ABLYNX SUBMITS A MARKETING AUTHORISATION APPLICATION TO THE EUROPEAN MEDICINES AGENCY FOR CAPLACIZUMAB, ITS ANTI-vWF NANOBODY, FOR THE TREATMENT OF aTTP

- **In the Phase II TITAN study, treatment with caplacizumab significantly reduced the time to platelet count normalisation and the number of recurrences of aTTP while on drug treatment**
- **Post-hoc analysis of the TITAN study demonstrated that caplacizumab dramatically reduced the number of patients experiencing major thromboembolic events while on drug treatment**
- **Ablynx is on track to report results of the confirmatory Phase III HERCULES study in the second half of 2017 and these results are expected to support a BLA filing in the United States in 2018**
- **Ablynx intends to lead the commercialisation of caplacizumab in Europe and North America**

GHENT, Belgium, 6 February 2017 - **Ablynx** ***[Euronext Brussels: ABLX; OTC: ABYLY]*** today announced that it has submitted a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for approval of caplacizumab, its first-in-class anti-von Willebrand factor (vWF) Nanobody® for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP), an ultra-rare, acute, life-threatening blood clotting disorder with a high unmet medical need.

The MAA includes data from the Phase II TITAN study in patients with aTTP which demonstrated a statistically significant and clinically meaningful benefit of caplacizumab treatment in reducing the time to platelet count normalisation and reducing recurrences while on drug treatment. Results of post-hoc analyses of the Phase II TITAN study further demonstrated that caplacizumab dramatically reduced the number of patients experiencing major thromboembolic events, as compared to placebo.

If approved, caplacizumab will be the first therapeutic specifically indicated for the treatment of aTTP.

Dr Edwin Moses, CEO of Ablynx, commented:
"As pioneers in the treatment of aTTP, we are committed to making caplacizumab available to patients suffering from this severe disease for which there is currently no specifically approved drug available. This is a very important moment in the development of Ablynx, as we prepare to commercialise our first product and become a fully vertically integrated biopharmaceutical company. We look forward to working with the EMA during this review process."

About caplacizumab

Caplacizumab is a highly potent and selective 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 microclots 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 conjunction with the standard of care of plasma exchange (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

nearly 40% 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 placebo[1]. 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%)[1]. In addition, fewer caplacizumab-treated patients, compared to those who received placebo, were refractory to treatment[2] (5.7% versus 21.6%; and 0% versus 10.8%, respectively depending on the definition of refractoriness[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 Phase III HERCULES study in patients with aTTP is currently ongoing and is expected to support a BLA filing in the United States. This randomised, double-blind, placebo-controlled study 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.

A three-year follow-up study of patients participating 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 an ultra-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 micro-clot formation in small blood vessels throughout the body[4], leading to thrombotic complications and widespread organ damage[5].

Despite the current standard-of-care treatment 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[6]. Furthermore, patients are at risk of acute thromboembolic complications (e.g. stroke, venous thrombosis and myocardial infarction) and of recurrence of disease. The recurrence rate has been reported to range from 10-84%[7] and recurrences typically occur within 1-2 years[8] but have been reported up to 30 years after the initial episode[9]. In addition, some patients are refractory to therapy[3], which is associated with a very poor prognosis for survival of an acute episode of aTTP. Long term, patients are at increased risk of hypertension, major depression, and premature death[10].

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[1] Press release June 2014; Manuscript in the NEJM, Feb 2016; presentation at EHA 2016; presentation at ECTH 2016
[2] Peyvandi *et al.*, notes to editor NEJM 2016
[3] Defined as: 'failure of platelet response after 7 days despite daily plasma exchange treatment' or 'absence of platelet count doubling after 4 days of standard treatment, and LDH>upper limit of normal'
[4] Veyradier, NEJM 2016: "von Willebrand Factor – A new target for TTP treatment?"
[5] Scully *et al.*, Br J Hem 2012; Sarode *et al.*, J Clin Apher 2014; Chaturvedi *et al.*, Am J Hem 2013
[6] Benhamou, Y. *et al.*, Haematologica 2012
[7] Thejeel *et al.*, Am J Hem 2016
[8] Kremer Hovinga *et al.*, Blood 2010
[9] Falter *et al.*, Hämostaseologie 2013
[10] Deford *et al.*, Blood 2013

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 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., Merck KGaA, Novartis, Novo Nordisk and Taisho Pharmaceuticals. The Company is headquartered in Ghent, Belgium. More information can be found on www.ablynx.com.

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