Outlook Therapeutics, Inc. Logo

Outlook Therapeutics® Announces Complete Twelve Week Efficacy and Safety Results of NORSE EIGHT Clinical Trial

January 16, 2025

- **ONS-5010 demonstrated to be non-inferior to Lucentis at 12 weeks**
- **BLA resubmission on track for calendar Q1 2025**
- **Entered into agreements for warrant inducement transaction expected to result in up to $20.4 million in gross proceeds**

ISELIN, N.J., Jan. 16, 2025 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Outlook Therapeutics, or the Company) (Nasdaq: OTLK), a biopharmaceutical company that achieved regulatory approval in the European Union and the United Kingdom 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 completed the analysis of the complete 12-week safety and efficacy results for NORSE EIGHT, the second of two adequate and well controlled clinical trials evaluating ONS-5010 in wet AMD patients. ONS-5010 demonstrated noninferiority to ranibizumab at week 12 in the NORSE EIGHT trial. Based on the completed analysis of the 12-week results, Outlook Therapeutics plans to resubmit the Biologics License Application (BLA) for ONS-5010 in the first quarter of calendar 2025.

Julia A. Haller, MD, Ophthalmologist-in-Chief at Wills Eye Hospital and an Outlook Therapeutics Board member, commented, “The 3-month data from NORSE EIGHT provides additional evidence to confirm what retina specialists expected. The clinical trial continues to demonstrate that ONS-5010 injections result in immediate and sustained anatomic efficacy, with steady gains in visual acuity and reliable, consistent safety.”

The difference in the mean between ONS-5010 and ranibizumab was -1.009 best corrected visual acuity (BCVA) letters with a 95% confidence interval of (-2.865, 0.848) in the NORSE EIGHT trial. Applying the statistical parameters from the week 8 primary endpoint with the lower bound of the non-inferiority margin at -3.5 with a 95% confidence interval, the noninferiority margin was met at week 12 (p=0.0043), indicating that the two study arms are not different at this timepoint. In the intent-to-treat (ITT) population, NORSE EIGHT demonstrated a mean 5.5 letter improvement in BCVA in the ONS-5010 arm and 6.5 letter improvement in BCVA in the ranibizumab arm.

	Mean change in BCVA at week 12	Non-Inferiority
ONS-5010 1.25 mg	+5.5 letters	95%CI: (-2.865, 0.848) P-value: 0.0043
Ranibizumab 0.5mg	+6.5 letters	

Additionally, the change in central retinal thickness, a measure of anatomical response, was similar in both study arms at all three study timepoints.

Mean change in central retinal thickness			
	Week 4	Week 8	Week 12
ONS-5010 1.25 mg	-106.6 microns	-117.7 microns	-123.9 microns
Ranibizumab 0.5mg	-108.4 microns	-120.9 microns	-127.3microns

As previously announced, 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, BCVA data across all study timepoints demonstrated an improvement in vision, increasing over time, and the presence of biologic activity. Overall, in NORSE EIGHT, ONS-5010 demonstrated mean visual acuity improvements of +3.3 letters at week 4, +4.2 letters at week 8, and +5.5 letters at week 12.

Additionally, in NORSE EIGHT, ONS-5010 was generally well-tolerated with overall ocular adverse event rates comparable to ranibizumab. The safety results demonstrated across the full duration of 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.

“We believe that the statistically significant 12-week results for ONS-5010 in NORSE EIGHT, combined with the complete NORSE EIGHT data set, confirms our successful NORSE TWO pivotal study and will support the resubmission of our BLA in the United States for the treatment of wet AMD,” added Lawrence Kenyon, Chief Financial Officer and Interim Chief Executive Officer of Outlook Therapeutics. “Our team continues the necessary work for the planned resubmission of our BLA in the first quarter of calendar 2025. We remain confident in the potential of ONS-5010/LYTENAVA™ to provide 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 retinal diseases here in the United States.”

