Project Brief: IMPAACT 2035

Full Title of Study/Programme	This is a Phase I/II, double-blinded, placebo-controlled, randomized multi-center study to assess the safety and immunogenicity of VPM1002 vaccination and BCG revaccination among South African pre-adolescents who received BCG vaccine at birth.
Technical Focus Area	Pre-adolescents (8-14 years of age, inclusive) living with or without HIV who received BCG vaccination at birth. Participants with HIV will be immunocompetent and virologically suppressed on antiretroviral therapy. For purposes of stratification as shown below, HIV status will be determined based on standard IMPAACT diagnostic testing algorithms. *M.tb* sensitization will be determined based on interferon gamma release assay (IGRA) testing.
Hypothesis	VPM1002 vaccination and BCG revaccination will be safe when administered to pre-adolescents who received BCG vaccine at birth.
	VPM1002 vaccination and BCG revaccination will induce anti-mycobacterial cellular immune responses when administered to pre-adolescents who received BCG vaccine at birth
Primary Objectives	To evaluate the safety of VPM1002 vaccination and BCG revaccination
	To evaluate the cellular immunogenicity of VPM1002 vaccination and BCG revaccination through Week 10
Secondary Objectives	To evaluate the cellular immunogenicity of VPM1002 vaccination and BCG revaccination at Week 24 and Week 48
	To evaluate the humoral immunogenicity of VPM1002 vaccination and BCG revaccination
	To assess the acceptability of VPM1002 vaccination and BCG revaccination in pre-adolescents
	To evaluate the association of HIV and IGRA status with the safety of VPM1002 vaccination and BCG revaccination
	To evaluate the association of HIV and IGRA status with cellular and humoral immune responses induced by VPM1002 vaccination and BCG revaccination.
	To describe early innate immune changes in whole blood in response to VPM1002 vaccination and to BCG revaccination
	To describe donor unrestricted T cell, natural killer (NK) cell, and monocyte responses elicited by VPM1002 vaccination and by BCG revaccination.
	To describe cytokine and chemokine production by vaccine induced CD4+ and CD8+ T cells following stimulation of whole blood with vaccine antigens.

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<tr><td>Exploratory Objectives</td><td>Evaluate differences in the epigenome of monocytes and NK cells by vaccine arm</td></tr>
<tr><td></td><td>Evaluate vaccine-induced changes in VPM1002-specific and BCG-specific antibodies by systems serology</td></tr>
<tr><td></td><td>Evaluate the effect of VPM1002 vaccination and BCG revaccination on frequency and phenotype of HIV-specific T cells in pre-adolescents living with HIV</td></tr>
<tr><td></td><td>Describe frequency of exploratory immune cell subsets by vaccine arm</td></tr>
<tr><td></td><td>Evaluate innate and adaptive cytokine and chemokine profiles following stimulation of whole blood with vaccine antigens</td></tr>
<tr><td></td><td>Evaluate the association between gut microbiome and vaccine immunogenicity</td></tr>
<tr><td>Primary Endpoint/Outcome</td><td></td></tr>
<tr><td>Secondary Endpoint/Outcome</td><td></td></tr>
<tr><td>Study Design (R)</td><td>The study will be conducted among approximately 480 participants, ranging in age from 8 to 14 years (inclusive). Participants will be randomly assigned to one of three study product arms (1:1:1) at enrollment, stratified by HIV and IGRA status. For each participant the assigned study product will be administered once by intradermal injection on the day of enrollment (randomization).</td></tr>
<tr><td>Study arms (R)</td><td>Overview of Study Population by Randomized Study Arm with Stratification by HIV and IGRA Status
<table>
<tr><th rowspan="2">Assigned Study Product</th><th colspan="2">With HIV</th><th colspan="2">Without HIV</th></tr>
<tr><th>IGRA Negative</th><th>IGRA Positive</th><th>IGRA Negative</th><th>IGRA Positive</th></tr>
<tr><td>VPM1002 Vaccine
0.1 mL (2-8x10^5 CFU)</td><td>40</td><td>40</td><td>40</td><td>40</td></tr>
<tr><td>BCG Vaccine
0.1 mL (2-8x10^5 CFU)</td><td>40</td><td>40</td><td>40</td><td>40</td></tr>
<tr><td>Placebo
0.1 mL sodium chloride for injection 0.9%</td><td>40</td><td>40</td><td>40</td><td>40</td></tr>
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<tr><td>Study population (R)</td><td>08-14 years of age inclusive.</td></tr>
<tr><td>Study sample size (R)</td><td>Approximately 480 participants will be enrolled.</td></tr>
<tr><td>Follow up/duration</td><td>Approximately 24 months. Accrual is expected to require approximately 12 months (48 weeks, counted from the date of first enrollment) and each participant will be followed for approximately 12 months (48 weeks).</td></tr>
<tr><td>Study/Programme sites</td><td>Wits RHI, Desmond Tutu, PHRU, FAMCRU, Umlazi, Klerksdorp, Emavundleni, Isipingo,Setshaba.</td></tr>
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Study/Programme duration	? February 2024 – 2026
Intervention (R)	VPM1002/ BCG / Placebo
Operations	
Investigators	**Dr Lee Fairlie, Principal Investigator** **Dr Faeezah Patel, Sub Investigator** **Dr Elizea Horne, Sub Investigator**
Other Partners & Collaborators	IQVIA, BARC,
Sponsors/Donors	NIAID, NICHD
Linked Sub Studies and post grad projects	
Publications/key presentations to date	
Progress Update as at Oct-2023	Enrolled: 00 On study: 00 Withdrawal 00 LTFU 00
Frequency of donor narrative report	
Overall Study/Project Contact	Dr Hermien Gous (
Briefing owner and date	Dr Lee Fairlie Oct-2023 reviewed Dr Hermien Gous Oct-2023