

Project Brief: CD388.SQ.3.06

Full Title of Study/Programme	A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Safety and Efficacy of CD388, a Novel Long-Acting Antiviral Conjugate, for the Prevention of Influenza in Adults and Adolescents at Higher Risk of Developing Influenza Complications.
Technical Focus Area/Key Words	Participants at higher risk of developing influenza complications.
Rationale	This study is being conducted to evaluate the safety and efficacy of CD388 in the prevention of symptomatic influenza infection. While human challenge studies can provide some insight into the preventive efficacy of a specific drug or vaccine, the mode and mechanism of real-world influenza exposure and acquisition cannot be mimicked. This study will assess the safety and efficacy of a single 450 mg dose of CD388 in a population with higher risk(s) for influenza complications during an entire influenza season. Follow-up will include close monitoring of symptoms and signs of influenza infection providing a real-world assessment of the intended effect of CD388. In the study, a placebo control will be used for comparison of safety and efficacy endpoints. A placebo-controlled design is selected to provide an untreated comparison for all endpoints. Randomization and blinding (Investigators and study site staff, study participants, Medical Monitors, the IAC, and the Sponsor) will be used to minimize bias in both the assignment of participants to treatment arms and the assessment of study endpoints.
Primary Objectives	To evaluate the clinical efficacy of CD388 in preventing symptomatic laboratory-confirmed influenza infections compared to placebo.
Secondary Objectives	- To evaluate the safety and tolerability of CD388 compared to placebo. - To evaluate the pharmacokinetics (PK) of CD388 in plasma. - To evaluate anti-drug antibodies (ADAs) in participants administered CD388.
Exploratory Objectives	- To evaluate the effect of CD388 in the reduction of symptoms and symptom severity in participants with laboratory-confirmed influenza infections compared to placebo. - To explore the effect of CD388 in the reduction of medical resource use (MRU), complications, and all-cause mortality compared to placebo. - To explore the impact of CD388 prophylaxis on work productivity and health-related quality of life measures associated with symptomatic laboratory-confirmed influenza infection when compared to placebo. - To evaluate the pharmacokinetic (PK)/ pharmacodynamic (PD) relationships of CD388 for selected clinical outcomes (efficacy and safety parameters). - To evaluate influenza A and B viral load and time to negativity.

	• To evaluate the emergence of hemagglutinin (HA) and neuraminidase (NA) mutations in the viral genome potentially associated with resistance to CD388. • Evaluate association of virus type and subtype in laboratory-confirmed influenza infections in participants administered CD388 compared to placebo. • Evaluate seroconversion to circulating strains of influenza at the end of the study period in participants administered CD388 compared to placebo.
Study Design (R)	This is a Phase 3 randomized, double-blind, placebo-controlled study. The purpose of the study is to evaluate safety, clinical efficacy (protection against reverse transcriptase-polymerase chain reaction positive [RT-PCR+] symptomatic influenza infection), tolerability, PK, and immunogenicity of 450 mg CD388 administered SQ as a single dose compared to placebo in approximately 7500 adults and adolescents (age 12 years or older) with higher risk(s) of developing influenza complications. This is a multicenter study that will be conducted globally. After screening, eligible participants will be randomized in a 1:1 ratio to receive 450 mg CD388 or placebo with approximately 3750 participants planned in each group. Participants will be stratified into Primary Stratum A (non-immunocompromised) or Primary Stratum B (immunocompromised either due to underlying disease or immunosuppressive medications). Approximately 6750 participants will be enrolled in Primary Stratum A and approximately 750 participants will be enrolled in Primary Stratum B. Within each of these 2 strata, participants will be further stratified by age (12 to less than 18 years, 18 to less than 65 years, and 65 years or older), and current seasonal influenza vaccination status (vaccinated or not vaccinated). From the time of study intervention administration, longitudinal surveillance for the occurrence of ARI will be conducted through the Day 197/EOS visit (ie, full study duration). Participants will be asked to complete an ARI surveillance screening question approximately twice per week. If a participant triggers an ARI Alert by responding “Yes” to the surveillance screening question, the ARI workflow will be initiated as outlined in the Schedule of Activities (SoA) (see Table 3; described further in Section 8.3.2 of the protocol). The participant will be prompted to conduct assessments to determine if they meet the criteria for an ARI Episode (described in Section 8.3.2.1 of the protocol). If an ARI Episode is triggered, the ARI workflow includes a study visit for collection of an NP sample to test for influenza by RT-PCR to confirm symptomatic influenza infection. Exploratory efficacy will be evaluated by patient-reported outcome (PRO) assessments, including an Influenza Symptom Self-Assessment Questionnaire (ISSQ), the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L), and the Work Productivity and Activity Impairment–General Health Questionnaire (WPAI-GH). Once the ARI Episode resolves (definition provided in Section 8.3.2.3 of the protocol), the participant will resume longitudinal ARI surveillance.

