Press Release

ISTH: Sanofi advances leadership in hemophilia with new data for ALTUVIIIO and fitusiran

- Seven oral presentations across the hemophilia portfolio reinforce Sanofi's commitment to bring potential first- and best-in-class treatments to the rare blood disorders community
- Interim results from the long-term XTEND-ed phase 3 study demonstrate once-weekly ALTUVIIIO continues to provide highly effective bleed protection
- New ATLAS phase 3 study data reinforce the potential of fitusiran to provide prophylaxis for people with hemophilia A or B, with or without inhibitors
- New Drug Application for fitusiran accepted for review by the US Food and Drug Administration, with a PDUFA date of March 28, 2025

Paris, June 21, 2024. Sanofi will present new data from its hemophilia portfolio at the 32nd Congress of the International Society on Thrombosis and Haemostasis (ISTH), taking place June 22-26, 2024, in Bangkok, Thailand. Notable presentations on ALTUVIIIO [Antihemophilic Factor (Recombinant), Fc-VWF-XTEN Fusion Protein] include long-term interim phase 3 data on the efficacy and safety of the treatment in adults and children with severe hemophilia A. Abstracts on fitusiran include information on surgical experience as well as long-term safety data from the ATLAS phase 3 clinical development program in adults and adolescents with hemophilia A or B, regardless of inhibitor status.

Dietmar Berger
Chief Medical Officer, Global Head of Development
"Our presence at this year's congress demonstrates our continued commitment to delivering innovative first- and best-in-class solutions to the hemophilia community. Hemophilia is a lifelong condition that significantly impacts people living with the disease—from risk of bleeds and poor joint health to increased risks during surgery. These data reinforce why it's critical to have treatment options, like ALTUVIIIO and fitusiran, that deliver effective outcomes in multiple scenarios and that can be used throughout a person's life. We look forward to working in partnership with regulatory agencies to keep bringing novel options to those living with hemophilia."

ALTUVIIIO

Interim analyses of XTEND-ed, a long-term extension phase 3 study, showed that in adult and pediatric populations, the use of ALTUVIIIO continued to provide highly effective bleed prevention leading to improvement or maintenance of joint health over a two-year period, and a safety profile consistent with that reported in the initial studies. The following abstracts will be presented at the meeting:

- **"First Interim Analysis of Clinical Outcomes in Adults and Adolescents With Severe Hemophilia A Receiving Efanesoctocog Alfa Prophylaxis in XTEND-ed, a Phase 3 Long-term Extension Study"**: In previously treated patients (≥12 years old) who had the completed the XTEND-1 (Arm A/B) trial, the mean annualized bleed rate (ABR) with ALTUVIIIO was 0.72 (standard deviation [SD])=1.26) for arm A and 0.42 (SD=0.89) for arm B. No factor VIII inhibitors were detected (abstract OC50.1).
- **"Interim Analysis of Joint Outcomes in Adult and Adolescent Patients with Severe Hemophilia A Receiving Efanesoctocog Alfa During the Phase 3 XTEND-ed Long-Term Extension Study"**: In patients who continued to receive once weekly ALTUVIIIO (50 IU/kg) in XTEND-ed, joint health had improved or been maintained in adults and adolescents over a two-year period, as measured by Hemophilia Joint Health Score total score, total joint score, and subdomain scores (abstract OC01.4).
- **"Long-term Outcomes With Efanesoctocog Alfa Prophylaxis for Previously**

Treated Children With Severe Hemophilia A, an Interim Analysis of the Phase 3 XTEND-ed Study": No factor VIII inhibitors were detected. The mean ABR was 0.70 (SD=1.27), a rate similar to the mean ABR observed in XTEND-Kids (abstract OC50.2).

Additional data being presented at ISTH show that across clinical studies, ALTUVIIIO demonstrated effective bleed protection when used for perioperative management in participants with severe hemophilia A:

- **"Perioperative Management with Efanesoctocog Alfa in Adults, Adolescents, and Children with Severe Hemophilia A in the Phase 3 XTEND Clinical Program"**: In 41 patients from the XTEND-1, XTEND-Kids, and XTEND-ed studies who underwent 49 major surgeries, hemostasis was maintained in all surgeries and hemostatic response with ALTUVIIIO was rated as excellent in most surgeries (43/49) (abstract OC14.1).

Fitusiran

Additional analyses will be presented at ISTH that support the potential of fitusiran as a first-in-class treatment offering consistent bleed protection for patients with hemophilia A or B, regardless of inhibitor status.

Novel results on the perioperative management of hemophilia using fitusiran prophylaxis in the ATLAS clinical development program demonstrated that major surgeries can be safely performed in patients on fitusiran:

- **"Surgical experience in people with hemophilia A or B with and without inhibitors receiving fitusiran"**: 60 major surgeries, including 24 in people with hemophilia with inhibitors, were conducted in the fitusiran clinical development program at the time of this analysis. Major surgeries were safely and effectively conducted with fitusiran prophylaxis following bleed management guidelines, irrespective of the patient's inhibitor status (abstract OC14.2).

Additional data presented at ISTH support the favorable safety profile for fitusiran and demonstrate that fitusiran prophylaxis under an antithrombin-based dosing regimen (AT-DR) successfully mitigated the risk of thrombotic events (TEs) and reduced the incidence of elevated liver enzymes and gallbladder inflammation or gallstones.

The following abstracts will be presented at ISTH:

- **"Incidence of thrombotic events in the fitusiran clinical development program"**: Fitusiran prophylaxis under an AT-DR led to a marked reduction in TEs with substantially greater exposure on the AT-DR (abstract OC40.2).
- **"Hepatobiliary events in the fitusiran clinical development program with the revised AT-based dose regimen"**: Fitusiran prophylaxis under an AT-DR led to reductions in liver transaminase elevations and cholecystitis/cholelithiasis events. Liver transaminase elevations were infrequent and transient, and events of cholecystitis/cholelithiasis resolved without clinical complications with no fitusiran dose interruptions or discontinuations (abstract OC40.3).

