At ASH, Extended Half-Life Therapies ELOCTATE® and ALPROLIX® Demonstrate Proven Efficacy and Well-Characterized Safety over Four Years

ASPIRE and B-YOND extension studies show no inhibitor development and consistently low annualized bleeding rates in study participants over four years with ELOCTATE and ALPROLIX, respectively

San Diego, Calif., December 1, 2018 – Bioverativ Inc., a Sanofi company, and Swedish Orphan Biovitrum AB (publ) (Sobi™) (STO:SOBI) today announced the final results of ASPIRE and B-YOND, the most comprehensive long-term studies of extended half-life factor therapies in hemophilia. The data from both studies confirm the established safety and sustained efficacy of ELOCTATE® [Antihemophilic Factor (Recombinant), Fc Fusion Protein], marketed as Elocta® in Europe and the Middle East, and ALPROLIX® [Coagulation Factor IX (Recombinant), Fc Fusion Protein] over four years of treatment in previously treated adult, adolescent, and pediatric patients with severe hemophilia A and B, respectively. These results were presented at the 60th Annual Meeting of the American Society of Hematology (ASH).

Factor replacement therapy is the cornerstone of hemophilia care and results from ASPIRE and B-YOND demonstrated that long-term prophylactic treatment with ELOCTATE and ALPROLIX consistently improved annualized bleed rates, including joint bleeds, across all patient populations studied and at extended dosing intervals. No inhibitors were observed in subjects enrolled in either of the two extension studies and the overall safety profile was consistent with the pivotal Phase 3 studies. Inhibitor development has been observed with ELOCTATE and ALPROLIX post market.

“These data add to a significant body of evidence showing that ELOCTATE and ALPROLIX provide protection from all types of hemophilia-related bleeds with individualized and flexible dosing regimens across all study populations,” said Tim Harris, PhD., D.Sc., Executive Vice President, Research and Development at Bioverativ. “We remain focused on and committed to providing complete protection for people with hemophilia.”

Debilitating joint disease, which is caused by repeated bleeds into joints over time, is one of the most common complications for people with hemophilia. In ASPIRE and B-YOND, subjects on prophylactic treatment experienced low joint and spontaneous joint annualized bleed rates (ABRs) across all dosing regimens. These results support that prophylactic dosing with ELOCTATE and ALPROLIX can effectively manage and control all types of joint bleeds.

“Joint protection remains a significant challenge in the long-term treatment of hemophilia, keeping individuals from living a life without constraints of their disease and these results confirm that our therapies can play a role in the effective prevention of joint bleeds,” said Milan Zdravkovic, Head of Research and Development and Chief Medical Officer, Sobi. “In addition to providing the clinical evidence to support the long-term use of our therapies, we continue to explore the impact of Fc fusion on joint health.”

An interim, post-hoc analysis of ASPIRE published in *Haemophilia* found that a prophylactic regimen of ELOCTATE can lead to continuous improvement in joint health, regardless of prior treatment regimen, severity of joint damage, or target joints[i]. This retrospective study evaluated joint health in adult and adolescent participants (n=47) using a modified version of the Hemophilia Joint Health Score (mHJHS), a first-line assessment tool that grades joints by specific domains including swelling, muscle atrophy,

alignment, range of motion, joint pain, strength, and global gait. Additional studies will be needed to confirm these findings and the mHJHS will require further validation.

ELOCTATE/Elocta and ALPROLIX are leading extended half-life therapies in the United States and Europe. They have been shown to treat all types of bleeds and can be used in all treatment scenarios, including acute, surgical, and emergency situations. The safety and efficacy of both therapies has been studied over hundreds of exposure days in adult, adolescent, and pediatric patients with hemophilia since 2010.

