Outlook Therapeutics, Inc. Logo

Outlook Therapeutics Reports New Positive 12-Month Safety Data from Pivotal Phase 3 NORSE TWO Trial

September 28, 2021

- **Full year data reinforce strong safety profile consistent with previous trials of ONS-5010 and with prior published data on ophthalmic bevacizumab**
- **Full data to be presented at American Academy of Ophthalmology's Retina Subspecialty Meeting, RET13 - Section X: Late Breaking Developments, Part II on November 13th at 9:17 AM ET**

ISELIN, N.J., Sept. 28, 2021 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Nasdaq: OTLK), a biopharmaceutical company working to develop and launch the first FDA-approved ophthalmic formulation of bevacizumab for use in retinal indications, today announced new 12-month safety data from the pivotal Phase 3 NORSE TWO trial that further confirm the strong safety profile in this study of ONS-5010 / LYTENAVA™ (bevacizumab-vikg) for treatment of neovascular age-related macular degeneration (wet AMD). In August 2021, Outlook Therapeutics announced the topline readout of pivotal data from its NORSE TWO trial, which included 11 months of safety data. The topline data previously reported from NORSE TWO demonstrated clinically relevant and highly statistically significant results as well as a robust safety profile indicating that in the trial ONS-5010 was well tolerated and showed no unanticipated safety signals.

"The full 12-month safety data results move us one step closer to providing patients with an FDA-approved, cGMP-produced drug product that meets ophthalmic FDA standards and avoids the potential risks of repackaged IV bevacizumab," said C. Russell Trenary III, President and CEO of Outlook Therapeutics. "Our goal is to offer patients, in the United States and globally, a safe and effective, approved ophthalmic bevacizumab. ONS-5010 is specifically formulated to meet requirements to treat retinal diseases like wet AMD. We continue to work towards submitting a Biologics License Application for ONS-5010 to the U.S. Food and Drug Administration for ONS-5010 in the first calendar quarter of 2022."

The NORSE TWO pivotal Phase 3 clinical trial enrolled a total of 228 subjects with wet AMD across 39 clinical trial sites in the United States. Participants in the trial were followed for 12 months. The primary endpoint for the study was the proportion of patients who gained at least 15 letters in the best corrected visual acuity (BCVA) at 11 months. The trial compared ONS-5010 dosed monthly to LUCENTIS®, which was dosed using one of the regimens listed in the LUCENTIS® label (i.e., patients were treated monthly for the first three months followed by less frequent dosing; the PIER regimen). The key secondary endpoint for NORSE TWO was the mean change in the BCVA through 11 months.

"The success of NORSE TWO continues to solidify the potential of ONS-5010 ophthalmic bevacizumab as a highly effective and safe treatment in treating wet AMD," added Terry Dagnon, Chief Operating Officer of Outlook Therapeutics. "We are excited that the highly statistically significant and clinically relevant results from NORSE TWO demonstrate the potential clinical value of ONS-5010 for patients and will work closely with the FDA and other global authorities to bring this new option to patients, clinicians and payors as quickly as possible."

Topline data from NORSE TWO showed that ONS-5010 bevacizumab-vikg met the primary and key secondary endpoints for efficacy with clinically impactful change observed for treated patients. The NORSE TWO primary endpoint difference in proportion of subjects gaining at least 15 letters BCVA was met and was highly statistically significant and clinically relevant. In the intent-to-treat (ITT) primary dataset, the percentage of patients who gained at least 15 letters who were treated with ranibizumab was 23%, and the percentage of patients who gained at least 15 letters who were treated with bevacizumab-vikg was 41% (p = 0.0052). The primary endpoint was also statistically significant and clinically relevant in the secondary per-protocol (PP) dataset (p = 0.04) where the percentages were almost identical, at 24% with ranibizumab and 41% with bevacizumab-vikg. The key secondary endpoint BCVA score change from baseline to month 11 in the primary ITT dataset was also highly statistically significant and clinically relevant (p = 0.0043). A mean change in BCVA was observed with ranibizumab of 5.8 letters and the mean change with bevacizumab-vikg was 11.2 letters. The results were also statistically significant in the secondary PP dataset (p = 0.05) with a mean change in letters with ranibizumab of 7.0 letters and with bevacizumab-vikg 11.1 letters.

The safety results demonstrated in NORSE TWO are consistent with previously reported safety results from Outlook Therapeutics' NORSE ONE and NORSE THREE clinical trials. Following exposure to bevacizumab-vikg, there was only one subject who reported an adverse event of ocular inflammation in all three trials. In NORSE TWO, there was only a single related ocular serious adverse event reported in the bevacizumab-vikg trial arm, which resolved, and no unanticipated safety signals were detected. The most common ocular adverse event was intravitreal injection-related hemorrhage in the tissues on the surface of the eye (conjunctival hemorrhage) that resolved without any sequela. The ONS-5010 safety database, now with 12 months of NORSE TWO data, continues to be consistent with previously published results for bevacizumab, such as in the 2011 CATT clinical trial.