These presentations reinforce pivotal data that were presented earlier this year from the phase 3 open-label extension study (ATLAS-OLE) of fitusiran prophylaxis showing that maintaining AT activity levels between 15-35% resulted in clinically meaningful bleed control and a substantially improved benefit risk profile in people with hemophilia A or B, with or without inhibitors.

Regulatory submissions for fitusiran for the treatment of hemophilia A or B in adults and adolescents with or without inhibitors have been completed in China, Brazil and the US with a US Food and Drug Administration (FDA) target action date of March 28, 2025. The FDA also granted fitusiran Breakthrough Therapy Designation for hemophilia B with inhibitors in December 2023.

About ALTUVIIIO

ALTUVIIIO [Antihemophilic Factor (Recombinant), Fc-VWF-XTEN Fusion Protein] is a first-in-class high-sustained factor VIII therapy that is designed to extend protection from bleeds with once-weekly prophylactic dosing for adults and children with hemophilia A. In adults and adolescents, ALTUVIIIO has a 3- to 4-fold longer half-life relative to standard and extended half-life factor VIII products, providing high-sustained factor activity levels within normal to near-normal range, allowing for once-weekly administration. ALTUVIIIO is the first factor VIII therapy that has been shown to break through the von Willebrand factor ceiling, which imposes a half-life limitation on other factor VIII therapies. ALTUVIIIO builds on the innovative Fc fusion technology by adding a region of von Willebrand factor and XTEN polypeptides to extend its time in circulation.

ALTUVIIIO is currently approved and marketed in the US, Taiwan, and Japan. On June 17, 2024, it was approved by the European Commission for the treatment and prevention of bleeds and perioperative prophylaxis in hemophilia A under the name Altuvoct.

ALTUVIIIO is the first factor VIII therapy to receive Breakthrough Therapy Designation by the FDA in May 2022, Fast Track Designation in February 2021, and Orphan Drug Designation in 2017. The European Commission granted Orphan designation in June 2019.

About the XTEND-ed study

XTEND-ed (NCT04644575) is a phase 3 multicenter, open-label three-arm study of the long-term efficacy and safety of once-weekly ALTUVIIIO (50 IU/kg) in previously treated patients with severe hemophilia A. The study enrolled participants with severe hemophilia A from previous phase 3 studies, including adult and adolescent patients (≥12 years old) who completed the XTEND-1 study (NCT04161495) and children (<12 years old) who completed the XTEND-Kids study (NCT04759131) (arm A), newly initiated patients (arm B, China only), and newly initiated patients with planned major surgery (arm C). Participants received ALTUVIIIO prophylaxis for a total of 100 exposure days, cumulative from the initial study (52 weeks) and this study.

About the Sanofi and Sobi collaboration

Sobi and Sanofi collaborate on the development and commercialization of Alprolix and Elocta/Eloctate. The companies also collaborate on the development and commercialization of efanesoctocog alfa, or ALTUVIIIO in the US, Taiwan, and Japan. Sobi has final development and commercialization rights in the Sobi territory (essentially Europe, North Africa, Russia, and most Middle Eastern markets). Sanofi has final development and commercialization rights in North America and all other regions in the world excluding the Sobi territory.

About Sobi

Sobi is a specialized international biopharmaceutical company transforming the lives of people with rare and debilitating diseases. Providing reliable access to innovative medicines in the areas of hematology, immunology, and specialty care, Sobi has approximately 1,800 employees across Europe, North America, the Middle East, Asia, and Australia. In 2023, revenue amounted to SEK 22.1 billion. Sobi's share (STO:SOBI) is listed on Nasdaq Stockholm. More about Sobi at sobi.com and LinkedIn.

About fitusiran

Fitusiran is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority. Fitusiran is a potential first-in-class, antithrombin-lowering therapy for the prophylactic treatment of people with hemophilia A or B, with or without inhibitors. It is an investigational small volume, subcutaneously administered small interference RNA (siRNA) therapeutic that aims to prevent bleeds and rebalance hemostasis by lowering antithrombin, a protein that inhibits blood clotting, to promote thrombin generation. Fitusiran utilizes Alnylam Pharmaceutical Inc.'s ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability. Fitusiran has the potential to enable prophylaxis for people around the world living with hemophilia A or B with or without inhibitors by virtue of its low overall treatment burden, with as few as six small-volume subcutaneous injections per year that do not require refrigeration.

About the ATLAS clinical development program

The efficacy and safety of fitusiran are being investigated in the ATLAS clinical development program. The program includes the completed phase 3 studies ATLAS-INH (NCT03417102), ATLAS-A/B (NCT03417245), or ATLAS-PPX (NCT03549871) and the ongoing ATLAS-OLE (NCT03754790) study, a single-arm, phase 3, open-label study evaluating the safety and efficacy of fitusiran with a revised AT-DR, which was designed to maintain an antithrombin target range of 15%-35%. This study includes lower doses and less-frequent dosing than earlier studies. ATLAS-NEO (NCT05662319) is an additional phase 3 study currently recruiting participants to assess the frequency of treated bleeding episodes with fitusiran under the AT-DR in male adult and adolescent (≥12 years old) participants with hemophilia A or B, with or without inhibitory antibodies to factor VIII or IX, who have switched from their prior standard-of-care treatment.

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 the world, 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.

Sanofi is listed on EURONEXT: SAN and NASDAQ: SNY

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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 pandemics or other global crises may 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. 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, 2023. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.