

Outlook Therapeutics Reports Topline Results and Positive Proof-of-Concept for ONS-5010 / LYTENAVA™ (bevacizumab-vikg) from NORSE 1

August 26, 2020

- **ONS-5010, an investigational ophthalmic formulation of bevacizumab-vikg for the treatment of wet AMD, demonstrated safety and efficacy profile consistent with previously published ophthalmic bevacizumab research**
- **NORSE 1 results support trial design and inclusion criteria for fully enrolled, ongoing pivotal NORSE 2 registration trial**

MONMOUTH JUNCTION, N.J., Aug. 26, 2020 (GLOBE NEWSWIRE) -- [Outlook Therapeutics, Inc.](#) (Nasdaq: OTLK), a late clinical-stage biopharmaceutical company working to develop the first FDA-approved ophthalmic formulation of bevacizumab-vikg for use in retinal indications, today announced topline results demonstrating anticipated safety and efficacy and positive proof-of-concept of ONS-5010 / LYTENAVA™ (bevacizumab-vikg) for the treatment of wet age-related macular degeneration (wet AMD) from its NORSE 1 clinical study, the first of two registration clinical trials. ONS-5010 is the first injectable ophthalmic formulation of bevacizumab-vikg seeking U.S. Food and Drug Administration (FDA) approval for the treatment of wet AMD under a new Biologics License Application (BLA).

"Although a small study, we are excited to see that both the efficacy signals that we anticipated in NORSE 1 for an ophthalmic bevacizumab as well as the clinical safety data are consistent with previously published results for ophthalmic bevacizumab," stated Mark Humayun, MD, PhD, Medical Advisor to Outlook Therapeutics. "We are looking forward to seeing the results of the NORSE 2 pivotal trial in the third quarter of 2021. If ONS-5010 is approved to treat wet AMD and other retinal diseases, it will be a significant development in the practice of ophthalmology. Bevacizumab is a well understood anti-VEGF therapy that is already widely used, and ONS-5010, if approved, will be a valuable, FDA-approved treatment option across the spectrum of retinal care."

In NORSE 1, there were no statistical differences between LUCENTIS® (ranibizumab) and ONS-5010 in the study. Overall, 2 of 25 (8%) patients on the ONS-5010 arm achieved > 15 letters best corrected visual acuity (BCVA) at Month 11 compared to 5 of 23 (22%) patients on the ranibizumab arm. In the subgroup analysis of treatment-naïve subjects, 2 of 6 (33%) patients on the ONS-5010 arm achieved > 15 letters at Month 11 compared to 4 of 13 (31%) patients in the ranibizumab arm. Additionally, the subgroup analysis of patients who had a baseline visual acuity of < 67 letters (20/50 or worse) at study entry included 2 of 4 (50%) patients in the ONS-5010 arm and 4 of 9 (44%) patients in the ranibizumab arm achieving > 15 letters at Month 11. These key subgroups represent the enrollment criteria for patients in the fully enrolled, pivotal NORSE 2 clinical trial.

The results from NORSE 1 indicate that the observed safety profile of ONS-5010 in this study is consistent with that of previously reported bevacizumab ophthalmology studies. There were no statistical differences in safety between LUCENTIS® (ranibizumab) and ONS-5010 in the study and zero cases of ocular inflammation.

"The results from NORSE 1 met our proof-of-concept expectations and, importantly, validate our confidence in the design of our ongoing NORSE 2 trial and the potential data we may see from that study. As anticipated in NORSE 1, ONS-5010 provided us with positive trends in efficacy in three-line visual acuity gains and was shown to be safe and well tolerated. In fact, ONS-5010 had no adverse events associated with inflammation, which has emerged as a concern for other anti-VEGFs in treating retinal diseases," said Lawrence Kenyon, President, CEO and CFO of Outlook Therapeutics. "On behalf of Outlook Therapeutics, I want to thank all of the patients and clinicians who have persevered through the COVID-19 pandemic to bring this clinical trial to completion."

The results from NORSE 1 provide support for the established design and protocol for the ongoing pivotal NORSE 2 clinical trial, the second of two registration clinical trials evaluating ONS-5010 for treatment of wet AMD; NORSE 2 excludes patients with vision better than 20/50 at baseline, as well as patients who have received prior treatment for wet AMD. NORSE 2 is powered for statistical significance, and by excluding such patients, Outlook Therapeutics believes that NORSE 2 has enrolled the optimal patients for meeting the endpoint of the study.

Mr. Kenyon concluded, "With these results now in hand, we turn our attention to our NORSE 2 Phase 3 pivotal trial, which is similar in design to NORSE 1 in length of treatment and dosing, but is designed with a larger, and treatment-naïve, patient population and powered to show statistical significance. Based on our end-of-Phase 2 discussions with the FDA, we believe that the results from NORSE 1 and NORSE 2, combined with our upcoming NORSE 3 safety study that is designed to ensure an adequate number of patient exposures to ONS-5010 are available, will be sufficient to support a new BLA submission in the second half of next year."

