Outlook Therapeutics, Inc. Logo

Outlook Therapeutics® Announces Acceptance of Biologics License Application by U.S. FDA for ONS-5010 as a Treatment for Wet AMD

October 28, 2022

- **Prescription Drug User Fee Act (PDUFA) goal date of August 29, 2023**

ISELIN, N.J., Oct. 28, 2022 (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 that the U.S. Food and Drug Administration (FDA) has accepted for filing a Biologics License Application (BLA) for ONS-5010 / LYTENAVA ™ (bevacizumab-vikg), an investigational ophthalmic formulation of bevacizumab for the treatment of wet age-related macular degeneration (wet AMD). The FDA set a Prescription Drug User Fee Act (PDUFA) goal date of August 29, 2023. ONS-5010, if approved, is expected to receive 12 years of regulatory exclusivity in the United States.

"This BLA acceptance and PDUFA date are significant milestones in our mission to offer clinicians and their patients the first and only on-label, ophthalmic bevacizumab to treat wet AMD," said Russell Trenary, President and CEO of Outlook Therapeutics. "If approved, ONS-5010 (bevacizumab-vikg) will meet the robust FDA requirements for use as an ophthalmic injectable. We estimate that approximately 50% of the millions of anti-VEGF injections in ophthalmology are off-label compounded bevacizumab that is administered with no FDA-approved labeling. That product configuration does not meet the same standards we must achieve to earn FDA approval in ophthalmology. We hope to enhance the standard of care in the anti-VEGF space, and we are proud of the entire team and our clinical partners and advisors for bringing ONS-5010 to this point in its journey towards FDA approval."

"We are pleased the FDA has begun its review of our application. ONS-5010 is designed and manufactured to be fully compliant with the FDA's criteria for ophthalmic intravitreal biologics and we are excited about the prospect of filling the public health need for an FDA-approved ophthalmic formulation of bevacizumab," added Terry Dagnon, Chief Operations Officer of Outlook Therapeutics.

As part of the Company's multi-year commercial planning process, and in anticipation of potential FDA approval in August 2023, Outlook Therapeutics and AmerisourceBergen recently announced a strategic commercialization agreement to expand the Company's reach for connecting to retina specialists and their patients. AmerisourceBergen will provide third-party logistics (3PL) services and distribution, as well as pharmacovigilance services in the United States. Through this agreement, Outlook Therapeutics expects to increase market access and efficient distribution of ONS-5010, while not duplicating services provided by AmerisourceBergen, thereby decreasing Outlook's otherwise needed expense for those same services.

Outlook Therapeutics also established best-in-class partnerships with FUJIFILM Diosynth Biotechnologies for drug substance manufacturing, and with drug product manufacturer Ajinomoto Bio-Pharma Services for finished drug product.

In addition to the U.S. filing, Outlook Therapeutics is also developing registration documents on a parallel path for approvals in Europe and expects to submit them in the fourth quarter of 2022. Outlook Therapeutics is assessing both direct commercialization and partnering in Europe and Asia on a country-by-country basis.

About the NORSE Registration Clinical Program for Wet AMD

NORSE ONE was a clinical experience trial involving 61 wet AMD participants at nine trial sites in Australia. NORSE ONE compared ONS-5010 to ranibizumab (LUCENTIS®) as a treatment for wet AMD and showed the first markers of efficacy and safety in humans for ONS-5010 ophthalmic bevacizumab. In the trial, ONS-5010 efficacy and safety data were consistent with historical published studies of bevacizumab in ophthalmology, and NORSE ONE also supported the trial design and inclusion/exclusion criteria for NORSE TWO, the pivotal Phase 3 registration clinical trial.

The NORSE TWO Phase 3 pivotal trial enrolled a total of 228 wet AMD patients at 39 clinical trial sites in the United States. It was designed as a superiority study comparing the safety and efficacy of ONS-5010 ophthalmic bevacizumab dosed monthly against ranibizumab (LUCENTIS®) dosed according to the PIER dosing regimen described in the LUCENTIS® label. The trial data met both the primary and secondary endpoints with high statistical significance and clinical relevance. For its primary endpoint, 41.7% ($p = 0.0052$) of patients gained ≥ 15 letters of vision, and for its secondary endpoints, 56.5% ($p = 0.0016$) of patients gained ≥ 10 letters of vision and 68.5% ($p = 0.0116$) gained ≥ 5 letters. The key secondary endpoint, mean change in BCVA from baseline to Month 11, was 11.2 letters gained ($p = 0.0043$) compared to 5.8 letters gained in the ranibizumab arm. The NORSE TWO data also showed that the drug was well-tolerated, consistent with previously reported data for ONS-5010 and prior research.

NORSE THREE was an open-label safety study of ONS-5010 in 197 patients conducted in the United States to provide the necessary number of retina patients dosed with ONS-5010 to complete the safety requirements for the BLA submission.

Safety results across the first three NORSE trials demonstrated a strong benefit-to-risk safety profile. Across all three ONS-5010 registration trials, there was only one ocular inflammation adverse event, which was reported in NORSE TWO; the event was treated topically and resolved without sequelae. The most common adverse reaction (≥ 5%) reported in patients receiving ONS-5010 was conjunctival hemorrhage associated with the needle injection procedure (5%).

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

ONS-5010 is an investigational ophthalmic formulation of bevacizumab under development 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 can replace the need to use unapproved repackaged oncologic IV bevacizumab from compounding pharmacies for the treatment of wet AMD.

Bevacizumab-vikg 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-vikg 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 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. The FDA accepted Outlook Therapeutics' BLA submission for ONS-5010 to treat wet AMD with a PDUFA goal date of August 29, 2023. The submission is supported by Outlook Therapeutics' wet AMD clinical program, which consists of three clinical trials: NORSE ONE, NORSE TWO, and NORSE THREE. 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. 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 "anticipate," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "will," 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, expectations concerning market exclusivity, Outlook's partnership with AmerisourceBergen, the services to be provided thereunder and the anticipated benefits thereof, Outlook's expected commercial reach, market access and distribution network, the timing of a commercial launch of ONS-5010, plans for regulatory submissions and potential launch in international markets, plans for submission of an sBLA and the related NORSE SEVEN clinical trial, 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 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, 2021, as supplemented by its Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, 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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