A LIVE ATTENUATED RSV VACCINE, PROCESS DEVELOPMENT STUDIES

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Respiratory Syncytial Virus (RSV) is the leading cause of lower respiratory tract disease in infants and young children. A vaccine to prevent the high burden of disease caused by RSV is urgently needed, but not available.

A live attenuated respiratory syncytial virus (RSV) vaccine for intranasal delivery is currently under development at Intravacc. The vaccine concept comprises a live Glycoprotein-complemented RSVΔG virus. This G-RSVΔG virus is generated by proliferation of an RSVΔG on G-expressing Vero cells. The vaccine thus contains virus particles that have the G-protein on their surface but not in their RNA genomes. This recombinant virus is highly attenuated compared to wild type RSV and therefore presents a live attenuated vaccine candidate for RSV infection.

A vaccine production process has been setup for the production of Phase I clinical lots. In short, the production process steps are: cell and virus culture, clarification, continuous flow density gradient ultracentrifugation, ultra/diafiltration, filling and lyophilization.

An example of process development is the design of the cell and virus culture method. Using the statistical design of experiment approach the virus culture has been optimized to both virus yield and harvest quality. As RSV is a filamentous virus, the optimization of harvest quality with respect to purification opportunities is pivotal. This DoE was done at lab-scale bioreactors (2-L) and the chosen conditions were successfully scaled-up to 50-L single use bioreactors. Preparation of preclinical and clinical lots is done at this scale.

The pre-clinical studies were successful. In the cotton rat model, the G-RSVΔG vaccine is safe, immunogenic and protects against challenge with wild type RSV. The following step, a clinical Phase I study, is planned.