Outlook Therapeutics, Inc. Logo

Outlook Therapeutics® Re-Submits Biologics License Application for ONS-5010 as a Treatment for Wet AMD to the U.S. Food and Drug Administration

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ISELIN, N.J., Feb. 28, 2025 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Nasdaq: OTLK), a biopharmaceutical company that achieved regulatory approval in the European Union (EU) and the United Kingdom (UK) for the first authorized use of an ophthalmic formulation of bevacizumab for the treatment of wet age-related macular degeneration (wet AMD), today announced it has re-submitted its Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for ONS-5010, an investigational ophthalmic product which, if approved, will be branded as LYTENAVA™ (bevacizumab-vikg) for the treatment of wet age-related macular degeneration (wet AMD).

"We remain committed to bringing an ophthalmic bevacizumab to market in the United States and providing retina patients suffering from wet AMD with a much needed treatment option that has the potential to address the problems associated with unapproved repackaged bevacizumab. Our team has worked diligently to address the FDA's requests and we believe this resubmission provides the necessary evidence to support approval of the ONS-5010 BLA in the United States," commented Lawrence Kenyon, Chief Financial Officer and Interim Chief Executive Officer of Outlook Therapeutics. "This resubmission marks a very significant milestone and puts us another step closer to a transformed Outlook Therapeutics."

The ONS-5010 BLA resubmission is based on the efficacy and safety demonstrated in NORSE EIGHT, as well as additional chemistry, manufacturing and controls (CMC) information requested by the FDA. As previously announced, following Type A meetings with the FDA in Q4 CY2023 to address the ONS-5010 Complete Response Letter (CRL), the FDA informed Outlook Therapeutics that, in order to meet the FDA's requirement for a second adequate and well-controlled clinical trial of ONS-5010, it could conduct a non-inferiority study evaluating ONS-5010 versus ranibizumab in a 12 week study of treatment naïve patients with a primary efficacy endpoint at 8 weeks (NORSE EIGHT). Outlook Therapeutics believes that the complete data set for NORSE EIGHT and the additional CMC information in the BLA resubmission, combined with the data from the other NORSE clinical trials, provides the required evidence to support approval of the ONS-5010 BLA in the United States. A decision from the FDA is expected within six months.

NORSE EIGHT was a randomized, controlled, parallel-group, masked, non-inferiority study of 400 newly diagnosed, wet AMD subjects randomized in a 1:1 ratio to receive 1.25 mg ONS-5010 / LYTENAVA ™ or 0.5 mg ranibizumab intravitreal injections. Subjects received injections at Day 0 (randomization), Week 4, and Week 8 visits. The primary endpoint is the mean change in best corrected visual acuity (BCVA) from baseline to week 8. In November 2024, Outlook Therapeutics reported that in NORSE EIGHT, ONS-5010 demonstrated a mean 4.2 letter improvement in best corrected visual acuity (BCVA), which did not meet the pre-specified non-inferiority endpoint at week 8 set forth in the special protocol assessment (SPA) with the FDA.

In January 2025, Outlook Therapeutics announced results from the completed analysis of the 12-week safety and efficacy results for NORSE EIGHT, which indicated that ONS-5010 demonstrated clinically meaningful anatomic and functional improvements at each study timepoint. BCVA data across all study timepoints demonstrated an improvement in vision, increasing over time, and the presence of biologic activity. Results from the 12-week analysis demonstrated a mean improvement in BCVA of 3.3 to 5.5 letters in the ONS-5010 arm across the 4, 8, and 12 week timepoints measured in the study, compared to a mean 4.5 to 6.5 letter improvement in the ranibizumab arm over the same timepoints. Additionally, the complete NORSE EIGHT data set showed that anatomical response was similar between treatments, with a reduction in central retinal thickness of -123.9 microns for ONS-5010 treated eyes and -127.3 microns for the ranibizumab group, virtually no difference between the arms. Central retinal thickness is a key indicator of effectiveness used by retina specialists in the treatment of wet AMD.

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

ONS-5010 / LYTENAVA™ is an ophthalmic formulation of bevacizumab for the treatment of wet AMD. LYTENAVA™ (bevacizumab gamma) is the subject of a centralized Marketing Authorization granted by the European Commission in the European Union (EU) and Marketing Authorization granted by the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) for the treatment of wet AMD.

In the United States, ONS-5010 / LYTENAVA™ (bevacizumab-vikg) is investigational.

Bevacizumab-vikg (bevacizumab gamma in the EU and UK) 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 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 focused on the development and commercialization of ONS-5010/LYTENAVA ™ (bevacizumab-vikg; bevacizumab gamma), for the treatment of retina diseases, including wet AMD. LYTENAVA™ (bevacizumab gamma) is the first ophthalmic formulation of bevacizumab to receive European Commission and MHRA Marketing Authorization for the treatment of wet AMD. Outlook Therapeutics is working to initiate its commercial launch of LYTENAVA™ (bevacizumab gamma) in the EU and the UK as a treatment for wet AMD, expected in the second quarter of calendar 2025. In the United States, ONS-5010/LYTENAVA™ is investigational, and a BLA has been resubmitted to the FDA in the United States. If approved in the United States, ONS-5010/LYTENAVA ™ , would be the first approved ophthalmic formulation of bevacizumab for use in retinal indications, including wet AMD.

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," "expect," "may," "plan," "potential," "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, Outlook Therapeutics' ability to remediate or otherwise resolve deficiencies identified in the CRL issued by the FDA in the resubmitted BLA, expectations concerning decisions of regulatory bodies and the timing thereof, expectations

concerning the therapeutic potential of LYTENAVA ™ as a treatment of wet AMD, ONS-5010/LYTENAVA™'s potential as the first FDA-approved ophthalmic formulation of bevacizumab for use in treating retinal indications, including wet AMD, in the United States, Outlook Therapeutics' plans for commercial launch of LYTENAVA™ in the UK and EU and timing thereof, Outlook Therapeutics' commercialization strategy, 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 and commercializing pharmaceutical product candidates, risks of conducting clinical trials and risks in obtaining necessary regulatory approvals, the content and timing of decisions by regulatory bodies, the sufficiency of Outlook Therapeutics' resources, as well as those risks detailed in Outlook Therapeutics' filings with the Securities and Exchange Commission (SEC), including the Annual Report on Form 10-K for the fiscal year ended September 30, 2024, filed with the SEC on December 27, 2024, and future quarterly reports Outlook Therapeutics files with the SEC, which include uncertainty of market conditions and future impacts related to macroeconomic factors, including as a result of the ongoing overseas conflicts, 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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