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Opportunity

To support funding stage 2 clinical trial for the second-generation COVID-19 vaccine through licensing or direct investment, contact:

Dr Anna Malinovitch
E: anna.malinovitch@unimelb.edu.au

Second-generation COVID-19 vaccine

Safe and Efficacious Protein-based COVID-19 vaccine based on Phase 1 Clinical Trial Data

The Technology

- Second generation recombinant protein RBD SARS-CoV-2 vaccine that focuses the immune response to the receptor-binding domain which is the primary target for neutralising antibodies including cross-protective determinants and offers potential production and manufacturing advantages as well as strong neutralizing activity against multiple SARS-CoV-2 variants of concern.

Market Need

- Emerging mutant variants of SARS-CoV-2 are less susceptible to the immunity produced by the first generation COVID-19 vaccines that are based on the S protein antigen.
- A highly stable vaccine that can be efficiently produced, stored and transported without freezing will be valuable in distribution across the globe including countries that have limited frozen/cold chain storage.

Technology Status

- The University RBD SARS-CoV-2 vaccine has been found to be both safe and efficacious in Phase 1 Clinical Trial.

Market Need

The COVID-19 pandemic caused by SARS-CoV-2 has infected over 689 million people, claimed more than 6 million lives and has had a significant adverse effect on economies globally. Safe and effective vaccines have a critical role in controlling the spread of COVID-19 and overcoming the pandemic.

Currently available 'first-generation' COVID-19 vaccines, including adenovirus-vectored, mRNA, and protein-subunit vaccines, use antigens based upon the SARS-CoV-2 full-length Spike (S) protein. These S protein vaccines are associated with relatively rare but serious adverse events including thrombocytopaenia with thrombosis syndrome with the adenovirus-vectored vaccines (e.g., Astra Zeneca), and myocarditis with the S mRNA vaccines (Pfizer and Moderna). Furthermore, as the pandemic evolves, mutations are emerging that are less susceptible to the immunity produced by these vaccines.

Solution and Technology Status

Professor Dale Godfrey and his team at the Doherty Institute for Infection and Immunity have developed an RBD-based SARS- CoV-2 protein vaccine candidate. The technology uses just the receptor-binding domain (RBD) region of the S protein as an antigen which offers potential advantages of focusing immunity to the key protective determinants. As an immunogen, the RBD shares multiple positive attributes with the full-length S protein, as well as potential production and manufacturing advantages such as delivery of abundant, temperature-stable vaccine doses at an affordable cost. Its highly efficient production means that, if necessary, the vaccine can also be rapidly modified to match new variants that arise.

This second generation COVID-19 vaccine induces high titres of RBD-specific antibodies, including high neutralising antibody titres, in mice following a prime and boost regimen. Immunity induced by this vaccine is durable and protects against virus challenge in a mouse model of SARS-CoV-2 infection, even 100 days following the boost. It induces strong neutralising antibody immunity activity against the original Wuhan strain, as well as against Beta, Delta and Omicron SARS-CoV-2 variants.

Technology Status

Phase 1 clinical trial to evaluate the safety and immunogenicity of SARS- CoV-2 beta variant RBD recombinant protein vaccine adjuvanted with MF59® as a 4th dose booster has now been completed. There were no safety concerns and the reactogenicity profile was mild and similar or better than licensed COVID vaccines. The beta RBD vaccine boosted immune responses against beta, ancestral and omicron BA5 strains based on microneutralisation assay. Based on the multiplex surrogate virus neutralization test and/or pseudovirus neutralisation test data, neutralising antibody titres against several other variants of concern, including omicron subvariants (BA.1, BA.2, XBB, XBB.1.5 and BQ.1.1) were also boosted by the vaccine. The vaccine also boosted CD4 and CD8 T cell responses.

