

**Title of Project:** Phase 2 placebo-controlled randomized trial of LACTIN-V (Lactobacillus crispatus CTV-05) among women at high risk of HIV acquisition in Durban, South Africa

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**Background:** The human vaginal microbiota affected by dysbiosis has long been considered a factor impacting women's risk for acquiring sexually transmitted infections (STIs) including HIV, but the extent of this contribution and the underlying mechanisms have not been well defined. Optimizing the vaginal microbiota by replenishing human lactobacilli strains with a live biotherapeutic product (LBP) containing *Lactobacillus crispatus* CTV-05 (LACTIN-V) is a new strategy to fight dysbiosis and vaginal inflammation.

**Methods:** Sixty eligible South African women aged 18-23 at high risk for HIV acquisition and diagnosed with bacterial vaginosis are receiving standard antibiotic treatment of oral metronidazole and then randomized 2:1 to vaginally administered LACTIN-V vs. placebo. Women receive study product for five consecutive days, followed by a twice weekly dose for three additional weeks. Participants are followed for a dosing (28 days) and post dosing phase (28 days) for a total of 56 days.

**Results:** Recruitment is ongoing with 28 randomized participants by August 1, 2022. The primary outcomes focus on the ability of LACTIN-V to decrease genital tract inflammation (as a marker of HIV susceptibility), and for *L. crispatus* CTV-05 to establish durable vaginal colonization in South African women. While LACTIN-V has been shown to be safe and well tolerated in US women, we will assess the safety and tolerability in this cohort of young South African women. After being initially slowed down by the COVID-19 pandemic in 2020 and damage to the clinic site after political unrest in 2021, recruitment is now at a steady pace. While data analysis will be completed in 2023, no severe adverse events have been recorded among the first 28 participants, and adherence to study product is high.

**Conclusion:** Should LACTIN-V be able to sustainably replenish vaginal lactobacilli and reduce genital inflammation, it could become a safe, effective, self-renewing, female-controlled product that promotes vaginal health and provides protection from HIV and potentially other STIs.