Outlook Therapeutics intends to complete development of ONS-5010 for submission to the FDA as a new BLA under the 351(a) PHS regulatory pathway for the treatment of wet AMD and also has plans to submit for regulatory approvals in Europe, the United Kingdom and Japan, as well as other countries. While bevacizumab is already widely used, if approved, ONS-5010 will be the first and only on-label ophthalmic formulation of bevacizumab-vikg approved for treating retinal diseases and has the potential to address a \$9.1 billion anti-VEGF market.

About NORSE 1

The NORSE 1 clinical trial is a small 30-subject-per-arm clinical experience trial designed to provide an initial safety and efficacy readout for ONS-5010 v. LUCENTIS® (ranibizumab) in treating patients with wet AMD, and to provide the initial safety data necessary to open an Investigational New Drug Application (IND) with the FDA in March 2019. The first of two registration clinical trials evaluating ONS-5010 in treating wet AMD, NORSE 1 enrolled a total of 61 treatment-naïve and previously treated patients diagnosed with wet AMD at nine sites in Australia. Patients on ONS-5010 were dosed monthly compared to those on ranibizumab, who were dosed using the PIER alternative dosing regimen of three monthly doses followed by quarterly dosing. Study design and randomization are consistent with an agreement reached with the FDA at an end-of-Phase 2 meeting in April 2018.

About NORSE 2

Outlook Therapeutics recently completed patient enrollment in NORSE 2, its 227-patient Phase 3 registration clinical trial evaluating ONS-5010 for the

treatment of patients with wet AMD. Patients in the trial are being treated for 12 months. The primary endpoint for NORSE 2 is the difference in proportion of patients who gain at least 15 letters in BCVA at 11 months for ONS-5010 dosed on a monthly basis, compared to LUCENTIS[®], which is being dosed quarterly per the PIER regimen. Outlook Therapeutics expects to report pivotal safety and efficacy data from NORSE 2 in the third calendar quarter of 2021.

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

ONS-5010 / LYTENAVA™ (bevacizumab-vikg) is an investigational ophthalmic formulation of bevacizumab-vikg under development to be administered as an intravitreal injection for the treatment of wet AMD and other retinal diseases. ONS-5010 is currently being evaluated in two registration clinical trials for wet AMD (NORSE 1 and NORSE 2) and, if successful, is expected to be submitted to the FDA as a new BLA for this ophthalmic indication under the PHS 351(a) regulatory pathway. Because no currently approved ophthalmic formulations of bevacizumab are available, clinicians wishing to treat retinal patients with bevacizumab use unapproved repackaged IV bevacizumab provided by compounding pharmacists, products that have known risks of contamination and inconsistent potency and availability.

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 new abnormal blood vessels. With wet AMD, abnormally high levels of VEGF are secreted in the eye and can lead to vision loss. Anti-VEGF injection therapy blocks this growth. Since the advent of anti-VEGF therapy, it has become the standard-of-care treatment option within the retina community globally.

If approved, ONS-5010 will be the first and only FDA-approved ophthalmic formulation of bevacizumab-vikg to treat retinal diseases. Outlook Therapeutics currently intends to commercialize ONS-5010 in both vials and single-use pre-filled syringes.

About Outlook Therapeutics, Inc.

Outlook Therapeutics is a late clinical-stage biopharmaceutical company working to develop ONS-5010 / LYTENAVA™ (bevacizumab-vikg) as the first FDA-approved ophthalmic formulation of bevacizumab-vikg for use in retinal indications, including wet AMD, DME and BRVO. If ONS-5010 is approved, Outlook Therapeutics expects to commercialize it as the first and only FDA-approved ophthalmic formulation of bevacizumab-vikg for use in treating retinal diseases in the United States, United Kingdom, Europe, Japan and other markets. Outlook Therapeutics expects to file ONS-5010 with the U.S. FDA as a new BLA under the PHS 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 statements about the timing of completion of, and pivotal safety and efficacy data from, NORSE 2, ONS-5010's potential as the first FDA-approved ophthalmic formulation of bevacizumab-vikg, including benefits therefrom to patients, payors and physicians, the timing of BLA submission and sufficiency of exposures to support such submission, statements about commercial launch of ONS-5010, and plans for regulatory approvals in other markets. 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, 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.

CONTACTS:

Media Inquiries:

Jessica Morris
Account Executive
LaVoie Health Science
T: 857.701.9731
jmorris@lavoiehealthscience.com

Investor Inquiries:

Jenene Thomas
Chief Executive Officer
JTC Team, LLC
T: 833.475.8247
OTLK@jtcir.com

