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.
- TEAEs 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
This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words “expects”, “anticipates”, “believes”, “intends”, “estimates”, “plans” and similar expressions. Although Sanofi’s management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi’s ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly, and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in Sanofi’s annual report on Form 20-F for the year ended December 31, 2020. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.