Project Brief: GBS6 Vaccine Study (C109-1002)

Full Title of Study/Programme	A phase 1/2, randomized, placebo-controlled, observer-blinded Trial to evaluate the safety, tolerability, and immunogenicity of a multivalent group b streptococcus vaccine in healthy non pregnant women and pregnant women 18 to 40 years of age and their infants.
Technical Focus Area	Research (Pediatric and Maternal)
Rationale	• Among young infants, GBS is a leading cause of invasive bacterial infection, a significant cause of infant morbidity and mortality globally. Serious GBS disease, including sepsis, meningitis, and pneumonia, is associated with mortality rates of 6% to 14% in high-income countries and 10% to 60% in low- and middle-income countries (LMICs). • Vaccination of pregnant women has been used globally in the prevention of neonatal tetanus and more recently for prevention of pertussis in young infants, and to protect women and their infants against influenza. • Pfizer is developing a 6-valent capsular polysaccharide (CPS) conjugate vaccine (group B streptococcus 6-valent polysaccharide conjugate vaccine [GBS6]) aimed at the prevention of group B streptococcal disease due to 6 serotypes in young infants by active immunization of pregnant women.
Primary Objectives	**Stage 1:** • To describe the safety and tolerability of various GBS6 formulations in healthy nonpregnant women 18 to 40 years of age. **Stage 2** • To describe the safety and tolerability of various GBS6 formulations when administered to healthy pregnant women 18 to 40 years of age vaccinated at 27 to 36 weeks' gestation. • To assess the safety of maternal immunization in infants born to women who were vaccinated with various GBS6 formulations during pregnancy. **Stage 3** • To describe the safety and tolerability of 1 selected dose/formulation of GBS6 when administered to healthy pregnant women 18 to 40 years of age vaccinated at 27 to 36 weeks' gestation. • To assess the safety of maternal immunization in infants born to women 18 to 40 years of age who were vaccinated with 1 selected dose/formulation during pregnancy.
Secondary Objectives	**Stage 1**: • To describe the immunogenicity of various GBS6 formulations when administered to healthy nonpregnant women. • **Stage 2**: To describe the immunogenicity of various GBS6 formulations when administered to healthy pregnant women.

	• **Stage 3**: To describe the immunogenicity of 1 selected dose level/formulation of GBS6 when administered to healthy pregnant women. **Stages 2 and 3** • To describe GBS6 antibody levels in infant subjects delivered to maternal subjects vaccinated with GBS6. • To assess placental transfer of antibody from maternal subjects vaccinated with GBS6 to their infant subjects.
Primary Endpoint/Outcome	**Primary Endpoints – Stage 1** • Proportions of nonpregnant women reporting prompted local reactions within 7 days following administration of investigational product (pain at the injection site, redness, and swelling). • Proportions of nonpregnant women reporting prompted systemic events within 7 days following administration of investigational product (fever, nausea/vomiting, diarrhea, headache, fatigue/tiredness, muscle pain, and joint pain). • Proportions of nonpregnant women reporting adverse events (AEs) through 1 month following administration of investigational product. • Proportions of nonpregnant women reporting medically attended adverse events (MAEs) and serious adverse events (SAEs) through 6 months following administration of investigational product. **Primary Safety Endpoints – Maternal Subjects (Stages 2 and 3**) • Proportions of sentinel-cohort maternal subjects (Stage 2 only) with clinical laboratory abnormalities following administration of investigational product at the 2-week follow-up visit. • Proportions of maternal subjects reporting prompted local reactions within 7 days following administration of investigational product (pain at the injection site, redness, and swelling). • Proportions of maternal subjects reporting prompted systemic events within 7 days following administration of investigational product (fever, nausea/vomiting, diarrhea, headache, fatigue/tiredness, muscle pain, and joint pain). • Proportions of maternal subjects reporting AEs through 1 month after administration of investigational product. • Proportions of maternal subjects with SAEs, MAEs, and obstetric complications (prepartum, intrapartum, and postpartum) throughout the study (Visit 1 through the 12-month postdelivery study visit). • Proportions of maternal subjects with each delivery outcome (live birth, delivery mode). **Primary Safety Endpoints – Infant Subjects (Stages 2 and 3**) • Proportions of infants with specific birth outcomes. • Proportions of infants with AEs from birth to 6 weeks of age.

	• Proportions of infants with SAEs, AEs of special interest (major congenital anomalies, developmental delay, and suspected or confirmed GBS infection), and MAEs through 12 months of age.
Secondary Endpoint/Outcome	**Secondary Endpoints – Stage 1** • GBS serotype-specific IgG geometric mean concentrations (GMCs) 1 month after vaccination in nonpregnant women. • GBS serotype-specific OPA geometric mean titers (GMTs) measured 1 month after vaccination in nonpregnant women. **Secondary Endpoints – Maternal Subjects (Stages 2 and 3**) • GBS serotype-specific IgG GMCs measured at 2 weeks and 1 month after vaccination and at delivery in maternal subjects. • GBS serotype-specific OPA GMTs measured at 2 weeks and 1 month after vaccination and at delivery in maternal subjects. **Secondary Endpoints – Infant Subjects (Stages 2 and 3**) • GBS serotype-specific IgG GMCs in infant subjects measured at birth. • GBS serotype-specific OPA GMTs in infant subjects measured at birth.
Study Design	This is a Phase 1/2, randomized, placebo-controlled, observer-blinded trial to evaluate the safety, tolerability, and immunogenicity of a multivalent GBS vaccine in healthy nonpregnant women and pregnant women aged 18 to 40 years and their infants.
Study Arms	**Stage 1**: Healthy nonpregnant women. **Stage 2**: Maternal subjects and their infant subjects (sentinel and expanded cohorts). **Stage 3**: Maternal subjects and their infant subjects (single cohort).
Study Population	Women
Study Sample Size	A total of approximately 586 subjects (66 nonpregnant women and 520 maternal subjects and their infant subjects) will be enrolled in this study by central randomization. • Stage 1: Approximately 66 subjects (nonpregnant women) • Stage 2: Approximately 360 maternal subjects • Stage 3: Approximately 160 maternal
Study/Programme Sites	• Wits RHI Shandukani Research Centre (SRC) • RMPRU • FAMCRU
Study/Programme Duration	December 2018 to September 2022
Intervention	For this study, the investigational product(s) are Group B Streptococcus 6-Valent Polysaccharide Conjugate Vaccine (GBS6), containing 5, 10, or 20 µg CPS/serotype/dose, each formulated with or without AlPO4; and placebo (saline control). The participants will receive 1 dose of either GBS6, with or without AlPO4, or placebo
Operations	
Investigators	• **Dr Lee Fairlie, Principal Investigator**

	• **Dr Masebole Masenya, Sub Investigator** • **Dr Faeezah Patel, Sub Investigator** • **Dr Elizea Horne, Sub Investigator**
Other Partners & Collaborators	• Bracket for the e-dairies • Covance laboratory • Impala data management • IHMA-cenral microbiology laboratary • RMPRU, Soweto • FAMCRU
Sponsors/Donors	Pfizer
Publications/Key Presentations to Date	None as yet
Progress Update as at 05/2019	Recruitment Stage 1: enrollment closed Enrolled: 10
Frequency of Donor Narrative Report	Monthly telecom calls
Overall Study/Project Contact	Dr Hermien Gous (hgous@wrhi.ac.za)
Briefing Owner and Date	Dr Lee Fairlie November 2018, reviewed Dr Mishal Bawa Nov-18 Hermien Gous Nov-18