



ABLYNX RECEIVES FAST TRACK DESIGNATION FROM THE FDA FOR CAPLACIZUMAB FOR THE TREATMENT OF ACQUIRED TTP

GHENT, Belgium, 26 July 2017 - Ablynx [*Euronext Brussels: ABLX; OTC: ABYLY*] today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation for caplacizumab, the Company's first-in-class anti-von Willebrand factor (vWF) Nanobody® being developed for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

The FDA's Fast Track programme is designed to facilitate the development and expedite the review of drugs that treat serious conditions and fill an unmet medical need. Drugs that receive this designation are eligible for more frequent interactions with the FDA, priority review and rolling review of the Biologics License Application (BLA). The purpose of this FDA programme is to get important new drugs to the patient earlier.

aTTP is a life-threatening, autoimmune blood clotting disorder manifested 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. Currently no products have been authorised for the treatment of aTTP and despite standard-of-care treatment with plasma exchange (PEX) and immunosuppressive therapy, patients remain at risk for thrombotic complications, recurrences and death.

The potential of caplacizumab to address this unmet need has been demonstrated in the Phase II TITAN study which supports the Marketing Authorisation Application (MAA) submitted to the European Medicines Agency (EMA) in February 2017. Caplacizumab is currently being further evaluated in the randomised, double-blind, placebo-controlled Phase III HERCULES study. Results from this Phase III study will be reported in the second half of 2017 and are expected to further support the MAA, as well as a planned BLA filing in the United States in 2018.

Dr Robert K. Zeldin, Chief Medical Officer at Ablynx, commented:

"The designation of Fast Track status by the FDA is recognition of the high unmet medical need in patients with aTTP and the potential for caplacizumab to improve outcomes in this very severe disease. We look forward to continuing to work with the FDA and accelerating the development of caplacizumab as potentially the first therapeutic specifically indicated for the treatment of aTTP."

About 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 (ULvWF) with platelets and, therefore, has an immediate effect on platelet aggregation 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 has the potential to protect the patient from the manifestations of the disease while the underlying disease process resolves.

The efficacy and safety of caplacizumab in conjunction with the standard of care of PEX and immunosuppression, were evaluated in the Phase II TITAN study in 75 patients with aTTP. Caplacizumab was well-tolerated and the primary endpoint was met ($p=0.005$), with caplacizumab treatment resulting in a 39% reduction in time to platelet count normalisation as compared to placebo (i.e., a faster reversion of

thrombocytopenia with consequent reduced use of PEX)¹. Moreover, during treatment, caplacizumab reduced recurrences of aTTP by 71% compared to placebo². Post-hoc analyses of the Phase II TITAN study data were performed to assess the impact of caplacizumab on a composite endpoint of major thromboembolic complications and aTTP-related mortality, as well as on refractoriness to standard treatment. The results demonstrate that a clinically meaningful lower proportion of subjects treated with caplacizumab experienced one or more major thromboembolic events, or died, as compared to placebo (11.4% versus 43.2%)². In addition, fewer caplacizumab-treated patients, compared to those who received placebo, were refractory to treatment (5.7% versus 21.6%)^{2, 3}. There were two deaths in the placebo group and both of those patients were refractory to treatment; no deaths were reported in the caplacizumab group.

The randomised, double-blind, placebo-controlled Phase III HERCULES study ([NCT02553317](#)) will evaluate the efficacy and safety of caplacizumab in patients with aTTP when administered in addition to the standard-of-care. The primary endpoint is time to platelet count normalisation, a measure of prevention of further microvascular thrombosis. Key secondary endpoints include a composite endpoint consisting of TTP-related mortality, recurrence of TTP and major thromboembolic events during study drug treatment, as well as the prevention of recurrence of TTP during the study period, refractoriness to treatment, and the effect on biomarkers of organ damage. Results from this Phase III study are expected in the second half of 2017 and these results are expected to support a BLA filing in the United States in 2018. In February 2017 a MAA has been submitted to the EMA for approval of caplacizumab in aTTP⁴. If approved by regulatory authorities, caplacizumab will be the first therapeutic specifically indicated for the treatment of aTTP.

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

About aTTP

aTTP is a rare, acute, life-threatening, blood clotting disorder. It has a sudden onset 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 body⁵, leading to ischemia and widespread organ damage⁶.

Despite the current standard-of-care treatment with 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 diagnosis⁷. Furthermore, patients are at risk of acute thromboembolic complications (e.g. stroke, myocardial infarction) and of recurrence of disease. Some patients are refractory to therapy³, which is associated with a poor prognosis for survival of an acute episode of aTTP. Long term, patients are at increased risk of hypertension, major depression, and premature death⁸.

About Ablynx

[Ablynx](#) is a biopharmaceutical company engaged in the development of [Nanobodies](#), proprietary therapeutic proteins based on single-domain antibody fragments, which combine the advantages of conventional

¹ Press release [June 2014](#); [Manuscript](#) in the NEJM, Feb 2016; [Manuscript](#) in the JTH, Apr 2017

² Peyvandi *et al.*, notes to editor NEJM 2016

³ Defined as: 'failure of platelet response after 7 days despite daily plasma exchange treatment'

⁴ Press release [February 2017](#)

⁵ Veyradier, NEJM 2016: "von Willebrand Factor – A new target for TTP treatment?"

⁶ Scully *et al.*, Br J Hem 2012; Sarode *et al.*, J Clin Apher 2014; Chaturvedi *et al.*, Am J Hem 2013

⁷ Benhamou, Y. *et al.*, Haematologica 2012

⁸ Deford *et al.*, Blood 2013

antibody drugs with some of the features of small-molecule drugs. Ablynx is dedicated to creating new medicines which will make a real difference to society. Today, the Company has more than [45 proprietary and partnered programmes](#) in development in various therapeutic areas including inflammation, haematology, immuno-oncology, oncology and respiratory disease. The Company has collaborations with multiple pharmaceutical companies including AbbVie; Boehringer Ingelheim; Eddingpharm; Merck & Co., Inc., Kenilworth, New Jersey, USA; Merck KGaA; Novartis; Novo Nordisk; Sanofi and Taisho Pharmaceuticals. The Company is headquartered in Ghent, Belgium. More information can be found on www.ablynx.com.

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