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Press Release

Source: Sanofi (EURONEXT: SAN) (NYSE: SNY)

CHMP recommends approval of Cablivi™ (caplacizumab)

- * First therapeutic to receive positive CHMP opinion for treatment of a rare blood disorder called acquired thrombotic thrombocytopenic purpura

Paris, France - June 29, 2018 - The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended approval of Cablivi (caplacizumab) in Europe for the treatment of adults experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP), a rare blood-clotting disorder. Cablivi was developed by Ablynx, a Sanofi Company.

The European Commission will review the CHMP recommendation and a final decision on the Marketing Authorisation Application for Cablivi in the European Union is expected in the coming months.

Directed against von Willebrand Factor (vWF), Cablivi is Ablynx's first Nanobody®-based medicine to receive a positive CHMP opinion and, if approved, will be the first therapeutic specifically indicated for the treatment of aTTP.

aTTP is a life-threatening, autoimmune-based blood clotting disorder characterized by extensive clot formation in small blood vessels throughout the body, leading to thrombocytopenia, ischemia and widespread organ damage especially in the brain and heart. There are currently no products authorised for the treatment of aTTP and despite treatment with plasma exchange (PEX) and immunosuppression, patients remain at risk for thrombotic complications, recurrences and death. The potential of Cablivi to address this unmet need has been demonstrated in 220 patients with aTTP, who participated in the phase II TITAN and phase III HERCULES studies. Data from the TITAN study were published in the New England Journal of Medicine in [February 2016](#) and the positive HERCULES results were presented at the 59th Annual Meeting of the American Society of Hematology (ASH) in [December 2017](#).

If approved, Cablivi will be made available to patients through Sanofi Genzyme, Sanofi's specialty care business, and will be part of the unit's new rare blood disorders franchise that will launch in 2019 and which will also include Bioverativ's treatments for Hemophilia A and B.

About Cablivi (caplacizumab):

Caplacizumab is a bivalent anti-vWF Nanobody that received Orphan Drug Designation in Europe and the United States in 2009. Caplacizumab blocks the interaction of ultra-large vWF multimers with platelets and, therefore, has an immediate effect on platelet adhesion and the ensuing formation and accumulation of the micro-clots that cause the severe thrombocytopenia, tissue ischemia and organ dysfunction in aTTP. This immediate effect of caplacizumab protects the patient from the manifestations of the disease while the underlying disease process resolves.

The efficacy and safety of caplacizumab in addition to daily PEX and immunosuppression were demonstrated in the phase II TITAN and Phase III HERCULES studies. In the HERCULES study, treatment with caplacizumab in addition to standard-of-care resulted in a significantly shorter time to platelet count response ($p < 0.01$), a significant reduction in aTTP-related death, recurrence of aTTP, or at least one major thromboembolic event during study drug treatment ($p < 0.0001$), and a significantly lower number of aTTP recurrences in the overall study period ($p < 0.001$). Importantly, treatment with caplacizumab resulted in a clinically meaningful reduction in the use of PEX and length of stay in the intensive care unit (ICU) and the hospital, compared to the placebo group. In addition, caplacizumab prevents refractory disease and has a positive impact on the normalisation of organ damage markers (lactate dehydrogenase, cardiac troponin I and serum creatinine). Caplacizumab has a favourable safety profile, consistent with its mechanism of action. No deaths were reported during study drug treatment in the caplacizumab group in the TITAN and HERCULES studies, while for the placebo group, two deaths were reported in the TITAN study and three deaths in the HERCULES study.

A three-year follow-up study ([NCT02878603](#)) of patients who have completed the HERCULES study is in progress and will further evaluate the long-term safety and efficacy of caplacizumab and repeated use of caplacizumab, as well as characterising the long-term impact of aTTP.

In Europe, a MAA for caplacizumab in aTTP was submitted to the EMA in [February 2017](#) based on the Phase II TITAN study results. The phase III HERCULES study results became available in the course of this procedure and were subsequently added to the Application.

In the United States, Fast Track designation was received from the Food and Drug Administration (FDA) for caplacizumab for the treatment of aTTP in [July 2017](#) and filing of a Biologics License Application (BLA) is planned in 2018.

About aTTP

aTTP is a rare, acute, life-threatening, autoimmune blood clotting disorder. It is caused by impaired activity of the ADAMTS13 enzyme, leaving ULvWF molecules uncleaved (vWF is an important protein involved in the blood clotting process). These ULvWF molecules spontaneously bind to blood platelets, resulting in severe thrombocytopenia

(very low platelet count) and clot formation in small blood vessels throughout the body, leading to ischemia and widespread organ damage.

Despite the current standard-of-care treatment consisting of PEX and immunosuppression, episodes of aTTP are still associated with a mortality rate of up to 20%, with most deaths occurring within 30 days of diagnosis. Furthermore, patients are at risk of acute thromboembolic complications (e.g. stroke, myocardial infarction) and of recurrence of disease. Some patients have refractory disease¹, which is associated with a poor prognosis for survival of an acute episode of aTTP. Long term, patients are at increased risk for hypertension, major depression, and premature death.

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

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