Study arms (R)	CD388 Injection: Double Blind <table border="0"> <tr> <td>Total injections: 3</td> <td>Total injections: 3</td> </tr> <tr> <td>Total active drug:</td> <td>Total placebo:</td> </tr> <tr> <td>150 mg (1 mL) × 3 = 450 mg (3 mL)</td> <td>1 mL × 3 = 3 mL</td> </tr> </table> CD388 Injection is a colourless to slightly yellow, clear to slightly opalescent liquid, essentially free of particulate matter, containing CD388, the active pharmaceutical ingredient. CD388 Injection is supplied as a sterile refrigerated solution in prefilled syringes for SQ injection. Placebo is a colourless to slightly yellow, clear to slightly opalescent liquid essentially free of particulate matter, containing the same buffers and excipients as the CD388 Injection active product, but without the active pharmaceutical ingredient. Placebo is supplied as a sterile refrigerated solution in prefilled syringes for SQ injection.	Total injections: 3	Total injections: 3	Total active drug:	Total placebo:	150 mg (1 mL) × 3 = 450 mg (3 mL)	1 mL × 3 = 3 mL
Total injections: 3	Total injections: 3						
Total active drug:	Total placebo:						
150 mg (1 mL) × 3 = 450 mg (3 mL)	1 mL × 3 = 3 mL						
Study population (R)	This study will enrol participants that are at higher risk of developing influenza complications. The need for an effective medication to prevent influenza is highest in these populations. The study population will be divided into 2 primary strata: Primary Stratum A will include non-immunocompromised participants who have chronic stable medical conditions which may include pulmonary disorders, asthma, cardiac disease, diabetes, and renal impairment that increase the risk of influenza complications, and otherwise healthy adults >65 years of age and Primary Stratum B will include participants who are immunocompromised either due to underlying disease or receipt of immunosuppressive medications. Participants must be ≥ 12 years of age at the signing of informed consent or assent (if applicable). This protocol will allow the enrollment of adolescent participants (aged 12-17 years) into either Primary Stratum A or B if such persons are known to be at higher risk of developing complications of influenza due to chronic illness or receipt of immunosuppressive medications. Adolescent participants with weights of 40 kg or higher are not considered to have risks of potential safety implications exceeding those of older participants. Participants must be in stable health as defined by the inclusion and exclusion criteria at the time of screening and randomization, per the Investigator's assessment. Participants in this study will have underlying comorbidities, but their screening signs and symptoms should be medically stable in the judgment of the Investigator at the time of randomization. Participants in this study who are ≥ 65 years of age may or may not have underlying comorbidities. All participants who have not received the current seasonal influenza vaccine will be encouraged to receive inactivated or recombinant influenza vaccine during the screening period as part of standard of care but at least 14 days prior to study intervention administration for inactivated influenza vaccine or up to the day of planned study intervention administration for recombinant influenza vaccine						
Study sample size (R)	The sample size is evaluated using PROC POWER in SAS. Based on the stated assumptions a sample size of 7500 (3750 per dosing group), would provide approximately 92.3% power. Assuming a 1.5% incidence in the placebo group, this planned number of participants will yield approximately 72 participants with protocol-						

	defined ILI and 8 participants with an imputed value of protocol-defined ILI due to missing data (ie, 80 total observed and imputed events).		
Follow up/duration	Total planned duration of study participation for each participant: 197 ($\pm$ 7) days (not including up to 21 days for Screening). If a participant has an acute respiratory infection (ARI) Episode between Day 168 and Day 197/end of study (EOS), the study duration could be up to 226 ($\pm$ 7) days. Of note, there is a $\pm$ 7-day allowable window for the final study visit, which could increase total duration of study participation by up to 1 week.		
Study/Programme sites	Wits RHI Shandukani		
Intervention (R)	Treatment Group Intervention Name Dose Formulation Dosage Level(s) Administered on Day 1 Route of Administration Dosing Instructions Total active drug: 150 mg (1 mL) $\times$ 3 = 450 mg (3 mL) Use IMP NIMP/AxMP	CD388 CD388 Injection Prefilled syringes Dose 450 mg Subcutaneous Total injections: 3 Total placebo: 1 mL $\times$ 3 = 3 mL Experimental Yes No	Placebo Placebo Prefilled syringes Dose 0 mg Subcutaneous Total injections: 3 Placebo Comparator Yes No
Investigators	• Dr Jeanne Coetzee: Principal-Investigator • Prof Lee Fairlie: Sub-Investigator • Dr Faezah Patel: Sub-Investigator • Dr Elizea Horne: Sub-Investigator • Dr Mrinmayee Dhar: Sub-Investigator • Tiffany Deborah Seef: Clinical Associate • Karabo Busisiwe Tloubatla: Clinical Associate		
Other Partners & Collaborators	None		
Sponsors/Donors	Cidara Therapeutics MSD (Pending Acquisition)		
Linked Sub Studies and post grad projects	None		
Publications/key presentations to date	None		
Progress Update as at Mar 2026	No yet, at start-up, likely site activation in April 2026		
Frequency of donor narrative report	6 Monthly		

Overall Study/Project Contact	Dr Jeanne Coetzee
Briefing owner and date	Nothando Faith Mtshali Mar 2026