Project Brief: Pfizer RSV Vaccine Study

Full Title of Study/Programme	A phase 3, randomized, double-or observer-blinded, placebo-controlled trial to evaluate the efficacy and safety of a respiratory syncytial virus (RSV) prefusion f subunit vaccine in infants born to women vaccinated during pregnancy
Technical Focus Area	Research (Paediatrics and Maternal)
Rationale	There is a large unmet medical need that could be addressed by an effective RSV prophylaxis in infancy. Given the global burden of disease in millions of cases each year, maternal immunization offers an attractive strategy for infant disease prevention. Both preclinical studies in animals and interim data from a Phase 1/2 study in healthy nonpregnant adults have demonstrated acceptable tolerability and safety of RSVpreF. A robust immune response has also been observed in population of the aforementioned trial at I month after vaccination. The combined RSV A and B serum neutralization geometric mean titers (GMTs) have been shown to be 12 to 20 times higher than those with 100 ug/ml of palivizumab, the concentration of monoclonal antibody that is known to provide near to complete protection of high risk infants from severe RSV disease. RSVpreF is currently under assessment in healthy pregnant women 18 through 49 years of age (Study C3671003: A Phase 2b,Randomized, Placebo-Controlled, Observer-Blinded Trial to Evaluate the Safety, Tolerability, and Immunogenicity of a Respiratory Syncytial Virus (RSV)Vaccine in Pregnant Women 18 Through 49 Years of Age and Their Infants; ClinicalTrials.gov identifier: NCT 04032093). This randomized, double-or observer-blinded, placebo-controlled Phase 3 study is designed to evaluate the efficacy and safety of maternal immunization with RSVpreF against medically attended RSV-associated LRTI in infants.
Primary Efficacy Objectives in Infant Participants	• To evaluate the efficacy of RSVpreF in reducing the incidence of MA-LRTI due to RSV and severe MA-LRTI due to RSV
Primary Safety Objectives- Infant Participants	• To describe the safety of RSVpreF
Secondary Efficacy Objectives – Infant Participants	• To evaluate the efficacy of RSVpreF in reducing the incidence of hospitalization due to RSV • To evaluate the efficacy of RSVpreF in reducing the incidence of all- cause MA-LRTI
Primary Efficacy Endpoints – Infant Participants	RSV-positive MA-LRTI as confirmed by endpoint adjudication committee (EAC) • Occurring within 90 days after birth • Occurring within 120 days after birth if analysis at 90 days meets efficacy criteria. • Occurring within 150 days after birth. If analysis at 120 days meets efficacy criteria • Occurring within 180 days after birth if analysis at 150 days meets efficacy criteria.

	Severe MA-LRTIs due to RSV as confirmed by EAC • Occurring within 90 days after birth • Occurring within 120 days after birth if analysis at 90 days meets efficacy criteria • Occurring within 150 days after birth if analysis at 120 days meets efficacy criteria • Occurring within 180 days after birth, if analysis at 150 days meets efficacy criteria
Primary Safety Endpoints Infant Participant	• Specific birth outcomes • Adverse events (A/Es) from birth to 1 month of age. • Serious adverse events (SAEs) and newly diagnosed chronic medical conditions (NDCMCs) i. From birth through to 6 months of age ii. From birth through 12 months of age iii. From birth through 24 months of age
Secondary Efficacy Endpoints Infant Participant	Hospitalization due to RSV • Occurring within 90 days of birth • Occurring within120 days after birth if analysis at 90 days meets efficacy criteria • Occurring within 150 days after birth if analysis at 120 days meets efficacy criteria • Occurring within 180 days after birth if analysis at 150 days meets efficacy criteria MA-LRTI due to any cause with protocol defined criteria: • Occurring within 90 days after birth • Occurring within 120 days after birth if analysis at 90 days meets efficacy criteria • Occurring within 150 days after birth if analysis at 120 days meets efficacy criteria • Occurring within 180 days after birth if analysis at 150 days meets efficacy criteria
MATERNAL PARTICIPANTS	
Primary Safety Objectives Maternal Participants	To describe the safety and tolerability of RSVpreF
Primary Safety Endpoints Maternal Participants	The incidence of: • Prespecified local reactions within 7 days after vaccination • Prespecified systemic events within 7 days after vaccination • AEs from the time of vaccination through to 1 month after vaccination. • SAEs throughout the study
Study design	Phase 3 multicentre, randomised, double or observer-blinded placebo-controlled study
Study Population	Healthy women between 18 and 49 years of age who are between 24/07- and 36/07-weeks gestation on the day of planned vaccination, with an uncomplicated, singleton pregnancy, who are at no known increased risk for complications

Study Sample size	Approximately 6900 mother-infant pairs
Follow up / Duration	Pregnant women will participate in the study from enrolment during their pregnancy, and for approximately 6 months after delivery. Total duration is approximately 6 months Eligible infant participants born to enrolled maternal participants during the first year of study will participate in the study from birth and will be followed for up to 24 months for RSV surveillance and safety for the secondary and exploratory endpoints of the study. All other infants will participate from time of birth and at least 12 months after birth.
Study Programme Sites	Wits RHI Shandukani Research Centre (SRC)
Study Programme Duration	5 years
Investigators	Dr Masebole Masenya, Principal Investigator Prof Lee Fairlie Sub Investigator Dr Elizea Horne Sub Investigator Dr Faeezah Patel Sub Investigator
Other Partners/ Collaborators	ICON - CRO
Sponsors / Donors	Pfizer
Publications/Key Presentations to Date	None yet
Progress update as at April 2020	Study started enrolment in October 2020
Frequency of Donor Narrative Report	Donor reports will be sent when available and/ or as requested. Progress reports will be sent to HREC and SAHPRA biannually.
Overall Study/ Project Contact	Dr M Masenya (mmasenya@wrhi.ac.za)
Briefing Owner and Date	Hedwig Kowo (hkowo@wrhi.ac.za) 17-June-2020