Outlook Therapeutics, Inc. Logo

Virtual Clinical Day Recap: Outlook Therapeutics Joined by Drs. Mark Humayun and Firas Rahhal to Discuss Need for FDA-Approved Ophthalmic Bevacizumab and Status of ONS-5010

May 27, 2021

- **Drs. Mark Humayun and Firas Rahhal, leading retinal specialists and Advisors to Outlook Therapeutics, stress clinical value of ONS-5010, if approved, over existing treatment options**
- **Registration clinical program and pre-commercialization planning for ONS-5010 remains ongoing with key catalysts expected over the next year**
- **Webcast replay is now available: click here**

ISELIN, N.J., May 27, 2021 (GLOBE NEWSWIRE) -- Outlook Therapeutics, Inc. (Nasdaq: OTLK), a late clinical-stage biopharmaceutical company working to develop the first FDA-approved ophthalmic formulation of bevacizumab for use in retinal indications, hosted a virtual Clinical Day on May 20, 2021 to provide an update on the clinical progress of ONS-5010 (bevacizumab-vikg) for treatment of wet age-related macular degeneration (wet AMD). If approved, ONS-5010 will be the first and only ophthalmic formulation of bevacizumab approved to treat retinal conditions.

The Outlook Therapeutics management team – Lawrence A. Kenyon, President, CEO and CFO, Terry Dagnon, COO, and Jeff Evanson, CCO – was joined by leading retina specialists Mark Humayun, MD, PhD, Medical Advisor to Outlook Therapeutics, and Firas Rahhal, MD, Senior partner at Retina-Vitreous Associates Medical Group and Associate Clinical Professor of Ophthalmology at the UCLA School of Medicine.

"As we near the end of the ONS-5010 registration program, we are excited to share the continued clinical progress that will culminate with the topline readout of pivotal data in just a few months," said Mr. Kenyon. "Together with Drs. Humayun and Rahhal, both of whom are practicing retina surgeons and well-known authorities in the retinal community, we are confident that ONS-5010, if approved, will offer a valuable new treatment option to clinicians and their retina patients and address many of the shortcomings that currently exist in the treatment landscape for wet AMD."

Treatment Landscape

For the past 15 years, major retinal diseases such as wet AMD, diabetic macular edema (DME) and branch retinal vein occlusion (BRVO) have been successfully treated with a class of medications called anti-VEGFs. Such retinal diseases are characterized by excessive growth of abnormal blood vessels under the retina, which if untreated leads to vision loss and even blindness. Anti-VEGF medications control this abnormal growth and have become the standard of care for treating these diseases.

Bevacizumab is an anti-VEGF drug that was developed for oncologic uses as an IV-administered drug known as Avastin®, but it is not approved for ophthalmic use. Although there are three anti-VEGF drugs currently approved to treat ophthalmic disease, they are extremely expensive. As a result, physicians who wish to treat their retinal patients with a less expensive anti-VEGF drug often use unapproved repackaged IV bevacizumab from compounding pharmacists. ONS-5010, if approved, will be the first and only on-label ophthalmic formulation for the treatment of retinal diseases.

Progress Report on Clinical Program for ONS-5010

The virtual Clinical Day opened with an in-depth discussion of Outlook Therapeutics' overall clinical program for ONS-5010. Of the three clinical trials that will form the data submission to the U.S. Food and Drug Administration (FDA) for a new Biologics License Application (BLA) in early 2022, two of them, NORSE ONE and NORSE THREE, have been completed. Topline results for ONS-5010 from the completed trials demonstrated positive proof-of-concept, anticipated safety and efficacy, and a safety profile consistent with that of prior published data on the use of bevacizumab for ophthalmic conditions. The remaining registration trial, NORSE TWO, is a Phase 3 trial that will provide pivotal data powered for statistical significance. Outlook Therapeutics expects to provide the topline readout of these data in the third calendar quarter of this year.

Mr. Dagnon commented, "In consultation with the FDA Ophthalmic Division, we have secured agreement to pursue an innovative clinical program as we move our investigational ophthalmic bevacizumab through its registration trials towards BLA filing. Based on the positive signals we have seen in NORSE ONE and NORSE THREE, we expect the data from NORSE TWO to show that ONS-5010 behaves the same as Avastin® bevacizumab does, as reported in the seminal CATT study and other prior published research on ophthalmic use of bevacizumab. Our goal is to provide the retina community with an approved ophthalmic bevacizumab that avoids the known risks of the unapproved repackaged IV bevacizumab currently supplied by compounding pharmacies."

