Development & Progression of a Candidate *Clostridium difficile* Vaccine for the Prevention of Symptomatic CDI

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Overview

- Sanofi Pasteur is developing a vaccine designed to prevent *Clostridium difficile* Infection(CDI) by using the immune system to neutralize the *C.diff* toxins that cause the symptoms of the disease.

- Sanofi Pasteur's investigational vaccine to prevent *C. difficile* infection (CDI) entered Phase III clinical trials in July of 2013 in the United States.

- Vaccination could be an efficacious, cost-effective and important public-health measure to help protect individuals from C. diff infection, which is emerging as a leading cause of life-threatening, healthcare-associated infections (HAIs) worldwide.

Unmet Medical Need

- The U.S. Food and Drug Administration (FDA) granted fast-track designation to Sanofi Pasteur's investigational C. diff vaccine candidate in 2010.

- The FDA's fast-track program is designed to facilitate the development and expedite the review of new drugs and vaccines that are intended to treat or prevent serious or life-threatening conditions and demonstrate the potential to address unmet medical needs.

How The Vaccine Works

- Like other toxoid vaccines (e.g. tetanus, diphtheria)
- The investigational *C. difficile* vaccine is designed to produce an immune response that targets the toxins generated by *C. difficile* bacteria.
- In previous clinical trials, the *C. difficile* candidate vaccine elicited antibody responses against Toxins A & B in the target population.

Target Population

- Adults at risk of CDI:
  - Adults with planned elective surgery
  - Long-term care residents
  - Adults with other health issues
  - Adults with frequent and/or prolonged antibiotic use

Phase I & II Clinical Data

- The investigational vaccine has progressed through Phase I and II clinical studies.
- The most recent Phase II study evaluated the vaccine for safety and immunogenicity in at-risk individuals, which included adults with imminent hospitalization.
- The Phase II trial met its primary objectives, reactions were generally mild and of short duration (not unlike licensed vaccines), and the candidate vaccine generated an immune response against C. difficile toxins A and B.
- The resulting data led to the selection of a vaccine formulation and dosing schedule for the Phase III global efficacy trial.

Phase III Trial - *Cdiffense*™

- a randomized, observer-blind, placebo-controlled, multi-center, multi-national Phase III trial called *Cdiffense*™.
- Recruitment began in late July of 2013 in the USA.
- The trial will include up to 15,000 volunteers across 200 trial sites in 20+ countries on 5 continents.
- Trial will last approximately 4.5 years based on the incidence of CDI and necessary follow-up required with the volunteers after vaccination.
- For more information, please visit www.Cdiffense.org

Trial Objectives

- Evaluate the safety, immunogenicity and efficacy of a toxoid vaccine for the prevention of symptomatic *C. difficile* infection (CDI).
- The study will evaluate the prevention of CDI.
- The primary endpoint of the trial is prevention of the first occurrence of symptomatic CDI.

Trial Requirements - Volunteers

- Have had at least two hospital stays, each lasting more than 24 hours, and has received systemic (not topical) antibiotics in the previous year before enrollment.

- Are anticipated to have an in-patient hospitalization for a planned surgical procedure within 60 days of enrollment.

    - **The impending hospital stay should be anticipated to last more than 72 hours and include an elective surgery conducted on the kidney/bladder/ urinary, musculoskeletal, respiratory, circulatory or central nervous system.**

Study Size & Dosing

- The 15,000 volunteers will be randomly assigned in a 2:1 ratio to either the vaccine or placebo group.
- The investigational vaccine will be tested as a three-dose immunization at 0, 7 and 30 days.
- The vaccine will be administered to 10,000 volunteers and the placebo to 5,000 volunteers.
- Of the up to 15,000 total volunteers, 1,500 will be enrolled into a subgroup that will test long-term immunogenicity of the vaccine.

Thank you