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Press Release

Source: Sanofi (EURONEXT: SAN) (NASDAQ: SNY)

Data from two Phase 3 studies demonstrating fitusiran significantly reduced bleeds in people with hemophilia A or B, with or without inhibitors, were featured at ASH's plenary and late-breaking sessions

- Both Phase 3 studies achieved their primary and secondary endpoints; fitusiran prophylaxis demonstrated significant and clinically meaningful improvements in bleed protection across all study populations
- A >89% reduction in annualized bleeding rate was demonstrated with fitusiran prophylaxis in both studies when compared to the control arms
- 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 inhibitors

Paris – December 14, 2021 - Positive data from two Phase 3 studies evaluating the efficacy and safety of fitusiran, an investigational small interference RNA (siRNA) therapy for the prophylactic treatment of adults and adolescents with hemophilia A or B, with or without inhibitors, are presented at the 63rd American Society of Hematology (ASH) Annual Meeting. Results from the ATLAS-A/B study, investigating fitusiran in people without inhibitors, are being presented today in the Late-Breaking Abstract Session and findings from the ATLAS-INH study, which evaluated fitusiran in people with inhibitors to factor VIII or IX, were shared in the Plenary Scientific Session on December 12, 2021.

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. Fitusiran is a novel subcutaneous siRNA prophylactic investigational therapy designed to lower antithrombin levels with the goal of enhancing thrombin generation to rebalance hemostasis in people with hemophilia, regardless of type or inhibitor status.

The Phase 3 studies compared once monthly fitusiran prophylaxis (80mg) with on-demand use of factor concentrates in the ATLAS-A/B study, and on-demand use of bypassing agents in the ATLAS-INH study. Across both clinical studies, prophylactic treatment with fitusiran reduced annualized bleeding rates by >89% compared to the control arms, showing a statistically significant and clinically meaningful improvement in bleeds when compared to on-demand treatments, and also showing significant improvement in quality of life.

> *"We are encouraged by the data from these initial Phase 3 studies demonstrating fitusiran's potential as a new therapeutic option for people with hemophilia A or B, regardless of inhibitor status,"* says Dietmar Berger, MD, PhD, Global Head of Development, Sanofi. *"There continues to be a significant need for transformative*

therapies that offer people with hemophilia consistent protection from bleeds while reducing treatment burden. These findings underscore fitusiran's potential to address these challenges and give hope to patients, caregivers, and physicians."

The fitusiran Phase 3 clinical program is ongoing. Sanofi is currently investigating the efficacy and safety of fitusiran under an amended protocol which includes lower doses and an extended dosing regimen in all ongoing adult and adolescent studies. Fitusiran has the potential to provide prophylactic treatment for all people with hemophilia A or B, with as few as six injections per year.

ATLAS-A/B Phase 3 Study (NCT03417245)

ATLAS-A/B is a Phase 3 randomized, open-label study investigating the efficacy and safety of fitusiran in males ≥12 years with severe hemophilia A or B without inhibitors who had previously been treated with on-demand factor therapy. Study participants (n=120) were randomized 2:1 to receive either once-monthly 80mg subcutaneous fitusiran prophylaxis or on-demand factor therapy for bleeding episodes. The primary endpoint is annualized bleeding rate (ABR).

The key findings in this study include the following:

- A statistically significant and clinically meaningful reduction in treated annualized bleeding rate of 89.9% in the fitusiran prophylaxis arm (95% CI 84.1%; 93.6%], P <0.0001) compared to the factor on-demand arm.
- Median (interquartile range) annual bleeding rate for treated bleeds is 0.0 (0.0; 3.4,) in the fitusiran arm compared to 21.8 (8.4; 41.0) in the factor on-demand arm.
- 50.6% (n=40) of study participants in the fitusiran prophylaxis arm had zero treated bleeds compared to 5.0% (n=2) of participants in the factor on-demand arm.
- The most common adverse events reported in at least five (6.3%) participants in the fitusiran prophylaxis arm were increased alanine aminotransferase (ALT), upper respiratory tract infection, nasopharyngitis, abdominal pain, increased aspartate aminotransferase (AST), cough, arthralgia, asthma, gastritis, and headache.
- Treatment emergent adverse events of special interest (TEAESIs) of any ALT or AST elevation >3 x upper limit of normal were reported in the fitusiran prophylaxis arm in 15 (19.0%) participants. There were no TEAESIs of suspected or confirmed thromboembolism reported.

Phase 3 ATLAS-INH Study (NCT03417102)

The ATLAS-INH study is a randomized, open-label Phase 3 study designed to evaluate the safety and efficacy of fitusiran in males ≥12 years with severe hemophilia A or B with inhibitors to factor VIII or IX. Study participants (n=57) receiving on-demand treatment with bypassing agents (BPA) were randomized in a 2:1 ratio to receive once-monthly 80mg subcutaneous fitusiran prophylaxis or continue with on-demand BPA. The primary endpoint is annualized bleeding rate.

The key findings in this study include the following:

- Fitusiran prophylaxis resulted in a statistically significant reduction in treated annualized bleeding rate of 90.8% (95% CI 80.8%; 95.6%), P<0.0001) in comparison to treatment with BPAs.
- The median (interquartile range) treated annualized bleeding rate is 0.0 (0.0; 1.7,) in the fitusiran prophylaxis arm compared to 16.8 (6.7; 23.5) in the on-demand BPA on-demand arm.
- 65.8% (n=25) participants in the fitusiran prophylaxis arm had zero treated bleeds compared to 5.3% (n=1)) in the BPA on-demand arm.
- The most common adverse events reported in at least five (12.2%) participants in the fitusiran prophylaxis arm were increased ALT, increased AST, upper abdominal pain, increased gamma-glutamyl transferase, headache, upper respiratory tract infection, arthralgia, increased blood alkaline phosphatase, and increased transaminases.
- TEAESIs of ALT or AST elevation >3 x upper limit of normal and suspected or confirmed thromboembolism were reported in the fitusiran prophylaxis arm in 10 (24.4%) and 2 (4.9%) participants, respectively.

Fitusiran significantly reduced annualized bleeding with a meaningful improvement in health-related quality of life. Reported TEAEs in the fitusiran prophylaxis arm of ATLAS-A/B and ATLAS-INH were generally consistent with previously identified risks of fitusiran, or risks associated with the underlying disease of severe hemophilia A or B.

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 sufficient 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

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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Sanofi Forward-Looking Statements

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