Outlook Therapeutics, Inc. Logo

Outlook Therapeutics Provides Regulatory Update on U.S. Food and Drug Administration Review of ONS-5010/LYTENAVA™ (bevacizumab-vikg) for the Treatment of Wet AMD

December 31, 2025

FDA issues Complete Response Letter (CRL) for resubmitted ONS-5010 BLA

ISELIN, N.J., Dec. 31, 2025 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Nasdaq: OTLK), a biopharmaceutical company focused on enhancing the standard of care for bevacizumab for the treatment of retina diseases, today announced that the U.S. Food and Drug Administration (FDA) has issued a complete response letter (CRL) to the ONS-5010/LYTENAVA ™ (bevacizumab-vikg) biologics license application (BLA) resubmission, indicating that the FDA cannot approve the application in its present form for the treatment of wet age-related macular degeneration (wet AMD).

In the CRL, the FDA noted that the additional mechanistic and natural history data information provided in the BLA resubmission does not alter the previous review conclusion that while the one adequate and well-controlled study demonstrated efficacy, the FDA has again recommended that confirmatory evidence of efficacy be submitted to support the application, however the FDA has not indicated what type of confirmatory evidence would be acceptable.

"Our goal has always been to provide wet AMD patients and their physicians with a safe, consistent, FDA-approved alternative to compounded Avastin manufactured in the United States, and that goal has not changed. We are disappointed and disagree with this decision, but we remain fully committed to taking all necessary steps to receive approval in the United States. We continue to believe strongly in the clinical need and commercial potential of the first on-label bevacizumab product for patients in the United States that is specifically formulated, manufactured, and packaged for intravitreal use," commented Bob Jahr, Chief Executive Officer of Outlook Therapeutics.

The ONS-5010 BLA resubmission was based on the complete data set from the NORSE clinical trial program, which included the successful NORSE TWO adequate and well-controlled pivotal clinical trial as well as confirmatory safety and efficacy data from all other NORSE trials, including NORSE EIGHT, an adequate and well-controlled 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. Outlook Therapeutics continues to believe that the complete data set for NORSE TWO, 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.

Outlook Therapeutics is currently exploring all available pathways for potential approval in the U.S. and intends to continue its efforts to expand into additional markets in Europe and other regions. As previously announced, LYTENAVA™ (bevacizumab gamma) was granted Marketing Authorization by the European Commission in the EU and Marketing Authorization by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK for the treatment of wet AMD. In June 2025, LYTENAVA™ (bevacizumab gamma) became commercially available in Germany and the UK for the treatment of wet AMD. In addition to current plans to expand its commercial presence in select countries in Europe, Outlook Therapeutics continues to speak with and explore collaborations with potential commercial and distribution partners in additional European countries, as well as outside of Europe. LYTENAVA™ (bevacizumab gamma) is the first and only authorized ophthalmic formulation of bevacizumab for use in treating wet AMD in adults in the European Union and UK.

About Wet AMD

Age-related macular degeneration, AMD, is a common eye condition and a leading cause of vision loss among people aged 50 and older. It causes damage to the macula, a small spot near the center of the retina and the part of the eye needed for sharp, central vision, which lets us see objects that are straight ahead. Wet AMD, a form of late-stage AMD, is also called neovascular AMD.

In wet AMD, abnormal blood vessels grow underneath the retina. These vessels leak fluid and blood, which may lead to swelling and damage to the macula, causing vision loss. Additionally, with wet AMD, abnormally high levels of vascular endothelial growth factor (VEGF) are secreted in the eyes. VEGF is a protein that promotes the growth of new abnormal blood vessels; anti-VEGF injection therapy blocks this growth and has become the standard-of-care treatment for wet AMD and other retinal diseases, such as diabetic macular edema and branch retinal vein occlusion.

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

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

In the United States, ONS-5010/LYTENAVA ™ (bevacizumab-vikg) is investigational. In certain European Union Member States ONS-5010/LYTENAVA™ must receive pricing and reimbursement approval before it can be sold.

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) to enhance the standard of care for bevacizumab for the treatment of retina diseases. 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 commenced commercial launch of LYTENAVA™ (bevacizumab gamma) in Germany and the UK as a

treatment for wet AMD.

In the United States, ONS-5010/LYTENAVA™ (bevacizumab-vikg) is investigational. 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," "on track," "plan," "potential," "target," "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, plans for commercial launch of LYTENAVA™ in additional markets and the timing thereof, expectations concerning decisions of regulatory bodies and the timing thereof, including market exclusivity, the future potential to receive approval from the FDA and the timing thereof, the potential of ONS-5010/LYTENAVA™ as a treatment for wet AMD, the market opportunity for LYTENAVA™ in Europe, the United States and other countries, the ability to successfully launch directly or via partnerships with other companies, 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, including the risk that the data from the NORSE EIGHT trial does not support the approval by the FDA of the ONS-5010 BLA, the content and timing of decisions by regulatory bodies, the acceptance of Outlook Therapeutics' products by healthcare professionals and patients as safe, effective, and cost-effective, the impact of governmental and semi-governmental laws, regulations and guidelines, reliance on third-party service providers, suppliers, and manufacturers, 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 (the SEC), including the Annual Report on Form 10-K for the fiscal year ended September 30, 2025, filed with the SEC on December 19, 2025, as supplemented by future 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, tariffs and trade tensions, fluctuations in interest rates and 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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