

PRESS RELEASE

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Interim data published in *Haemophilia* show improvements in long-term joint health for haemophilia A patients after prophylactic treatment with Elocta®

Positive results seen in study participants regardless of prior treatment regimen, severity of joint damage or target joints

First study to demonstrate continuous improvement in joint health with an extended half-life factor therapy

[Swedish Orphan Biovitrum AB \(publ\)](#) (Sobi™)(STO:SOBI) and [Bioverativ Inc.](#) (NASDAQ: BIVVV) today announces the publication of interim results from a longitudinal study of joint health in patients treated prophylactically with Elocta® (efmoroctocog alfa)/ELOCTATE® [Antihemophilic Factor (Recombinant), Fc Fusion Protein] for the treatment of haemophilia A. Interim data show participants enrolled in the ASPIRE extension study demonstrated continuous improvement in joint health over a nearly three-year period with prophylactic dosing of Elocta/ELOCTATE, regardless of prior treatment regimen, severity of joint damage or target joints. Joint health improvements were most notable in haemophilia A patients with poor joint health. These results were published online 30 October, 2017 in *Haemophilia*.

“Gradual joint destruction, which is the leading cause of morbidity for people with haemophilia, remains a significant challenge in the treatment of haemophilia A,” says Professor Johannes Oldenburg, MD, Institute of Experimental Haematology and Transfusion Medicine at the University of Bonn, Germany, and lead author of the published manuscript. “This is the first study to show that functional joint health can continue to improve using prophylactic treatment with an extended half-life factor therapy, even for those who have severe joint disease at the start of treatment.”

This interim post hoc analysis evaluated joint health in adult and adolescent participants in the A-LONG and ASPIRE studies using the modified Haemophilia 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. The study examined mHJHS measurements (a decrease in score reflecting improvement) taken at A-LONG baseline and ASPIRE baseline and annually thereafter for nearly three years of treatment.

“These findings demonstrate the potential long-term benefit of prophylactic treatment with Elocta/ELOCTATE on joint health for people with haemophilia A, particularly for those with severe joint damage, regardless of their pre-study prophylaxis or episodic treatment regimens,” said Maha Radhakrishnan, MD, Senior Vice President of Medical at Bioverativ. “Similar positive results were observed in people with haemophilia B for the first time when treated with Alprolix® in the long-term extension study B-YOND. Through our partnership with Sobi, we are focused on finding ways to help people with haemophilia

better manage their joint health through our extended half-life therapies. This work also supports Bioverativ's innovative imaging collaboration with Invicro that is focused on advancing the use of imaging for diagnosis and management of joint health."

In the study, adults and adolescents (n=47) treated prophylactically with Elocta/ELOCTATE experienced a mean improvement in joint health score of -4.1 at ASPIRE year 2, compared with A-LONG baseline. Regardless of pre-study treatment regimen, subjects showed continuous improvement in mHJHS from A-LONG baseline through ASPIRE year 2 (pre-study prophylaxis: -2.4; pre-study episodic treatment: -7.2) and benefits were seen in subjects with target joints (-5.6) as well as those with severe joint destruction (-8.8). The mHJHS components with the greatest improvement at ASPIRE year 2 were swelling (-1.4), range of motion (-1.1) and strength (-0.8)ⁱ.

"We are very encouraged by the results of this study as they reinforce the positive impact prophylactic treatment with Elocta/ELOCTATE has the potential to provide on joint health and patient outcomes," said Krassimir Mitchev, MD, PhD, Vice President and Medical Therapeutic Area Head of Haemophilia at Sobi. "Along with Bioverativ, we are dedicated to the further study of Fc fusion technology in order to better understand and address the significant unmet needs that remain in haemophilia."

Debilitating joint disease, which is caused by frequent bleeds into joints over time, is one of the most common complications for people with haemophilia and often results in chronic pain and disability. The ability to minimize joint damage over the long term should have a positive impact on patient outcomes.

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 percent) of those who completed A-LONG and 61 (91 percent) of those who completed Kids A-LONG. The primary endpoint was the development of inhibitors. Secondary endpoints included the annualized number of bleeding episodes per subject, Elocta®/ELOCTATE® exposure days and a participant's assessment of response to treatment of a bleeding episode.

