Outlook Therapeutics, Inc. Logo

Outlook Therapeutics® Submits Special Protocol Assessment (SPA) to FDA for Non-Inferiority Study of ONS-5010

December 19, 2023

- **NORSE EIGHT study on track to commence in Q1 2024**
- **Resubmission of ONS-5010 Biologics License Application (BLA) in the U.S. expected by the end of calendar year 2024**

ISELIN, N.J., Dec. 19, 2023 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Nasdaq: OTLK), a biopharmaceutical company working to achieve FDA approval for the first ophthalmic formulation of bevacizumab for the treatment of retinal diseases, today announced that, following receipt of written confirmation of the NORSE EIGHT proposed clinical trial protocol with the U.S. Food and Drug Administration (FDA), Outlook Therapeutics has submitted a Special Protocol Assessment (SPA) request for the required additional adequate and well-controlled study of ONS-5010.

As previously announced, following the Type A meeting with the FDA held in October 2023, the FDA informed Outlook Therapeutics that it can conduct a non-inferiority study evaluating ONS-5010 versus ranibizumab in a 3-month study of treatment naïve patients with a primary efficacy endpoint at 2 months. Subsequently, as discussed with and recommended by the FDA, Outlook Therapeutics submitted a clinical trial protocol and requested a Type A meeting with the FDA for feedback. The FDA has since provided written feedback on the protocol, which Outlook Therapeutics has incorporated. The revised protocol is the subject of the SPA request, in which Outlook Therapeutics is seeking further confirmation from the FDA that NORSE EIGHT, if successful, addresses the FDA's requirement for a second adequate and well-controlled clinical trial to support the resubmission of the ONS-5010 BLA for wet AMD. The FDA is expected to provide a response to the SPA in early February 2024.

NORSE EIGHT will be a randomized, controlled, parallel-group, masked study of neovascular age-related macular degeneration subjects randomized in a 1:1 ratio to receive 1.25 mg ONS-5010 or 0.5 mg ranibizumab intravitreal injections. Subjects will receive injections at Day 0 (randomization), Week 4, and Week 8 visits. Approximately 400 patients are expected to be enrolled in the study.

Outlook Therapeutics expects to resubmit the ONS-5010 BLA by the end of calendar year 2024 to include the results of NORSE EIGHT and the additional CMC work to address the issues identified by FDA in the Complete Response Letter issued in August 2023 to support approval.

"We have been working closely with FDA to meet the remaining requirements provided by the Agency to support approval of ONS-5010. Based on our ongoing discussions with FDA, we believe we have agreement on a clinical trial protocol. With the SPA now submitted, we are preparing to start NORSE EIGHT in the first quarter of 2024," commented Russell Trenary, President and Chief Executive Officer of Outlook Therapeutics. "We remain dedicated in our pursuit to achieve U.S. FDA approval for the first ophthalmic formulation of bevacizumab and look forward to providing further updates."

About ONS-5010 / LYTENAVA™ (bevacizumab-vikg)

ONS-5010 is an investigational ophthalmic formulation of bevacizumab under development as an intravitreal injection for the treatment of wet AMD and other retinal diseases. Because no FDA-approved ophthalmic formulations of bevacizumab are available currently, clinicians wishing to treat retinal patients with bevacizumab have had to use unapproved repackaged IV bevacizumab provided by compounding pharmacies—products that have known risks of contamination and inconsistent potency and availability. If approved, ONS-5010 would provide an FDA-approved option for physicians that currently prescribe unapproved repackaged oncologic IV bevacizumab from compounding pharmacies for the treatment of wet AMD.

Bevacizumab-vikg is a recombinant humanized monoclonal antibody (mAb) that selectively binds with high affinity to all isoforms of human vascular endothelial growth factor (VEGF) and neutralizes VEGF's biologic activity through a steric blocking of the binding of VEGF to its receptors Flt-1 (VEGFR-1) and KDR (VEGFR-2) on the surface of endothelial cells. Following intravitreal injection, the binding of bevacizumab-vikg to VEGF prevents the interaction of VEGF with its receptors on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation in the retina.

About Outlook Therapeutics, Inc.

Outlook Therapeutics is a biopharmaceutical company working to achieve FDA approval for the launch of ONS-5010/ LYTENAVA™ (bevacizumab-vikg) as the first FDA-approved ophthalmic formulation of bevacizumab for use in retinal indications, including wet AMD, DME and BRVO. If ONS-5010 ophthalmic bevacizumab is approved, Outlook Therapeutics expects to commercialize it as the first and only FDA-approved ophthalmic formulation of bevacizumab for use in treating retinal diseases in the United States, United Kingdom, Europe, Japan, and other markets. As part of the Company's multi-year commercial planning process, Outlook Therapeutics and Cencora, formerly AmerisourceBergen, entered into a strategic commercialization agreement to expand the Company's reach for connecting to retina specialists and their patients. Cencora will provide third-party logistics (3PL) services and distribution, as well as pharmacovigilance services and other services in the United States. For more information, please visit www.outlooktherapeutics.com.

Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical facts are "forward-looking statements," including those relating to future events. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "may," "might," "intend," "potential," "predict," "should," "will," or "would" the negative of terms like these or other comparable terminology, and other words or terms of similar meaning. These include, among others, statements about ONS-5010's potential as the first FDA-approved ophthalmic formulation of bevacizumab-vikg, expectations concerning our ability to remediate or otherwise resolve deficiencies identified in the CRL issued by the FDA, including with respect to an additional clinical trial and CMS issues, expectations concerning the NORSE EIGHT trial design, the timing for initiation and completion of an additional clinical trial and resubmission of the BLA for ONS-5010, expectations concerning decisions of regulatory bodies, and the timing thereof, plans for potential commercial launch of ONS-5010, expectations concerning the relationship with Cencora and the benefits and potential expansion thereof and other statements that are not historical fact. Although Outlook

Therapeutics believes that it has a reasonable basis for the forward-looking statements contained herein, they are based on current expectations about future events affecting Outlook Therapeutics and are subject to risks, uncertainties and factors relating to its operations and business environment, all of which are difficult to predict and many of which are beyond its control. These risk factors include those risks associated with developing pharmaceutical product candidates, risks of conducting clinical trials and risks in obtaining necessary regulatory approvals, the content and timing of decisions by the FDA, as well as those risks detailed in Outlook Therapeutics' filings with the Securities and Exchange Commission (the "SEC"), including the Annual Report on Form 10-K for the fiscal year ended September 30, 2022 as supplemented by the Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, in each case as filed with the SEC and future quarterly reports we file with the SEC, which include the uncertainty of future impacts related to macroeconomic factors, including as a result of the ongoing overseas conflict, high interest rates, inflation and potential future bank failures on the global business environment. These risks may cause actual results to differ materially from those expressed or implied by forward-looking statements in this press release. All forward-looking statements included in this press release are expressly qualified in their entirety by the foregoing cautionary statements. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Outlook Therapeutics does not undertake any obligation to update, amend or clarify these forward-looking statements whether as a result of new information, future events or otherwise, except as may be required under applicable securities law.

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