



## ABLYNX ANNOUNCES POSITIVE TOPLINE RESULTS FROM THE PHASE III HERCULES STUDY OF CAPLACIZUMAB FOR THE TREATMENT OF ACQUIRED TTP

- **Caplacizumab meets primary endpoint and key secondary endpoints**
  - **Statistically significant reduction in time to platelet count response, with at any given time patients treated with caplacizumab 50% more likely to achieve platelet count response**
  - **74% relative reduction in the percentage of patients with aTTP-related death, a recurrence of aTTP, or at least one major thromboembolic event during the study drug treatment period**
  - **67% relative reduction in the percentage of patients with aTTP recurrence during the overall study period**
- **No caplacizumab-treated patients had refractory disease**
- **Trend to faster normalisation of organ damage markers**
- **Safety profile consistent with Phase II TITAN results and mechanism of action**
- **Data will be used to drive the registration process for caplacizumab in Europe and the USA**

**[Conference call and webcast](#) today at 4pm CET/10am ET**

**GHENT, Belgium, 2 October 2017** - Ablynx [*Euronext Brussels: ABLX; OTC: ABYLY*] today announced positive topline results from the Phase III HERCULES study with caplacizumab, the Company's anti-von Willebrand factor (vWF) Nanobody® being developed for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

Treatment with caplacizumab in addition to standard-of-care resulted in a statistically significant reduction in time to platelet count response ( $p < 0.01$ ), the primary endpoint of the study and a measure of prevention of further microvascular thrombosis. Patients on caplacizumab were 1.5 times more likely to achieve platelet count response at any given time point, compared to patients treated with placebo.

The Phase III HERCULES study also met the first two key secondary endpoints. Treatment with caplacizumab resulted in a 74% reduction in the percentage of patients with aTTP-related death, recurrence of aTTP, or at least one major thromboembolic event during study drug treatment ( $p < 0.0001$ ), with recurrences being the driver for achievement of this endpoint. In addition, the proportion of patients with a recurrence of aTTP in the overall study period (including the 28 day follow-up after discontinuation of study drug treatment) was 67% lower in the caplacizumab arm compared to the placebo arm ( $p < 0.001$ ), demonstrating the durability of the treatment effect.

Analysis of the third key secondary endpoint showed that no patients treated with caplacizumab were refractory to treatment compared to three patients treated with placebo ( $p = 0.057$ ).

The analysis of the fourth key secondary endpoint showed a trend to faster normalisation of the organ damage markers (lactate dehydrogenase, cardiac troponin I and serum creatinine) in patients treated with caplacizumab.

Based on the topline data, the safety profile of caplacizumab is consistent with its mechanism of action and the Phase II TITAN study results. The number and nature of treatment-emergent adverse events (TEAEs) were similar between the treatment groups. Serious TEAEs were more common in the placebo group, driven by the percentage of patients experiencing a recurrence of aTTP. Consistent with the mechanism of action of caplacizumab, the percentage of subjects with any bleeding-related TEAE was higher in the caplacizumab treatment group than in the placebo treatment group (66.2% vs. 49.3%). Most bleeding-related TEAEs were mild or moderate in severity. There were three deaths in the placebo group and none in the caplacizumab group during the study drug treatment period. One patient in the caplacizumab group died in the follow-up period after completing the study drug treatment and this was assessed by the investigator not to be related to study drug.

Caplacizumab is wholly-owned by Ablynx and today's reported data will be used to support the registration process for caplacizumab in Europe and the USA.

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

“Patients with aTTP are at risk for significant morbidity and early death. We believe these positive Phase III study results confirm the potential for caplacizumab to address the high unmet medical need in the treatment of aTTP and to have a meaningful impact on the lives of affected patients. We continue to analyse the data and look forward to sharing the results with regulatory authorities and the scientific community.”

“We thank the study participants and their families as well as the investigators and staff who contributed to this study.”

**Dr Edwin Moses, CEO of Ablynx, commented:**

“I am delighted by this outcome as it reinforces all our beliefs in the potential for caplacizumab to change the lives of patients affected by aTTP. This is a very important milestone for the Company as it further validates our Nanobody platform and demonstrates our ability to discover and develop medicines that make a real difference for society. These results strengthen our resolve to obtain marketing approval as quickly as possible so that caplacizumab rapidly becomes available to patients suffering from this severe disease for which there is currently no approved drug available.”

**Professor Marie Scully, leading TTP specialist from the University College Hospital in London and Investigator in the HERCULES study commented:**

“The results of this landmark trial constitute a complete game changer for patients with aTTP. They will revolutionise how we manage the acute phase of the disease, which is when patients are at highest risk for organ damage, recurrence and death.”

**Investor conference call and webcast information**

Ablynx will host a conference call/webcast today at 4pm CET, 10am ET. The webcast may be accessed by clicking [here](#). To participate in the Q&A, please dial +32 (0)2 620 01 38, using confirmation code 4097559. Shortly thereafter, a replay of the webcast will be available on the Company's website: <http://www.ablynx.com/news/events-presentations/>.

**About HERCULES**

The HERCULES study recruited 145 patients and is the largest randomised, double-blind, placebo-controlled study conducted in patients with aTTP. Patients with an acute episode of aTTP were randomised 1:1 to

receive either caplacizumab or placebo in addition to standard-of-care treatment (i.e. daily plasma exchange [PEX] and immunosuppression). Patients received a single intravenous bolus of 10mg caplacizumab or placebo followed by daily subcutaneous dose of 10mg caplacizumab or placebo until 30 days after the last daily PEX. If, at the end of this treatment period, there was evidence of persistent underlying disease activity indicative of an imminent risk for recurrence, the treatment could be extended for additional seven-day periods up to a maximum of 28 days. Patients were followed up for a further 28 days after discontinuation of treatment.

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.

### **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.

In February 2017, based on the Phase II TITAN study results, a Marketing Authorisation Application (MAA) was submitted to the European Medicines Agency (EMA) for approval of caplacizumab in aTTP<sup>1</sup>. In July 2017, Ablynx received Fast Track designation from the Food and Drug Administration (FDA) for caplacizumab for the treatment of aTTP.<sup>2</sup> Results from the Phase III HERCULES study are expected to further support the MAA, as well as a planned Biologics License Application (BLA) filing in the United States in 2018. If approved by regulatory authorities, caplacizumab would be the first therapeutic specifically indicated for the treatment of aTTP.

### **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<sup>3</sup>, leading to ischemia and widespread organ damage<sup>4</sup>.

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<sup>5</sup>. Furthermore, patients are at risk of acute thromboembolic complications (e.g. stroke, myocardial infarction) and of recurrence of disease. Some patients are refractory to therapy<sup>3</sup>, 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<sup>6</sup>.

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<sup>1</sup> Press release [February 2017](#)

<sup>2</sup> Press release [July 2017](#)

<sup>3</sup> Veyradier, NEJM 2016: "von Willebrand Factor – A new target for TTP treatment?"

<sup>4</sup> Scully *et al.*, Br J Hem 2012; Sarode *et al.*, J Clin Apher 2014; Chaturvedi *et al.*, Am J Hem 2013

<sup>5</sup> Benhamou, Y. *et al.*, Haematologica 2012

<sup>6</sup> 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., 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](http://www.ablynx.com).

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