About ASPIRE

ASPIRE is an open-label, non-randomized, multi-year extension study for people who completed the pivotal, Phase 3 A-LONG or Kids A-Long studies. The study enrolled 211 males, including 150 (98%) of those who completed A-LONG and 61 (91%) of those who completed Kids A-LONG. The primary endpoint is the development of inhibitors. Secondary endpoints include the annualized number of bleeding episodes per subject, ELOCTATE exposure days, and a participant's assessment of response to treatment of a bleeding episode. Key findings include:

- Overall median ABRs for those on prophylactic treatment remained low throughout ASPIRE, particularly in the individualized dosing arm.
- Zero spontaneous joint bleeds were reported in subjects in all age groups in the individualized dosing arm. Median joint ABRs of <0.66 were also reported in the cohorts.
- In the study, adult and adolescent subjects (n=72) treated prophylactically with ELOCTATE experienced a mean improvement in modified hemophilia joint health (mHJHS) score of -2.5 (negative shows improvement) compared to their baseline score in A-LONG.
- Over 92% of subjects either lengthened or experienced no change in dosing intervals during the length of the study.
- Low ABRs as well as improved joint health scores reported in ASPIRE demonstrate clinical benefit of ELOCTATE that goes beyond just bleed prevention.

About B-YOND

B-YOND is an open-label, non-randomized, multi-year extension study for people who completed the pivotal, Phase 3 B-LONG or Kids B-Long studies. B-YOND enrolled 116 previously-treated males, including 93 participants (81%) who completed B-LONG, and 27 (100%) of those who completed Kids B-LONG. The primary outcome measure is development of inhibitors. Secondary endpoints include the annualized number of bleeding episodes per subject (including spontaneous joint bleeding rates), ALPROLIX exposure days per participant, ALPROLIX consumption (total IU/kg per subject per year), and the participant's assessment of response to treatment of a bleeding episode. Key findings include:

- For subjects on prophylactic treatment, ABRs remained low throughout the study across all age groups, especially related to joint and spontaneous joint bleeds.
- In adult and adolescent subjects following a prophylactic regimen with ALPROLIX, median joint and spontaneous joint ABRs were <1.58 and <0.38, respectively.
- In study participants <12 years on prophylactic treatment, median joint and spontaneous joint ABRs were <0.85 and zero, respectively.
- Data showed 85% of adult and 93% of pediatric subjects either lengthened or experienced no change in dosing intervals during the extension study.
- ALPROLIX provides flexible dosing while maintaining consistently low bleeding rates with extended interval dosing of up to 14 days.

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- The B-YOND study reflects real-world use of ALPROLIX with flexible dosing and adjustments based on individualized preference and clinical needs.

About ELOCTATE® /Elocta®
ELOCTATE® [Antihemophilic Factor (Recombinant), Fc Fusion Protein] is a recombinant clotting factor therapy developed for hemophilia A using Fc fusion technology to prolong circulation in the body. It is engineered by fusing factor VIII to the Fc portion of immunoglobulin G subclass 1, or IgG1 (a protein commonly found in the body), enabling ELOCTATE to use a naturally occurring pathway to extend the time the therapy remains in the body. While Fc fusion technology has been used for more than 15 years, Bioverativ and Sobi have optimized the technology and are the first companies to utilize it in the treatment of hemophilia. ELOCTATE is manufactured using a human cell line in an environment free of animal and human additives.

ELOCTATE is approved and marketed by Bioverativ in the United States, Japan and Canada. It is also approved in Australia, New Zealand, Brazil and other countries, and Bioverativ has marketing rights in these regions. It is also approved as Elocta® in the European Union, Switzerland, Iceland, Liechtenstein, Norway and other countries where it is marketed by Sobi.

As with any factor replacement therapy, allergic-type hypersensitivity reactions and development of inhibitors may occur in the treatment of hemophilia A. Inhibitor development has been observed with ELOCTATE/Elocta, including in previously untreated patients. For more information, please see the full U.S. prescribing information for ELOCTATE. Note that the indication for previously untreated patients is not included in the EU Product Information for Elocta.

About ALPROLIX®
ALPROLIX® [Coagulation Factor IX (Recombinant), Fc Fusion Protein] is a recombinant clotting factor therapy developed for hemophilia B using Fc fusion technology to prolong circulation in the body. It is engineered by fusing factor IX to the Fc portion of immunoglobulin G subclass 1, or IgG1 (a protein commonly found in the body), enabling ALPROLIX to use a naturally occurring pathway to extend the time the therapy remains in the body (half-life). While Fc fusion technology has been used for more than 15 years, Bioverativ and Sobi have optimized the technology and are the first companies to utilize it in the treatment of hemophilia. ALPROLIX is manufactured using a human cell line in an environment free of animal and human additives.