Phase 1 Clinical Trial Data

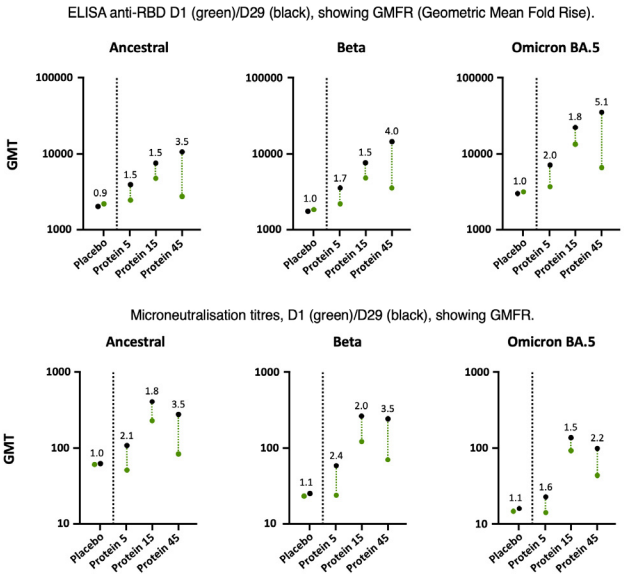

Figure 1. (a) ELISA anti-RBD D1 (green) /D29 (black), showing GMFR. Serial dilutions of sera were tested. The RBD vaccine demonstrated effects against non-target SARS-CoV types and strains, including the ancestral strain, omicron variants (BA1, BA2, BA5, BQ.1.1, XBB, and XBB.1.5), alpha, delta, gamma, lambda, mu and SARS-CoV-1. There was a clear positive dose-response relationship for the booster responses (GMFR).

(b). Micro-neutralisation titres, D1 (green)/D29 (black), showing GMFR. Serial dilutions of sera were incubated with 100 TCID50 (50% tissue culture infectious dose) of SARS-CoV-2 ancestral, beta or omicron BA.5 viruses, and residual virus infectivity was assessed in Vero E6-TMPRSS2 cells. Viral CPE was read on day 5. Dilution of serum that completely prevented CPE in 50% of the wells (ID50) was calculated.

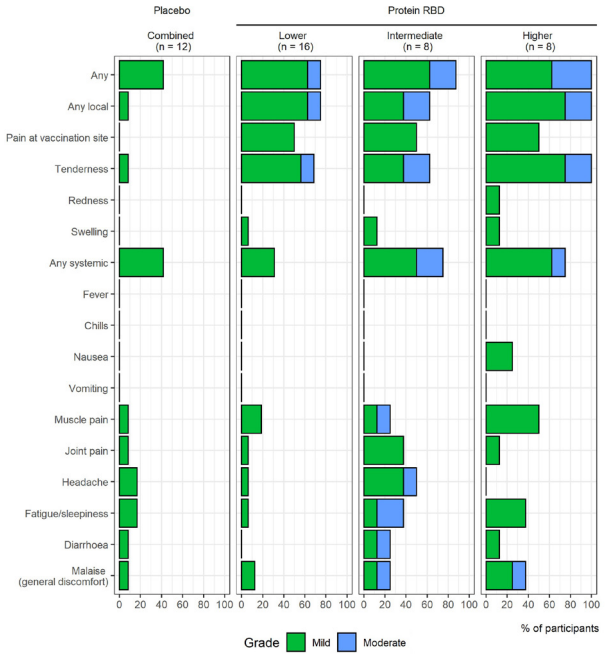

Figure 2. No vaccine-related Serious Adverse Event (SAEs) occurred. The protein RBD vaccine reactogenicity profile was mild (no Grade-3 reactions).

More Phase 1 Clinical trial data is available upon request.

Tech name and number	2020-111 Second-generation RBD COVID-19 vaccine
Researchers	Prof. Terry Nolan, Dr. G. Deliyannis, Dr. N. Gherardin, Prof. D. Purcell, Professor D. C. Jackson, Prof. D. Godfrey
Publications	Deliyannis et al. Broad immunity to SARS-CoV-2 variants of concern mediated by a SARS-CoV-2 receptor-binding domain protein vaccine. eBioMedicine, vol. 92, 104574, JUNE 2023 https:// doi.org/10.1016/j.ebiom.2023.104574 T. Nolan et al. Phase I trial of novel SARS-CoV-2 beta variant receptor-binding domain recombinant protein and mRNA vaccines as a 4th dose booster. Poster presentation at the ECCMID 2023 https://www.eccmid.org/online-platform
Patents	PCT/AU2021/051553 "Coronavirus vaccine" filed on 23/03/2022 International Publication NO.: WO 2022/133547, priority date 23 December 2020 PCT/ AU2023/050093PCT "Coronavirus vaccination regimen" filed on 10 February 2023, priority date 11 February 2022
Keywords	COVID-19 vaccine, RBD, Phase 1 clinical trials

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