

Fitusiran prophylaxis reduced bleeds by 61% in people with hemophilia A or B, with or without inhibitors, compared to prior factor or bypassing agent prophylaxis

- A median annualized bleeding rate (ABR) of 0.0 was reported in the overall study population during fitusiran prophylaxis (80 mg monthly)
- Fitusiran is a novel, investigational subcutaneously administered small interference RNA therapy, in development for the prophylactic treatment of people with hemophilia A or B, with or without inhibitor

Paris – July 10, 2022 – Positive data from the Phase 3 ATLAS-PPX study evaluating the efficacy and safety of once-monthly fitusiran (80 mg) in adults and adolescents with severe hemophilia A or B who were previously treated with prior factor or bypassing agent (BPA) prophylaxis were presented today in a late-breaking session at the International Society on Thrombosis and Haemostasis (ISTH) 2022 Congress. The study met the primary endpoint and demonstrated fitusiran prophylaxis significantly reduced bleeding episodes compared to prior factor or BPA prophylaxis.

Gili Kenet, MD

Investigator, professor of Hematology, Director of the Israeli National Hemophilia Center at Sheba Medical Center and head of the Amalia Biron Thrombosis Research Institute of Tel Aviv University, Tel Aviv, Israel

“There is a continued need for transformative therapies that offer people with hemophilia consistent protection while also reducing treatment burden. These phase 3 results are encouraging and support fitusiran’s potential to provide people with hemophilia A or B, regardless of inhibitor status, with a meaningful reduction in bleeding episodes.”

Key findings in the Phase 3 ATLAS-PPX study include the following:

- The overall median annualized bleeding rate (ABR) was 0.0 for fitusiran prophylaxis, compared to a median ABR of 4.4 with prior prophylaxis.
- Fitusiran prophylaxis resulted in a statistically significant reduction in estimated ABR of 61.1% ($p= 0.0008$) versus factor or BPA prophylaxis.
- 63.1% ($n=41$) of adults and adolescents treated with fitusiran experienced zero treated bleeds compared to 16.9% ($n=11$) with prior factor or BPA prophylaxis.
- Median ABR for treated bleeds was 0.0 with fitusiran prophylaxis for both participants with and without inhibitors compared to 6.5 and 4.4 for participants with and without inhibitors, respectively, on prior prophylaxis.
- Of the 67 participants exposed to a least one dose of fitusiran, the most common adverse events (≥ 6 participants) were increased alanine aminotransferase, nasopharyngitis, and upper respiratory tract infection.
- Consistent with the previously identified risk of fitusiran, suspected or confirmed thromboembolic events were reported in 2 participants (3.0%).

Dietmar Berger MD, PhD

Global Head of Development and Chief Medical Officer

“These positive data support fitusiran’s potential to transform prophylaxis treatment for people with hemophilia A or B, with or without inhibitors, with a median annual bleed rate of zero across all patient populations. Moreover, we are excited to continue to explore fitusiran under an

amended protocol that focuses on dose optimization, including lower doses and less frequent dosing regimens, with the potential for as few as six injections per year.”

Additional data from the fitusiran clinical program will be shared at the congress including:

- *Consumption of On-demand Factor Concentrates and Bypassing Agents for Management of Breakthrough Bleeds with Fitusiran Prophylaxis in People with Haemophilia A or B: An Analysis of Two Phase 3 Studies. Oral presentation: OC40.3.* July 11, 2:45 pm – 4:00 pm CET.
- *Fitusiran, an Investigational siRNA Therapeutic Targeting Antithrombin: Analysis of Antithrombin Levels and Thrombin Generation from a Phase 3 Study in People with Haemophilia A or B Without inhibitors. Oral presentation: OC.50.2.* July 12, 10:45 am – 12:00 pm
- *Fitusiran, an Investigational siRNA Therapeutic Targeting Antithrombin: Analysis of Antithrombin Levels and Thrombin Generation from a Phase 3 Study in People with Haemophilia A or B With inhibitors. Poster presentation: PB1152.* July 12, 6:30 pm - 7:30 pm CET)

Collectively, these data add to a growing body of evidence, including results from the [ATLAS A/B and ATLAS-INH Phase 3 studies](#), supporting fitusiran’s potential to transform treatment for all people with hemophilia. Hemophilia A and B are rare congenital bleeding disorders caused by a deficiency of factor VIII and IX, respectively, resulting in insufficient thrombin generation and ineffective clot formation further complicated in patients who develop inhibitors to their factor treatment.

Sanofi is currently investigating the efficacy and safety of fitusiran under an amended protocol which includes lower doses and a less frequent dosing regimen maintaining an antithrombin target range of 15-35% in all ongoing studies. Fitusiran has the potential to provide prophylactic treatment for all people with hemophilia A or B, with or without inhibitors, with as few as six subcutaneous injections per year.

ATLAS-PPX Phase 3 study design (NCT03549871)

ATLAS-PPX is a multinational, open-label, Phase 3 study designed to evaluate the efficacy and safety of fitusiran in adult and adolescents aged ≥ 12 years with severe hemophilia A or B, with or without inhibitors, who have switched from prior factor or bypassing agent prophylaxis. A total of 80 participants were enrolled. In the study, participants continued their pre-study prophylaxis regimen with factor or bypassing agents for a six-month period followed by a switch to once-monthly fitusiran (80 mg) administered subcutaneously for seven months.

The primary endpoint of the study was annualized bleeding rate.

About fitusiran

Fitusiran is an investigational, subcutaneously administered small interference RNA therapeutic in development for the prophylactic treatment of people with hemophilia A or B, with or without inhibitors. Fitusiran is designed to lower antithrombin, a protein that inhibits blood clotting, with the goal of promoting thrombin generation to rebalance hemostasis and prevent bleeds. Fitusiran utilizes Alnylam Pharmaceutical Inc.’s ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability. Fitusiran is currently under clinical investigation and has not been evaluated by any regulatory authority.

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people’s lives. Our team, across some 100 countries, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

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