ASX Announcement

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Long COVID-19 study identifies novel blood markers as potential diagnostic and therapeutic targets

- World first study utilizing Somalogic SomaScan® assay# to assess up to 7,000 plasma proteins in Long COVID-19 patients has elucidated novel blood markers as potential diagnostic and therapeutic targets
- Provisional patent applications have been filed in the United States (US) to seek protection for these new inventions
- A potential therapeutic marker known to be modulated by ATL1102 in DMD patients has been identified as suggestive of its therapeutic potential as a treatment for Long COVID-19
- Collaboration with global leader in the clinical research of neurological aspects of Long COVID-19 Dr Koralnik to continue with application for grant funding
- Company plans to review its new patent applications with targeted pharmaceutical and diagnostic companies for potential commercial discussions

Antisense Therapeutics Limited [ASX: ANP | US OTC: ATHJY | FSE: AWY] (the Company) is pleased to advise of outcomes from its collaboration to study the neurological aspects of Long COVID-19 (Long Neuro COVID-19) with US based researchers led by global leader in the field, Dr Igor Koralnik, at the Northwestern Medicine Neuro-COVID clinic in Chicago, USA. The study has elucidated novel blood markers as potential diagnostic and therapeutic targets in the treatment of Long COVID-19 patients. Three (3) provisional patent applications have been filed in the US to seek protection for these new inventions.*

Under the collaboration, blood samples that had been collected from Long COVID-19 patients who had not been hospitalized (focused on those with neurological symptoms including brain fog, where blood immune cell changes were observed[1]), were used to generate data on up to 7,000 proteins in the blood utilising a large-scale protein analysis known as proteomics. Industry leading proteomics group Somalogic in Boulder Colorado USA undertook the analysis, successfully testing the samples using their SomaScan® assay and then the data was statistically analyzed using their Dataviz program[2].

The analyzed data has identified a number of proteins that are significantly modulated in the blood of Long Neuro COVID-19 patients when compared to convalescent subjects who had recovered from Long COVID-19 infection with no persistent symptoms and to healthy subjects. This data has been included in recently filed patent applications as potential diagnostic and therapeutic targets for the treatment of Long COVID-19. Certain targets when combined (as few as 5) identified all 48 Neuro Covid-19 patients and the 42 of 44 subjects who were convalescent or healthy controls suggestive of these targets' diagnostic potential. A number of targets (<15) have been identified as potentially amenable to treatment by currently available drugs or other therapeutic approaches on the market. The mechanisms of action of those drugs are known to modulate the discovered target proteins, therefore the marketers/developers of those drugs have been identified as initial prospects for partnering interest. A smaller number of diagnostic markers have been detected that could assist in the identification of Neuro Long Covid patients for better designed clinical trials and potentially for earlier treatment intervention. Accordingly, the Company also plans to review its newly generated intellectual property (IP) with targeted pharmaceutical and diagnostic companies for potential commercial discussions, noting that for these discussions to progress, the Company and potential partner companies would need to agree on licensing and/or joint development of this newly generated IP to advance as either diagnostic or therapeutic programs.

Of the 94.7 million people in the US diagnosed as infected and surviving COVID-19[3], approximately 82 million (87%) people are non-hospitalized[4], and 45% of non-hospitalized patients[5] have developed some manifestation of Long COVID-19 syndrome which suggests more than 24 million people are afflicted by the condition to some extent. The main neurological symptom is brain fog (defined with the established memory tests conducted) and reported in 81% suggesting an impact on nearly 20 million people in the US.

Identification of appropriate biomarkers of Long COVID-19 have proved elusive.[6] The National Institute of Health (NIH) in the US is funding a national research effort focused on understanding and treating Long COVID-19 beyond US$1billion it has already committed.[7]

One of the aims of the proteomics analysis was to assess if Neuro Long COVID-19 patients may have been amendable to treatment with ANP's immunomodulatory drug ATL1102 which has previously demonstrated biologic activity in MS patients[11] and the ability to reduce T cells and modulate proteins involved in the blood of DMD patients (data presented at the 2021 World Muscle Society conference WMS-ATL1102-DMD-PROTEOMICS-Poster). Encouragingly, one of the potential therapeutic markers in Long COVID-19 patients identified from this proteomics analysis is also known as having the potential to be significantly modulated by ATL1102 in DMD patients and therefore is suggestive of its therapeutic potential in Long COVID-19. The Company is looking to further explore the clinical potential of ATL1102 in this setting via applying for grant funding opportunities (such as that as offered by NIH) in collaboration with Professor Koralnik.

Dr Koralnik said, "The collaboration with Antisense Therapeutics has generated promising novel data in Long COVID-19 patients in identifying potential disease biomarkers and represents an important advance towards the goal of establishing effective disease diagnostics and interventional treatments. We look forward to continuing our scientific collaboration with Antisense Therapeutics and to advancing such endeavors through our active involvement and support in seeking grant applications including with bodies such as the NIH."

Dr George Tachas Director of Drug Discovery at Antisense Therapeutics said, "We are delighted to report on the initial outcomes from this novel and leading scientific collaboration with Professor Koralnik and his team. Our data has identified potential new avenues towards diagnoses and treatment of a disease that has negatively impacted the lives of over a hundred million people around the world. We look forward to continuing scientific advancements in the space in collaboration with Professor Koralnik and the further important IP that we anticipate emerging from this important scientific collaboration."

For further details please refer to the presentation following this announcement.

This announcement has been authorised for release by the Board.

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ANP is the first Company to utilize Somalogic's 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/

* Patent application names:
"Biomarkers and Uses thereof"
"Methods for treating neurological post-acute sequelae of COVID-19 (NPASC)"
"Methods for diagnosing and treating neurological post-acute sequelae of COVID-19 (NPASC)"

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 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[9] 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".[10] Confirmed infections numbers which increases daily can be followed on these links below[3]. Long COVID-19 cases in Australia were recently estimated at 475,000[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[9]. 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.[4] 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. https://somalogic.com/stats-data-viz/ and https://somalogic.com/life-sciences/ 7,000 analytes, 450,000+ samples run, >400 publications, >500 patents.
3. https://coronavirus.jhu.edu/map.html and https://www.worldometers.info/coronavirus/country/us/ as of 16 August 2022, 94.7 million people in the USA were diagnosed with COVID-19, 1.063 million deaths have been recorded, and 89.9 million people have recovered.
4. 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
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.msn.com/en-us/health/medical/brain-fog-and-other-long-covid-symptoms-can-last-more-than-a-year-according-to-study/vi-AA10gBis
7. https://www.cbsnews.com/news/long-covid-research-funding/.
8. 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/
9. 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
10. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-clinical-eval.html
11. https://www.abc.net.au/news/2022-08-11/long-covid-and-chronic-fatigue-syndrome-pathology-overlap/101318522
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
13. "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