Outlook Therapeutics, Inc. Logo

Outlook Therapeutics® Announces Preliminary Topline Results of NORSE EIGHT Clinical Trial

November 27, 2024

- **Final efficacy data expected in January 2025**
- **Anticipate resubmission of BLA in calendar Q1 2025**

ISELIN, N.J., Nov. 27, 2024 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Nasdaq: OTLK), a biopharmaceutical company that achieved regulatory approval in the European Union and the United Kingdom earlier this year for the first authorized use of an ophthalmic formulation of bevacizumab for the treatment of wet age-related macular degeneration (wet AMD), today announced preliminary topline results of NORSE EIGHT, the second of two adequate and well controlled clinical trials evaluating ONS-5010 in wet AMD patients. Upon the completion of analysis of the final results of NORSE EIGHT, Outlook Therapeutics plans to resubmit the Biologics License Application (BLA) application for ONS-5010 in the first quarter of calendar 2025.

In the NORSE EIGHT trial, ONS-5010 did not meet the pre-specified non-inferiority endpoint at week 8 set forth in the special protocol assessment (SPA) with the U.S. Food and Drug Administration (FDA). However, the preliminary data from the trial demonstrated an improvement in vision and the presence of biologic activity, as well as a continued favorable safety profile for ONS-5010. Analysis of the data is ongoing as the month 3 data from NORSE EIGHT is being collected, which is expected to be available in January 2025. Upon receipt of the full month 3 efficacy and safety results for NORSE EIGHT, Outlook Therapeutics plans to resubmit the BLA application for ONS-5010 in the first quarter of calendar 2025. In addition, plans for a potential 2025 launch in the UK and Germany are ongoing, where LYTENAVA ™ has received European Commission and MHRA Marketing Authorization for the treatment of wet AMD. Outlook Therapeutics remains confident that ONS-5010/ LYTENAVA ™ is an important therapy for the treatment of wet AMD in place of off-label repackaged bevacizumab that has not received regulatory approval for use in ophthalmology.

The pre-specified non-inferiority endpoint at week 8 set forth in the SPA with the FDA was measured by mean change in best corrected visual acuity (BCVA) from baseline to week 8. The difference in the means between the ONS-5010 and ranibizumab in the NORSE EIGHT trial was -2.257 BCVA letters with a 95% confidence interval of (-4.044, -0.470) while the lower bound of the pre-specified non-inferiority margin in the SPA was -3.5 at a 95% confidence interval; the hypothesis of noninferiority was not met (p>0.025). In the intent-to-treat (ITT) primary dataset, NORSE EIGHT demonstrated a mean +4.2 letter improvement in BCVA in the ONS-5010 arm and +6.3 letter improvement in BCVA in the ranibizumab arm.

	Mean change in BCVA at week 8	Non-Inferiority
ONS-5010 1.25 mg	+4.2 letters	95%CI: (-4.044, -0.470) P-value: 0.0863
Ranibizumab 0.5mg	+6.3 letters	

In NORSE EIGHT, ONS-5010 was generally well-tolerated with overall ocular adverse event rates comparable to ranibizumab. The safety results demonstrated in NORSE EIGHT are consistent with previously reported safety results from the NORSE ONE, NORSE TWO, and NORSE THREE clinical trials, with no cases of retinal vasculitis reported in either study arm. Additional safety and efficacy data from the NORSE EIGHT trial will be analyzed after all subjects complete their final visit at month 3.

Remediation of the Chemistry, Manufacturing and Controls (CMC) comments in the Complete Response Letter (CRL) is complete and has been closely aligned with the FDA in type C and type D meetings**.**

In the European Union and the United Kingdom, ONS-5010/LYTENAVA™ (bevacizumab gamma) has already been granted Marketing Authorization. Outlook Therapeutics intends to continue efforts to begin launching in Europe in 2025 either directly or with a licensing partner. Discussions with potential licensing partners for markets outside of the United States are ongoing.

About NORSE EIGHT

NORSE EIGHT was a randomized, controlled, parallel-group, masked, non-inferiority study of newly diagnosed, wet AMD subjects randomized in a 1:1 ratio to receive 1.25 mg ONS-5010 or 0.5 mg ranibizumab intravitreal injections. Subjects received injections at day 0 (randomization), week 4, and week 8 visits. The primary endpoint was mean change in best corrected visual acuity (BCVA) from baseline to week 8. For more information about the NORSE EIGHT study, visit clinicaltrials.gov and reference identifier NCT06190093.

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 age-related macular degeneration (wet AMD).

In the United States, ONS-5010/LYTENAVA™ (bevacizumab-vikg) is investigational and is being evaluated in an ongoing non-inferiority study for the treatment of wet AMD.

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 first half of calendar 2025. In the United States, ONS-5010/LYTENAVA ™ is investigational, is being evaluated in an ongoing non-inferiority study for the treatment of wet AMD, and the data may be sufficient for Outlook to resubmit a BLA 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,” “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, ONS-5010’s status as the first and only European Commission, MHRA approved ophthalmic formulation of bevacizumab for use in treating retinal diseases in the EU and UK, and plans to continue analyzing data for the NORSE EIGHT trial and the potential to resubmit the BLA for ONS-5010 and the timing thereof, expectations concerning Outlook Therapeutics’ ability to remediate or otherwise resolve deficiencies identified in the CRL issued by the FDA, including with respect to an additional clinical trial and CMC issues, expectations concerning decisions of regulatory bodies and the timing thereof, plans for commercial launch of ONS-5010 in the UK and EU and the timing thereof, including the potential to launch with a partner, expectations concerning the sufficiency of the Company’s cash resources 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, including the risk that the data from the NORSE EIGHT trial does not support the resubmission or subsequent filing by the FDA of the ONS-5010 BLA, 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, 2023, filed with the SEC on December 22, 2023, and 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, 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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