In the European Union and the United Kingdom, ONS-5010/LYTENAVA™ (bevacizumab gamma) has already been granted Marketing Authorization. Outlook Therapeutics intends to begin launching in Europe in the first half of calendar 2025.

Warrant Inducement Transaction

The Company has entered into warrant exercise inducement offer letters (the Inducement Letters) with certain holders of existing warrants to purchase the Company’s common stock, exercisable for an aggregate of 8,146,066 shares of common stock (the Existing Warrants), pursuant to which the holders agreed to exercise their Existing Warrants at a reduced exercise price of $2.51 per share, in exchange for the Company’s agreement to issue, for each Existing Warrant exercised, two new warrants to purchase common stock (the Inducement Warrants). The reduction of the exercise price of the Existing Warrants and the issuance of the Inducement Warrants was structured as an at-the-market transaction under Nasdaq rules.

The gross proceeds to the Company from the exercise of the Existing Warrants are expected to be up to approximately $20.4 million prior to deducting capital markets advisory fees and estimated offering expenses.

In consideration for the immediate exercise of the Existing Warrants for cash at the Reduced Exercise Price, holders will receive Inducement Warrants. The Inducement Warrants will be exercisable for an aggregate of up to 16,292,132 shares of Common Stock at an exercise price of $2.26 per share. The Inducement Warrants will only be exercisable for cash, except in limited circumstances. Half of the Inducement Warrants will be exercisable immediately and have a term of five years from the date of issuance. The remaining Inducement Warrants will be exercisable upon the effectiveness of an amendment to the Company's certificate of incorporation to increase the number of shares of common stock authorized for issuance and will have a term of five years from the effectiveness of such amendment. At its 2025 annual meeting of stockholders, the Company will submit a proposal to approve the amendment to its certificate of incorporation.

The Company intends to use the net proceeds from the exercise of the Existing Warrants to fund its ONS-5010 clinical development programs, European commercial launch of LYTENAVA™ and for working capital and general corporate purposes.

In connection with the transaction described above, BTIG, LLC served as capital markets advisor.

The Inducement Warrants and shares of common stock issuable upon exercise thereof were offered in a private placement in reliance on the exemptions provided by Section 4(a)(2) of the Securities Act of 1933, as amended (the Securities Act), and similar exemptions under applicable state laws and have not been registered under the Securities Act or applicable state securities laws. Accordingly, the Inducement Warrants and the underlying shares of common stock may not be offered or sold in the United States except pursuant to an effective registration statement or an applicable exemption from the registration requirements of the Securities Act and such applicable state securities laws. As part of the transaction, the Company has agreed to file a resale registration statement on Form S-3 to register the resale of the shares of common stock underlying the Inducement Warrants.

The warrant inducement transaction with respect to an aggregate of 7,074,637 Existing Warrants for gross proceeds of $17.8 million is expected to close on or about January 17, 2025, subject to the satisfaction of certain customary closing conditions. The closing of the warrant inducement transaction with Syntone, which accounts for the exercise of an aggregate of 1,071,429 Existing Warrants for gross proceeds of $2.7 million, is subject to receipt of certain regulatory approvals.

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, and returned for a final study visit at week 12. The primary endpoint was mean change in 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 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 theUK 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 if successful, 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," "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' plans for commercial launch of LYTENAVA™ in the UK and EU and timing thereof, as well as the potential to launch with a partner, expectations concerning Outlook Therapeutics' ability to remediate or otherwise resolve deficiencies identified in the CRL issued by the FDA, plans to resubmit the BLA for ONS-5010 and the timing thereof, Outlook Therapeutics' commercialization strategy, expectations concerning decisions of regulatory bodies and the timing thereof, 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, expectations concerning the warrant inducement transaction, including the amount and use of proceeds therefrom, the expected timing of closing, and the stockholder approval required in connection therewith, 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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