Physicians' Perspectives: Clinical Need for an Approved Ophthalmic Bevacizumab

Drs. Humayun and Rahhal stressed that the clinical retina community already is comfortable with the safety and efficacy of the bevacizumab molecule itself in treating retinal disease. The concern with using an unapproved form arises from the ancillary issues that can arise during the repackaging process outside of a cGMP facility when compounding pharmacies repackage large vials of oncologic IV Avastin into dozens of small non-ophthalmic syringes for use in the eye.

"Bevacizumab is a validated drug with a known target and mode of action; we know how well it behaves," said Dr. Humayun. "The NORSE TWO trial is not attempting to demonstrate new science. The strength of the ONS-5010 clinical program is that it is structured to provide the retina community with an approved ophthalmic formulation of a drug that we already use, but in a form that offers physicians and our patients all the safety, efficacy and consistency that FDA approval and cGMP manufacturing provide. I believe ONS-5010, if approved, would be a significant improvement over the unapproved bevacizumab that many doctors are currently using."

Dr. Rahhal described potential problems with using unapproved repackaged IV bevacizumab, including possible lack of sterility, inconsistent potency or availability, syringe malfunctions, and silicone droplets or other particulates inadvertently injected into patients' eyes. "Although the compounding pharmacists who repackage IV bevacizumab do the best they can, there are certainly challenges and likely also some limitations on consistency. My biggest concern is that both the process of repackaging and the syringes themselves may often result in patients receiving sub-potent dosing," said Dr.

Rahhal. “I suspect that underdosing is more common than we realize and could lead to suboptimal clinical outcomes for our patients. Having a specific ophthalmic syringe prepared in an appropriately credentialed facility would solve this problem.”

Progress Towards Commercialization

The virtual Clinical Day concluded with an overview of the pre-commercialization initiatives that are underway in anticipation of a potential FDA approval in 2022. Mr. Evanson detailed how Outlook Therapeutics is working to position ONS-5010, if approved, to address both unmet clinical and market needs. If approved, ONS-5010 is not only expected to provide retina patients with the safety and efficacy of an FDA-approved bevacizumab, but Outlook Therapeutics intends to work collaboratively with payors and the retina community to offer it at a responsible price that meets their needs while still delivering value to Outlook Therapeutics’ shareholders.

Mr. Evanson also discussed the potential value to clinicians and patients of providing ONS-5010 in a pre-filled ophthalmic syringe. “Assuming we receive FDA approval for ONS-5010 in 2022, we plan at that time to file a supplementary application for approval to provide the product in a pre-filled ophthalmic syringe; we would expect syringe approval within four to six months of that application submission. Based on our market research, we believe the retina community will welcome a pre-filled, silicone-free syringe that meets the strict specifications for ophthalmic use,” said Mr. Evanson.

Outlook Therapeutics has early launch planning well underway, including distribution, sales force planning, physician and patient outreach, key opinion leader support and payor community engagement. Outlook Therapeutics is also developing registration documents on a parallel path for approvals in Europe and expects to submit them shortly after completing the filing to the FDA. Mr. Evanson emphasized that while Outlook Therapeutics remains in discussion with potential strategic commercialization partners, particularly for European markets, Outlook Therapeutics is preparing to launch ONS-5010 in the United States by itself, pending FDA approval.

The ONS-5010 BLA will be submitted to the FDA under the PHSA 351(a) regulatory pathway for new biologics, and if approved will have 12 years of exclusivity in the $13.1 billion global market for anti-VEGF retina therapies. In addition to pursuing approval for wet AMD, Outlook Therapeutics holds FDA SPA Agreement Letters from the FDA to conduct pivotal registration clinical trials for DME and BRVO. Outlook Therapeutics expects to initiate NORSE FOUR for BRVO and NORSE FIVE and NORSE SIX for DME in late 2021.

A webcast replay of the virtual Clinical Day is available on the Events page of the Investors section of Outlook Therapeutics’ website (outlooktherapeutics.com).

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 pharmacists, products that have known risks of contamination and inconsistent potency and availability. If approved, ONS-5010 will reduce the need for use of unapproved repackaged IV bevacizumab from compounding pharmacists for retinal disease.

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 lead to loss of vision. 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.

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 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 file ONS-5010 ophthalmic bevacizumab with the U.S. FDA as a new 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 the timing of topline data from NORSE 2, plans for submission of a BLA and supplemental applications, ONS-5010’s potential as the first FDA-approved ophthalmic formulation of bevacizumab-vikg, including benefits therefrom to patients, payors and physicians, including expectations regarding market exclusivity, the timing of 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, including its 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.

CONTACTS:

Media Inquiries:
Harriet Ullman
Vice President
LaVoie Health Science
T: 617-669-3082
hullman@lavoiehealthscience.com

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

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