARS-CoV-2 virus causes long COVID-19 with impacts that last by definition for 28 days post COVID-19 symptom onset[1] and that can last for 12 weeks and well beyond[6]. Long COVID-19 can occur post severe COVID-19, and post mild to moderate COVID-19. In the US Long COVID-19 patients comprise 13% of subjects post severe COVID-19 who have previously being hospitalized and 87% of subjects post mild-moderate COVID-19 who have not been hospitalized. In the latter there is ~2:1 ratio of females to males, like in autoimmune disease multiple sclerosis and the main neurological symptoms reported were 81% brain fog (defined with the established memory tests conducted), 68% headache, 60% numbness/tingling 59% dysgeusia, 55% anosmia, and 55% myalgias, and additionally 85% experienced fatigue, which are not well understood.[2] While COVID-19 incidence and severity is being reduced with vaccines numerous studies connect the SARS-CoV-2 virus infection to long term neurological conditions in both hospitalized and non-hospitalized patients after vaccination[12].

References

1. Visvabharathy L, and Koralnik, I.J et al " Neuro-COVID long-haulers exhibit broad dysfunction in T cell memory generation and responses to vaccination." https://www.medrxiv.org/content/10.1101/2021.08.08.21261763v3
2. Graham E.L and Koralnik I.J et al. "Persistent neurological symptoms and cognitive dysfunction in non-hospitalized COVID-19 "Long Haulers" ". Ann. Clinical and Translational Neurol 2021, 8(5):1073-1085 https://onlinelibrary.wiley.com/doi/epdf/10.1002/can3.51350
3. https://coronavirus.jhu.edu/map.html and https://www.worldometers.info/coronavirus/country/us/ as of 21 February, 80.1 million people in the USA were diagnosed with COVID-19, 959,000 deaths have been recorded, and 51.6 million people have recovered.
4. Chen Chen et al "Global prevalence of Post-Acute Sequelae of COVID-19 (PASC) or Long COVID: A meta-Analysis and Systematic Review. https://www.medrxiv.org/content/10.1101/2021.11.15.21266377v1
5. Estiri H et al "Evolving phenotypes of non-hospitalized patients that indicated long COVID". BMC Medicine (2021) 19: 249 https://doi.org/10.1186/s12916-021-02115-0
6. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-clinical-eval.html
7. Su Y et al, "Multiple Early Factors Anticipate Post-Acute COVID-19 Sequelae". Cell, 2022; DOI: 10.1016/j.cell.2022.01.014 and https://www.livescience.com/long-covid-four-potential-risk-factors
8. Bjornevik K et al., Science 375, 296–301 (2022) DOI: 10.1126/science.abj8222
9. Limmroth V, Barkhof F, Desem N, Diamond M.P and Tachas G. "CD49d antisense drug ATL1102 reduces disease activity in patients with relapsing-remitting MS". Neurology, 2014; 83(20): 1780-1788) https://pubmed.ncbi.nlm.nih.gov/25239835/
10. https://somalogic.com/life-sciences/ 7,000 analytes, 450,000+ samples run, >400 publications, >500 patents.
11. "Mass disability event" warning as huge numbers diagnosed with Long Covid" Matt Young https://www.news.com.au/technology/science/human-body/mass-disability-event-warning-as-huge-numbers-diagnosed-with-long-covid/news-story/d541286fc71ac1b2a262ac798238d4ec
12. Ledford H "Do vaccines protect against Long COVID? What the data say", Vaccines reduce the risk of developing COVID-19- but studies disagree on their protective effect against long COVID. 23November 2021 https://www.nature.com/articles/d41586-021-03495-2