About haemophilia A and B

Haemophilia is a rare, genetic disorder in which the ability of a person's blood to clot is impaired. Haemophilia A occurs in about one in 5,000 male births annually, and more rarely in females. Haemophilia 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 haemophilia A and B world-wideⁱⁱ.

People with haemophilia A and B experience bleeding episodes that can cause pain, irreversible joint damage and life-threatening haemorrhages. Prophylactic injections of factor VIII and factor IX can temporarily replace the clotting factors that are needed to control bleeding and prevent new bleeding episodesⁱⁱⁱ. The World Federation of Hemophilia (WFH) recommends prophylaxis as the optimal therapy as it can prevent bleedings and joint destruction^{iv}.

About Elocta®/ELOCTATE®

Elocta® (efmoroctocog alfa), is a recombinant clotting factor therapy developed for haemophilia A with prolonged circulation in the body using Fc fusion technology. 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 Elocta 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, Sobi and Bioverativ have optimised the technology and are the first companies to utilise it in the treatment of haemophilia. Elocta is manufactured using a human cell line in an environment free of animal and human additives.

Elocta is approved and marked by Sobi for the treatment of haemophilia A in the European Union, Iceland, Liechtenstein, Norway, Switzerland, Kuwait and Saudi Arabia. In the United States, Japan, Canada, Australia, New Zealand, Brazil, and other countries, it is approved as ELOCTATE® [Antihemophilic Factor (Recombinant), Fc Fusion Protein], and Bioverativ has marketing rights in these regions.

As with any factor replacement therapy, allergic-type hypersensitivity reactions and development of inhibitors may occur in the treatment of haemophilia A. Inhibitor development has been observed with Elocta/ELOCTATE, 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® (eftrenonacog alfa) is a recombinant clotting factor therapy developed for haemophilia 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 optimised the technology and are the first companies to utilise it in the treatment of haemophilia. Alprolix is manufactured using a human cell line in an environment free of animal and human additives.

Alprolix is approved for the treatment of haemophilia B in the European Union, Iceland, Liechtenstein, Norway, Switzerland, Kuwait and Saudi Arabia and marketed by Sobi. It is also approved in the United States, Canada, Japan, Australia, New Zealand, Brazil and other countries, and Bioverativ has marketing rights in these regions.

Allergic-type hypersensitivity reactions and development of inhibitors have been observed with Alprolix in the treatment of haemophilia B, including in previously untreated patients. For more information, please see the full [U.S. prescribing information](#) for Alprolix. Note that the indication for previously untreated patients is not included in the [EU Product Information](#).

About Bioverativ

Bioverativ is a global biopharmaceutical company dedicated to transforming the lives of people with hemophilia and other rare blood disorders through world-class research, development and commercialization of innovative therapies. Launched in 2017 following separation from Biogen Inc., Bioverativ builds upon a strong heritage of scientific innovation and is committed to actively working with the blood disorders community. The company's mission is to create progress for patients where they need it most 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. Sobi's mission is to develop and deliver innovative therapies and services to improve the lives of patients. The product portfolio is primarily focused on Haemophilia, Inflammation and Genetic diseases. Sobi also markets a portfolio of specialty and rare disease products across Europe, the Middle East, North Africa and Russia for partner companies. Sobi is a pioneer in biotechnology with world-class capabilities in protein biochemistry and biologics manufacturing. In 2016, Sobi had total revenues of SEK 5.2 billion (USD 608 M) and about 760 employees. The share (STO: SOBI) is listed on Nasdaq Stockholm. More information is available at www.sobi.com.

About the Bioverativ and Sobi collaboration

Sobi and Bioverativ collaborate on the development and commercialisation of Elocta®/ELOCTATE® and Alprolix®. Sobi has final development and commercialisation rights in the Sobi territory (essentially Europe, North Africa, Russia and most Middle Eastern markets). Bioverativ has final development and commercialisation rights in North America and all other regions in the world excluding the Sobi territory, and has manufacturing responsibility for Elocta/ELOCTATE and Alprolix.

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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://www.wfh.org/en/data-collection>

ⁱⁱⁱ World Federation of Hemophilia. About Bleeding Disorders – Frequently Asked Questions. Available at: http://www.wfh.org/en/page.aspx?pid=637#Difference_A_B. Accessed on: June 17, 2016.

^{iv} Guideline for the management of hemophilia, World Federation of Hemophilia, 2nd edition, <http://www1.wfh.org/publication/files/pdf-1472.pdf>. Accessed on December 2015