ALPROLIX is approved and marketed by Bioverativ for the treatment of hemophilia B in the United States, Japan and Canada. It is also approved in Australia, New Zealand, Brazil and other countries, and Bioverativ has marketing rights in these regions. It is also authorized in the European Union, Iceland, Liechtenstein, Norway and other countries, where it is marketed by Sobi.

Allergic-type hypersensitivity reactions and development of inhibitors have been observed with ALPROLIX in the treatment of hemophilia B, including in previously untreated patients. For more information, please see the full US prescribing information for ALPROLIX. Note that the indication for previously untreated patients is not included in the EU Product Information.

About Hemophilia A and B
Hemophilia is a rare, genetic disorder in which the ability of a person's blood to clot is impaired. Hemophilia A occurs in about one in 5,000 male births annually, and more rarely in females. Hemophilia B occurs in about one in 25,000 male births annually, and more rarely in females. The World Federation of Hemophilia estimates that approximately 180,000 people are currently diagnosed with hemophilia A and B worldwide.[ii]

People with hemophilia A or B experience bleeding episodes that can cause pain, irreversible joint damage and life-threatening hemorrhages. Prophylactic infusions of factor VIII or IX can temporarily replace the clotting factors that are needed to control bleeding and prevent new bleeding episodes.[iii] The World Federation of Hemophilia recommends prophylaxis as the optimal therapy as it can prevent bleedings and joint destruction.[iv]

About Bioverativ
Bioverativ, a Sanofi company, is dedicated to transforming the lives of people with hemophilia and other rare blood disorders through world-class research, development, and commercialization of innovative therapies. Bioverativ is committed to actively working with the blood disorders community, and its hemophilia therapies, when launched, represented the first major advancements in hemophilia treatment in more than two decades. For more information, visit www.bioverativ.com or follow @bioverativ on Twitter.

About Sobi™
Sobi is an international specialty healthcare company dedicated to rare diseases. Our vision is to be recognised as a global leader in providing access to innovative treatments that transform lives for individuals with rare diseases. The product portfolio is primarily focused on treatments in Haemophilia and Specialty Care. Partnering in the development and commercialisation of products in specialty care is a key element of our strategy. Sobi has pioneered in biotechnology with world-class capabilities in protein biochemistry and biologics manufacturing. In 2017, Sobi had total revenues of SEK 6.5 billion and approximately 850 employees. The share (STO:SOBI) is listed on Nasdaq Stockholm. More information is available at www.sobi.com.

About the Bioverativ and Sobi Collaboration
Bioverativ and Sobi collaborate on the development and commercialization of ALPROLIX and ELOCTATE®/Elocta® [Antihemophilic Factor (Recombinant), Fc Fusion Protein]. Bioverativ has final development and commercialization rights in North America and all other regions in the world excluding the Sobi territory, and has manufacturing responsibility for ELOCTATE and ALPROLIX. Sobi has final development and commercialization rights in the Sobi territory (essentially Europe, North Africa, Russia and most Middle Eastern markets). Sobi has elected to add the rFVIIIFc-VWF-XTEN fusion molecule and the rFIXFc-XTEN for the potential treatment of haemophilia A and B respectively to its collaboration agreement with Bioverativ.

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[i] Oldenburg J, Kulkarni R, Srivastava A,et al. Improved joint health in subjects with severe haemophilia A treated prophylactically with recombinant factor VIII Fc fusion protein. *Haemophilia*. 2017;00:1–8. https://doi.org/10.1111/hae.13353

[ii] World Federation of Hemophilia. Annual Global Survey 2015, published in October 2016. Available at: http://www1.wfh.org/publication/files/pdf-1669.pdf. Accessed on May 23, 2017.

[iii] World Federation of Hemophilia. About Bleeding Disorders – Frequently Asked Questions. Available at: http://www.wfh.org/en/page.aspx?pid=637. Accessed on May 23, 2017.

[iv] World Federation of Hemophilia. Guideline for the management of hemophilia, 2nd edition. Available at: http://www1.wfh.org/publication/files/pdf-1472.pdf. Accessed on May 23, 2017.