ABLYNX INITIATES THE PHASE IIb "RESPIRE" STUDY OF ITS WHOLLY-OWNED, FIRST-IN-CLASS, INHALED ANTI-RSV NANOBODY, ALX-0171, FOR THE TREATMENT OF RSV INFECTIONS IN HOSPITALISED INFANTS

- **ALX-0171 is a first-in-class inhaled Nanobody® developed for the treatment of RSV infections**
- **ALX-0171 was safe and well tolerated in a Phase IIa study in hospitalised infants with a RSV infection**
- **ALX-0171 had an immediate and significant impact on viral replication and an encouraging initial therapeutic effect in a Phase IIa study in hospitalised infants with a RSV infection[1]**

GHENT, Belgium, 11 January 2017 - Ablynx *[Euronext Brussels: ABLX; OTC: ABYLY]* today announced that it has dosed the first patient in the Phase IIb "RESPIRE" dose-ranging efficacy study of ALX-0171, its novel inhaled drug candidate to treat RSV infections. Topline results from this Phase IIb study of inhaled ALX-0171 are expected in the second half of 2018.

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections and the leading viral cause of severe lower respiratory tract disease in infants and young children worldwide. It is the primary cause of infant hospitalisation and virus associated deaths in infants, with estimated global annual infection and hospitalisation rates of 34 million and 3-4 million respectively[2]. Current treatment of RSV infections is primarily focused on symptomatic relief, hence the need for an effective and specific anti-RSV therapeutic.

This Phase IIb study is a randomised, double-blind, placebo-controlled, international, multicentre dose-ranging study of three different doses of inhaled ALX-0171 in approximately 180 infants (aged 1-24 months) diagnosed with RSV and hospitalised for a lower respiratory tract infection. ALX-0171 will be administered once daily for three consecutive days. The study consists of a sequential dose escalation part, which is expected to enrol approximately 36 infants, followed by a parallel part in which approximately 144 infants will be randomly assigned to one of the three dose groups of inhaled ALX-0171, or placebo.

The primary endpoint of the study is to evaluate the anti-viral effect of treatment measured in nasal swabs. Secondary endpoints include safety, pharmacokinetics, clinical activity with assessment of composite clinical scores such as the Global Severity Score (using data on feeding intolerance, medical interventions, respiratory distress, apnoea, general condition and fever)[3], and time to clinical response (i.e. time needed to achieve adequate oxygen saturation and oral feeding).

Dr Edwin Moses, CEO of Ablynx, commented: "Ablynx is a pioneer in the development of a specific treatment for RSV infections. The start of this efficacy study in hospitalised infants with a RSV infection is another important step forward. If recruitment goes to plan then the study is expected to be completed in the first half of 2018 with results anticipated by the end of 2018."

About the RESPIRE study

The primary objective of the recently reported first-in-infant Phase I/IIa study in 53 hospitalised RSV-infected infants, aged 1-24 months, was to evaluate the safety and tolerability of an inhaled dose (1.5 mg/kg) of ALX-0171, administered once daily for three consecutive days. The results from this study demonstrated that ALX-

[1] Webcast presentation of 3 May 2016
[2] Nair *et al*, Lancet 2010
[3] Based on the ReSVinet Scale: Justicia-Grande *et al*, Plos One, June 2016

0171 was safe and well tolerated, had a significant and immediate impact on viral replication and that it had an encouraging initial indication of therapeutic effect.

The benign safety profile of inhaled ALX-0171 observed so far supports the study of increased doses of inhaled ALX-0171 in the Phase IIb RESPIRE efficacy trial, to evaluate the maximum potential of this novel drug candidate and to support selection of the optimal dose for future development and commercialisation.

The RESPIRE study will consist of two parts. The first part will be a sequential dose escalation that will include three cohorts of 12 subjects each of whom will be randomly (3:1 ratio) assigned to receive inhaled ALX-0171 or inhaled placebo. The first cohort will evaluate the safety of inhaled ALX-0171 at a dose of 3.0 mg/kg. After the last subject in this cohort has completed treatment, an independent data monitoring committee (DMC) will review the safety data and advise the Company on proceeding to the next cohort with a dose of 6.0 mg/kg, and the same procedure will then be used prior to the third cohort which will be dosed at 9.0 mg/kg. Recruitment will be paused while the DMC reviews each data set. Following completion of the sequential dose escalation part, the remaining 144 subjects will be randomly assigned in a 1:1:1:1 ratio to one of the three dose groups of inhaled ALX-0171 (3.0 mg/kg, 6.0 mg/kg and 9.0 mg/kg) or inhaled placebo. Subjects will receive once daily doses for three consecutive days and the total study duration per subject will be 28 days.

The primary endpoint of the study is to evaluate the anti-viral effect of inhaled ALX-0171 measured in nasal swabs, which will be determined by the time needed for the viral load (as assessed by plaque assay) to drop below the quantification limit. Secondary endpoints include safety, pharmacokinetics, clinical activity with assessment of composite clinical scores such as the Global Severity Score (using data on feeding intolerance, medical interventions, respiratory distress, apnoea, general condition and fever)[4]; and time to clinical response (i.e. time needed to achieve adequate oxygen saturation and oral feeding).

About RSV and ALX-0171

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections and the leading viral cause of severe lower respiratory tract disease in infants and young children worldwide. It is the primary cause of infant hospitalisation and virus associated deaths in infants, with estimated global annual infection and hospitalisation rates of 34 million and 3-4 million respectively[2]. It is associated with an estimated 3,000-8,500 deaths in infants <2 years globally per year[5], and it has been linked to an increased risk of asthma development later in life[6].

Current treatment of RSV infections is primarily focussed on symptomatic relief, hence the need for an effective and specific anti-RSV therapeutic.

Ablynx's ALX-0171 has been developed to address this unmet medical need and is a potential breakthrough for the treatment of RSV infection. This wholly-owned trivalent Nanobody binds to the F-protein of RSV, thereby inhibiting viral replication and neutralising RSV activity by blocking virus uptake into cells. The physical robustness of the Nanobody allows administration via inhalation directly to the site of infection, i.e. the respiratory tracts. ALX-0171 has shown a potent anti-viral effect against a broad range of RSV strains *in vitro* and it has demonstrated a marked therapeutic effect following administration via nebulisation in a neonatal animal model for infant RSV infection[7]. Repeated daily inhalation of ALX-0171 was proven to be well-tolerated in multiple Phase I clinical studies in adults and a Phase I/IIa study in hospitalised infants with a RSV infection. In addition, repeated daily inhalation of ALX-0171 had an immediate and significant impact on viral replication and an encouraging initial therapeutic effect in a Phase I/IIa study in hospitalised infants with a RSV infection.

[4] Based on the ReSVinet Scale: Justicia-Grande *et al*, Plos One, June 2016
[5] Byington et al, Pediatric 2014
[6] Sigurs *et al*, Thorax 2010; Backman *et al*, Acta Pediatr 2014
[7] Oral presentation at the 9th International RSV Symposium (November 2014); presentation available on the Ablynx website

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, Genzyme, 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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