

FDA approves Cablivi® (caplacizumab-yhdp), the first Nanobody®-based medicine, for adults with acquired thrombotic thrombocytopenic purpura (aTTP)

- * First medicine approved in the U.S. specifically for the treatment of aTTP, a rare blood-clotting disorder
- * Cablivi is the first U.S. approval for Sanofi's new rare blood disorders franchise

PARIS – February 6, 2019 – The U.S. Food and Drug Administration (FDA) has approved Cablivi® (caplacizumab-yhdp) in combination with plasma exchange and immunosuppression for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP) in adults. Cablivi is the first FDA approved therapy specifically indicated for the treatment of aTTP.

“The U.S. approval of Cablivi provides a much-needed treatment option for people facing this challenging disease. There have been limited medicines available to treat aTTP until now,” says Olivier Brandicourt, M.D., Chief Executive Officer, Sanofi. *“Cablivi marks the first U.S. approval in our newly formed rare blood disorders franchise, and we look forward to continuing to provide important medicines for people living with these very serious diseases.”*

Cablivi targets von Willebrand factor (vWF), a protein in the blood involved in hemostasis. It is designed to inhibit the interaction between vWF and platelets. Cablivi is an anti-vWF Nanobody and Sanofi's first Nanobody®-based medicine to receive approval in the U.S. Nanobodies® are a novel class of proprietary therapeutic proteins based on single-domain antibody fragments that contain the unique structural and functional properties of naturally-occurring heavy chain only antibodies.

Cablivi received FDA Fast Track designation and was evaluated under Priority Review, which is reserved for medicines that represent significant improvements in safety or efficacy in treating serious conditions.

An Unmet Need in a Rare Blood Disorder

aTTP is a rare, life-threatening, autoimmune blood disorder. aTTP is considered an urgent, medical emergency. For some patients, resuscitative measures might be required and the immediate outcome might not be predictable. In most cases, patients are routinely treated in intensive care units during the first few days following their aTTP diagnosis. It is estimated that up to 20% of patients die from TTP episodes, despite currently available

treatments (plasma exchange and immunosuppression), with most deaths occurring within 30 days of diagnosis. In the U.S., aTTP affects fewer than 2,000 adults each year.

“aTTP is a very severe, life-threatening disease. For those faced with this rare diagnosis, the treatment and care can be difficult and the threat of recurrence is ever-present,” said Spero R. Cataland, M.D., Professor of Internal Medicine, Division of Hematology, Wexner Medical Center at the Ohio State University. *“Cabliivi provides new hope for adults in the U.S. suffering with aTTP and provides a much needed treatment option to help effectively manage aTTP episodes.”*

In aTTP, accumulation of ultra-large vWF causes extensive clot formation in small blood vessels throughout the body, leading to severe thrombocytopenia (very low platelet count), microangiopathic hemolytic anemia (loss of red blood cells through destruction), and ischemia (restricted blood supply to parts of the body).

Cabliivi Clinical Program and Results

The approval of Cabliivi in the U.S. is based on the results of the pivotal multicentre, randomized, double-blind, placebo-controlled Phase 3 clinical study known as HERCULES. This trial evaluated the efficacy of Cabliivi in combination with plasma exchange and immunosuppressive therapy (n=72) versus placebo, plasma exchange and immunosuppressive therapy (n=73) in 145 adults experiencing an episode of aTTP.

In the HERCULES study, treatment with Cabliivi in combination with plasma exchange and immunosuppression resulted in a significantly shorter time to platelet count response versus plasma exchange and immunosuppression alone (Hazard Ratio 1.55 [1.10; 2.20] p=0.01), the study's primary efficacy endpoint; in secondary endpoints, Cabliivi showed a significant reduction on a composite endpoint of aTTP-related death, recurrence of aTTP, or a major thromboembolic event during study drug treatment versus plasma exchange and immunosuppression alone (12.7% vs. 49.3%; p <0.0001); and a significantly lower percentage of aTTP recurrences in the overall study period versus plasma exchange and immunosuppression alone (13% vs. 38%; p<0.001). Results of this study were published in the *New England Journal of Medicine* in [January 2019](#).

In the HERCULES and TITAN (Phase 2) clinical trials, the most frequently reported adverse reactions were epistaxis (bleeding from the nose) 29%, headache 21% and gingival (gums) bleeding 16%. In the placebo group, two deaths were reported in the TITAN study and three deaths in the HERCULES study. No deaths were reported during the study drug treatment period in the Cabliivi group in the TITAN and HERCULES studies. However, one death was reported in the HERCULES study during the treatment free follow up period, which was determined not to be Cabliivi treatment related.

About Cabliivi

Cabliivi should be administered upon initiation of plasma exchange therapy, based on a diagnosis of aTTP. Cabliivi is first administered as an 11 mg intravenous injection prior to

plasma exchange, followed by an 11 mg subcutaneous injection after completion of plasma exchange on day 1. During the daily plasma exchange period and 30 days following daily plasma exchange, patients will take daily 11 mg subcutaneous injections. If after the initial treatment symptoms of the underlying disease are unresolved the treatment can be further extended for a maximum of 28 days. Subcutaneous injection can be administered by a patient/caregiver following proper training.

Cablivi is expected to be available in the U.S. late in the first quarter. The U.S. list price, or wholesale acquisition cost, for treating a typical aTTP episode with Cablivi is \$270,000. Sanofi is committed to helping U.S. patients who have been prescribed Cablivi access their medication and get the support they need, and will be launching Cablivi Patient Solutions, a comprehensive patient support program. For patients with aTTP who are prescribed Cablivi, Cablivi Patient Solutions will provide support to eligible patients who require financial assistance.

Cablivi was developed by Ablynx, which was acquired by Sanofi in 2018. Cablivi was approved in the European Union in August 2018. Cablivi is part of the company's rare blood disorders franchise within Sanofi Genzyme, the specialty care global business unit of Sanofi.

For full prescribing information, please visit www.cablivi.com.

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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Media Relations Contact

Ashleigh Koss

Tel.: +1 (908) 981-8745

ashleigh.koss@sanofi.com

Investor Relations Contact

George Grofik

Tel.: +33 (0)1 53 77 45 45

ir@sanofi.com

Sanofi Forward-Looking Statements

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commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation and the ultimate outcome of such litigation, and volatile economic conditions, as well as those risks 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, 2017. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.