ONS-5010 (bevacizumab) registration clinical trial program

Outlook Therapeutics' wet AMD ONS-5010 clinical program for the planned BLA consists of three clinical trials: NORSE ONE, a proof-of-concept clinical experience trial in wet AMD patients; NORSE TWO, the pivotal Phase 3 wet AMD trial; and NORSE THREE, a supplemental safety study in patients with wet AMD and other retina diseases undertaken to ensure that a sufficient number of patients have been dosed with ONS-5010 to support the BLA submission. Results from NORSE ONE and NORSE THREE demonstrated positive proof-of-concept and a safety profile consistent with that of prior published research on bevacizumab for ophthalmic use. NORSE TWO provided pivotal data that demonstrated positive and highly statistically significant and clinically relevant efficacy and safety data for treatment of patients with wet AMD.

With the registration clinical trials now completed, Outlook Therapeutics plans to submit a BLA under the Public Health Service Act (PHSA) 351(a) regulatory pathway in the first quarter of calendar 2022. If the BLA is approved, it is expected to result in 12 years of marketing exclusivity for ONS-5010 as the first and only ophthalmic formulation of bevacizumab approved by the FDA to treat wet AMD.

Full data from NORSE TWO will be presented at the American Academy of Ophthalmology's Retina Subspecialty Meeting, RET13 - Section X: Late Breaking Developments, Part II on November 13, 2021, at 9:17 AM ET. The NORSE TWO data will also be submitted for publication in a

peer-reviewed journal.

Pre-commercialization planning underway

Per the National Eye Institute (NEI), use of unapproved repackaged IV bevacizumab from compounding pharmacies is estimated to account for approximately 50% of all wet AMD prescriptions in the United States each year. Globally, the nine major markets account for an estimated $13.1 billion market for anti-VEGF drugs to treat retina diseases.

In anticipation of potential FDA marketing approval in 2022 for ONS-5010, Outlook Therapeutics has begun commercial launch planning, including manufacturing with drug substance manufacturer FUJIFILM Diosynth Biotechnologies and best-in-class drug product manufacturer Aji Biopharma Services, distribution, sales force planning, physician and payor advisory board outreach, key opinion leader support and payor community engagement. To bring ONS-5010 to market in a way that benefits all stakeholders – patients, clinicians, and payors – Outlook Therapeutics has already commenced collaborative discussions with payors and the retina community. Outlook Therapeutics expects ONS-5010, if approved, to be a safe and cost-effective choice for patients, payors and clinicians worldwide for retinal indications.

Outlook Therapeutics is also developing registration documents on a parallel path for approvals in Europe and expects to submit them shortly after completing the submission to the FDA. Outlook Therapeutics continues to explore potential strategic commercialization partners, such as Syntone Biopharma JV in China.

In addition to the clinical development program evaluating ONS-5010 for wet AMD, Outlook Therapeutics has received agreements from the FDA on three Special Protocol Assessments (SPAs) for three additional registration clinical trials. These SPAs cover the protocols for a planned registration clinical trial evaluating ONS-5010 to treat branch retinal vein occlusion (BRVO, NORSE FOUR), and two planned registration clinical trials evaluating the drug candidate for the treatment of diabetic macular edema (DME, NORSE FIVE and NORSE SIX). Outlook Therapeutics expects to initiate registration clinical trials for ONS-5010 for DME and BRVO later in 2021 or in early 2022.

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

ONS-5010 is an investigational ophthalmic formulation of bevacizumab under development to be administered as an intravitreal injection for the treatment of wet AMD and other retinal diseases. Because no currently approved ophthalmic formulations of bevacizumab are available, 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 will replace the need to use unapproved repackaged IV bevacizumab from compounding pharmacies for the treatment of wet AMD.

ONS-5010 is a full-length, humanized anti-VEGF (Vascular Endothelial Growth Factor) recombinant monoclonal antibody (mAb) that inhibits VEGF and associated angiogenic activity. VEGF is a protein that promotes the growth of abnormal new blood vessels and promotes leakage from these vessels leading to retinal edema and hemorrhage. With wet AMD, abnormally high levels of VEGF are secreted in the eye and lead to loss of vision. Anti-VEGF injection therapy treats the vision-threatening leakage and hemorrhage as wells as blocks the growth of the abnormal blood vessels. Since the advent of anti-VEGF therapy, it has become the standard-of-care treatment option within the retina community globally.

About Outlook Therapeutics, Inc.

Outlook Therapeutics is a biopharmaceutical company working to develop and launch 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. Outlook Therapeutics expects to submit ONS-5010 ophthalmic bevacizumab to the U.S. FDA as a BLA under the PHSA 351(a) regulatory pathway. 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 “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “project,” “believe,” “estimate,” “predict,” “potential,” “intend” or “continue,” 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, including benefits therefrom to patients, payors and physicians, including expectations of market exclusivity, the timing of BLA submission and commercial launch of ONS-5010, plans for regulatory approvals in other markets and plans for future clinical trials. 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, as well as those risks detailed in Outlook Therapeutics’ filings with the Securities and Exchange Commission, including the Annual Report on Form 10-K for the fiscal year ended September 30, 2020, as amended, and subsequent Quarterly Reports on Form 10-Q, which include the uncertainty of future impacts related to the ongoing COVID-19 pandemic. 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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