First-in-Human Phase 1/2 Clinical Trial of SIG-001, an Innovative Shielded Cell Therapy Platform, for Hemophilia A

Amy D. Shapiro1, Barbara A. Konkle2, Stacy E. Croteau3, Wolfgang Miesbach4, Charles Hay5, Rashid Kazmi6, Marina Mihova7, Savita Rangarajan8, K. John Pas9
1. Indiana Hemophilia & Thrombosis Center, Indianapolis, IN, USA; 2. Bloodworks Northwest and the University of Washington, Seattle, WA, USA; 3. Boston Children’s Hospital, Boston, MA, USA; 4. University Hospital Frankfurt, Frankfurt, Germany; 5. Manchester University, Manchester, UK; 6. University of Southampton, Southampton, UK; 7. Sigilon Therapeutics, Cambridge, MA, USA; 8. Barts and the London School of Medicine and Dentistry, London, UK.

Introduction

- Hemophilia A arises from pathogenic variants in the F8 gene, affecting ~1/5000 males.
- Treatment options include frequent IV factor and subcutaneous (SC) non-factor therapies; however, they have limitations such as:
  - non-ideal factor kinetics
  - morbidity from breakthrough bleeding, including chronic joint disease
  - impaired quality of life
  - inhibitor development
  - treatment burden
  - risk of thrombotic events and coagulation test interference with newer non-factor therapies.
- Cell therapy with allogeneic, genetically modified cells, is a new potential approach for many diseases, including hemophilia A.
- Genetically modified allogeneic cells have to be physically protected from the host’s immune cells as well as the prevention of PFO.
- This platform provides both the physical shield to cell-to-cell interaction, as well as the prevention of PFO.
- The shielded spheres are placed in the peritoneal space where they can absorb nutrients while the released therapeutic protein can enter the blood compartment.

Summary of Preclinical Data for SIG-001

Given the expected immune response to human FVIII exposure in immunocompetent mice, NSG mice were used in this long-term transgenic study. Low or high doses of SIG-001 were placed in the 8-week hFVIII levels measured by ELISA. Spheres were assessed at the study completion (131 days) and evaluated for viability and hFVIII productivity.

SIG-001-121 Clinical Trial Design

- Investigational Product SIG-001: Cell Line Modified with a Non-Viral Vector to Express hFVIII, Encapsulated within Modified Alginite Spheres

SIG-001-121 Study Schema

- Patients will be followed for 5 years after SIG-001 administration.

SIG-001-121 Study Endpoints

**Primary endpoints:**
- Safety: including clinically significant changes in vital signs, physical exam, hematology and blood chemistry
- Treatment emergent adverse events

**Secondary endpoints include:**
- FVIII levels by one-stage and chromogenic assays (central lab)
- Annualized bleeding rate
- Annualized FVIII use
- FVIII inhibitors

**Exploratory endpoints include changes in:**
- Health, QoL, and Physical Activity Questionnaires
- Number and frequency of bleeds in target joints
- Hemophilia Joint Health Score (HJHS)

SIG-001-121 Patient Population

- **Key Inclusion Criteria:**
  - Adult males (≥18 years of age)
  - Severe (rFVIII activity) or moderately-severe HA (≥15 - 52% FVIII activity)
  - ≥150 exposure days to FVIII product(s)

- **Key Exclusion Criteria:**
  - Prior administration of a gene therapy product
  - History of allergic reaction to recombinant FVIII products
  - Unable to undergo anesthesia or laparoscopy

**Reference**


Contact/Further Information

- **SIG-001 has been granted orphan designation by the US FDA**
- **ClinicalTrials.gov Study Number:** NCT04451208
- **EudraCT Study Number:** 2019-004210-33
- **Sponsor Contact:** clinicaltrials@sigilon.com

References