RAPID RESPONSE PIPELINE FOR STABILIZED SUBUNIT VACCINES

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The Coalition for Epidemic Preparedness Innovations (CEPI) have recently put out a call for proposals aimed at platform technologies that can enable rapid vaccine development for novel or previously unrecognized viruses. We have proposed a streamlined process for the generation of stabilized subunit vaccines. This project brings together unique proprietary recombinant technology for generating stabilized subunit vaccines (the molecular clamp), a highly skilled team from some of Australia's leading scientific organizations and world-class facilities. Molecular clamp is a broadly applicable platform technology that facilitates expression of recombinant viral glycoproteins in subunit form without loss of native antigenicity. The molecular clamp imparts superior stability over alternative trimerization domains, efficiently stabilizing soluble viral fusion proteins in their native trimeric 'pre-fusion' form. This form is equivalent to that expressed on the virion surface and the principle target for a protective neutralizing antibody response. Through stabilization of the pre-fusion form, the molecular clamp promotes the production of highly neutralizing and broadly cross-reactive antibodies. Importantly, the molecular clamp does not required prior knowledge of a proteins quaternary structure.

The goal of this project is to establish a holistic and robust pipeline to rapidly generate novel subunit vaccines purely from sequence information. Within this pipeline, pre-clinical development, including the generation of evidence for safety and immunogenicity in animal models, is to be completed within a 16 week window allowing candidate vaccines to then progress directly into Phase I clinical trials. Phase I trials, including regulatory approval, patient immunization and analysis of safety and immunogenicity will be completed within 10 weeks (week 17-26 of the pipeline). As part of the project, large-scale manufacture of >200,000 vaccine doses will be completed within a further 8 weeks. Vaccine produced through this pipeline will therefore be available for rapid deployment and provide the best possible opportunity to counter emerging viral epidemics.

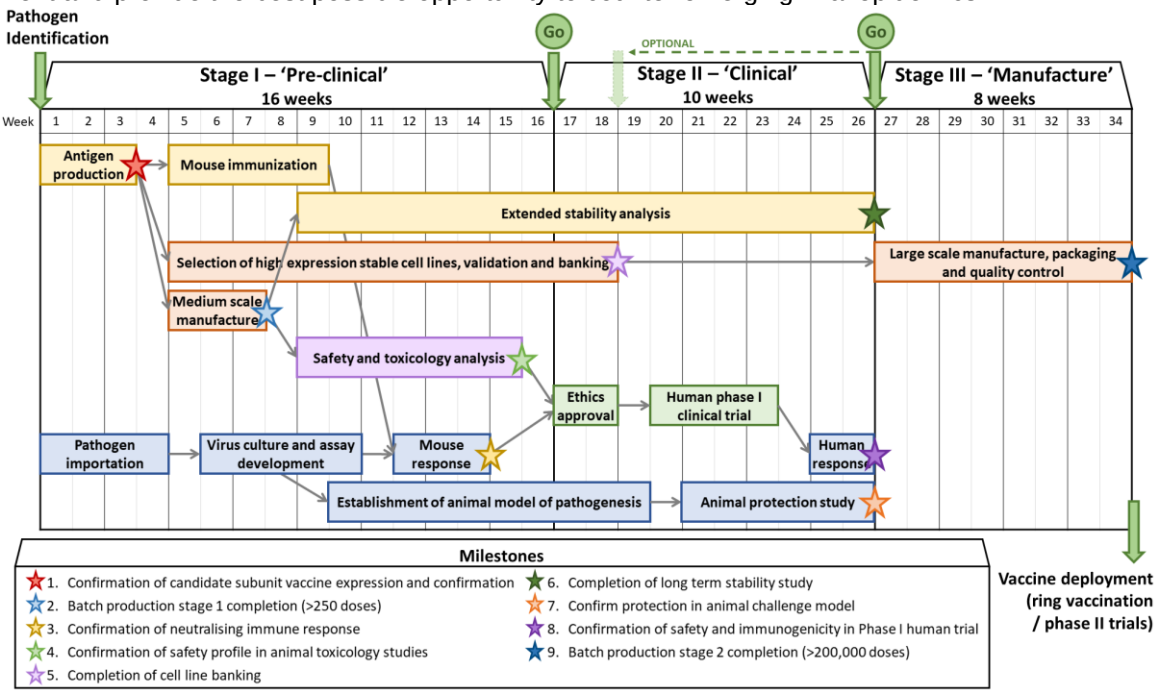

Figure 1. Overview of rapid response pipeline design. Key pipeline components are designated by color. Yellow: Vaccine design and animal immunizations; Red: Vaccine manufacture; Purple: Toxicology analysis; Blue: Immunogenicity and animal protection studies; Green Phase I clinical trials. Note: stage III is able to be optionally triggered at week 18, prior to completion of stage II. Early triggering of stage III at week 18 in the event of a 'worst case scenario' will decrease the total time to deployment to 26 weeks from pathogen identification.