**PRESS RELEASE**
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# ANNEXIN ADVANCES THE NEXUS STUDY TO INCLUDE PATIENTS WHO RECEIVED AN ANTI-VEGF INJECTION

**Annexin Pharmaceuticals AB announces a next patient cohort in the NEXUS study. The company continues to study the effects of the drug candidate vanexin (formerly ANXV) in patients with retinal vein occlusion (RVO) and expands the study to also include patients who have received one injection of anti-VEGF, the current standard-of-care treatment. The objective is to evaluate the safety, tolerability and signals of effect data when administering anti-VEGF and thereafter vanexin within a short timeframe. This is a preparatory step in line with the company´s intention to include the use of standard-of-care anti-VEGF in a forthcoming Phase 2b study.**

Thus far, effects of vanexin have been studied as monotherapy in treatment-naïve RVO patients. Anti-VEGF, the current standard of care, has only been administered when considered clinically necessary by the responsible investigator in order to reduce retinal swelling (macular edema, ME). Multiple patients with RVO who have received vanexin have been deemed not to require subsequent anti-VEGF treatment during the duration of the study. So far, clinical data using vanexin indicate that rebound swelling and use of anti-VEGF may be less frequent than expected, but for patients with significant MEand impaired vision, clinical improvements from receiving an anti-VEGF injection have been noted, and it is therefore justified to include this in a clinical study.

The mechanisms of action of vanexin and anti-VEGF differ. Vanexin acts to improve retinal blood perfusion, reduce inflammation and support the survival of cells at risk, while anti-VEGF rapidly neutralizes pre-existing VEGF, the main driver of ME. Therefore, the intended Phase 2b design allows for one anti-VEGF injection for patients presenting with ME in order to provide a rapid anti-ME effect, with vanexin treatment following shortly afterwards. This approach is expected to provide short- and long-term benefits and allow maintenance of visual function with significantly less subsequent need for anti-VEGF treatment. This study design is supported by the company's Medical Advisory Board but is pending regulatory advice. The NEXUS clinical study protocol, in which this expansion of RVO patient characteristics has been introduced, has recently been approved by the German regulatory authority (BfArM). Regulatory approval in the UK by MHRA is pending.

*"This development in the NEXUS study is positive and possible due to the continued favorable safety and tolerability in patients, as well as encouraging signals of effect observed to date. In the end, it is about providing short- and long-term benefits to patients, mainly supporting their ability to achieve and maintain the best possible vision," says Anna Frostegård, Chief Scientific and Medical Officer at Annexin Pharmaceuticals.*

*"The estimates of the potential commercial value of vanexin have taken the use of a loading dose, i.e. an initial anti-VEGF injection, into consideration. This approach is also expected to facilitate a more rapid patient inclusion in the NEXUS as well as in the future clinical studies, since standard of care is provided without delay alongside vanexin. We plan to enroll an initial cohort of three patients, pending safety and signal of effect data that we will receive on a rolling basis. We believe this preparative step for a Ph2b trial will facilitate the licensing discussions,"* says Anders Haegerstrand, CEO of Annexin Pharmaceuticals.

**About the NEXUS study**
Annexin's Phase 2a/proof of concept study NEXUS has an adaptive design and includes patients with diabetic retinopathy (DR), where there is a clear impact on retinal blood vessels and blood supply, as well as newly diagnosed RVO patients. It is an open-label study without a placebo group or comparison with another treatment. The study is being conducted at The Retina Clinic London, UK, with Professor Paulo-Eduardo Stanga as Principal Investigator, and from May 2026 also at STZ eye trial, Department for Ophthalmology, University Hospital Tübingen, Germany, with Dr Immanuel P. Seitz as Principal Investigator.

The study is adaptive and initially planned to include three patients with DR and RVO respectively, followed by a data analysis. After this data analysis, safety, tolerability and effect signals supported a reduction from 5 to 3 days of vanexin treatments and as recently amended, also including patients who have received an initial anti-VEGF treatment. Patients are treated with vanexin and followed up with detailed assessments up to 30 days and thereafter followed less frequently up to 120 days after the first vanexin treatment.

Both standard and high-advanced image analyses, functional and anatomical ophthalmological assessments, are performed at least monthly for four months following ANXV treatment. Evaluation is made of safety, tolerability and any signals of effect that may be related to vanexin. In addition to standardized tests of best corrected visual acuity (BCVA), the degree of diabetes-caused retinal damage, swelling of the retina and the need for anti-VEGF injections, objective functional tests and analyses of blood flow and vascular changes are performed. Initially, up to twelve patients in total are planned to be included in the study and the regulatory approvals allow for enrolment of up to 18 patients.

**About diabetic retinopathy (DR)**
DR is a serious eye disease and one of the leading causes of vision loss and blindness in people with diabetes. A significant proportion of patients suffer from vision loss during their working life. The disease occurs when high blood sugar levels damage the small blood vessels in the retina, leading to leakage, lack of oxygen and the formation of new, fragile blood vessels. Today's treatments include anti-VEGF injections, laser treatment, and surgery, but these are often costly, require repeated interventions, and do not always provide sufficient effect as they do not target the loss of blood flow in the retina. Therefore, there is a great need for new, more effective and long-term effective treatment options. Globally, it is estimated that over 100 million people are living with DR, and with an increasing prevalence of diabetes, the number of people affected is expected to rise sharply.

**About Retinal Vein Occlusion (RVO)**
RVO is a vascular disease of the eye in which blood flow in the retinal veins is acutely blocked. The disease often leads to severe visual impairment or blindness and the need for long-term treatment. Today's standard treatment for RVO consists of injections directly into the eye, usually once every 4 to 8 weeks, to treat swelling of the macula, the central area of the retina that we use to see details and distinguish between faces, but has no effect on the actual blockage of blood vessels that is the cause of RVO. Sources put the prevalence of RVO in the world at between 16 and 28 million people being affected. Most patients only have one eye affected. However, some patients may have a second occlusion in the same eye or an occlusion in the other eye.

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**About Annexin Pharmaceuticals AB**
Annexin Pharmaceuticals is a clinical stage biotechnology company active in the therapeutic areas ophthalmology and oncology. The company develops vanexin (previously ANXV), a recombinant human Annexin A5 protein, as a first-in-class biologic with potentially disease-modifying mechanisms of action. The vanexin program is currently in Phase 2 in ophthalmology for retinal vein occlusion (RVO) and diabetic retinopathy (DR) and in pre-clinical stage in oncology.
The company is based in Stockholm and listed on Nasdaq First North Growth Market Sweden under the ticker ANNX. Redeye Nordic Growth AB is the company's Certified Adviser.

**Attachments**
**Annexin advances the NEXUS study to include patients who received an anti-VEGF injection**