Ocular Therapeutix™ Shares SOL-R Enrollment Progress and Next Steps for AXPAXLI™ in NPDR

January 14, 2025

311 subjects enrolled across various stages of loading and randomization in SOL-R, Ocular's second registrational trial of AXPAXLI™ in wet AMD, as of January 10, 2024

First wet AMD registrational trial, SOL-1, completed randomization in December 2024 with topline data anticipated in Q4 2025

Company plans to seek FDA feedback in H1 2025 on clinical trial design for AXPAXLI in NPDR

BEDFORD, Mass., Jan. 14, 2025 (GLOBE NEWSWIRE) -- Ocular Therapeutix, Inc. (NASDAQ: OCUL, "Ocular", the "Company"), a biopharmaceutical company committed to redefining the retina experience, outlined exceptional clinical progress across its registrational program for AXPAXLI™ in wet age-related macular degeneration (wet AMD), plans to advance AXPAXLI in non-proliferative diabetic retinopathy (NPDR), and the Company's strategic outlook for 2025 in its presentation at the 43 rd Annual J.P. Morgan Healthcare Conference (JPM 2025).

"Wet AMD is the leading cause of blindness in the U.S., but it does not need to be. Diabetic retinopathy is the leading cause of blindness in the working population in the U.S., but it does not need to be. We have a proven target, VEGF, and proven treatments for decades, the anti-VEGFs. Unfortunately, we also have a treatment regimen that is simply not sustainable for many patients. Our mission at Ocular is to correct this," said **Pravin U. Dugel, MD, Executive Chairman, President and Chief Executive Officer** of Ocular Therapeutix. "Last year, we started with wet AMD. We recruited SOL-1 well ahead of schedule and, yesterday at JPM 2025, I announced that we have already enrolled 311 patients in various stages of loading and randomization in SOL-R, our second registrational study in wet AMD. The historic pace of recruitment in both studies underscores the enthusiasm in the retina community for AXPAXLI. In 2025, we will also target diabetic retinopathy. Our HELIOS study has demonstrated that a single injection of AXPAXLI has the potential to reduce the risk of vision loss in NPDR to literally zero at 48 weeks. In HELIOS, every single patient with non-center involved DME treated with a single injection of AXPAXLI, improved at week 48. Therefore, AXPAXLI has the potential to not only prevent vision loss, but also to treat existing vision threatening complications, such as DME."

Dr. Dugel concluded, "In 2025, Ocular will target the two most impactful global diseases in retina, wet AMD and diabetic retinopathy. We believe we have the infrastructure, finances and expertise to succeed and redefine the global retina experience."

J.P. Morgan Presentation Highlights

- **Complementary wet AMD registrational program.** Ocular's wet AMD registrational program for AXPAXLI is comprised of two complementary studies, SOL-1 and SOL-R, strategically designed with the intent of de-risking patient populations, aligning with regulatory standards, enhancing each other's enrollment, and providing a broad evaluation of AXPAXLI's durability, repeatability, and flexibility. SOL-1 is being conducted under a Special Protocol Agreement (SPA) with the U.S. Food and Drug Administration (FDA), while SOL-R received alignment with the FDA through a written Type C response. The FDA previously agreed that together, these studies could constitute two adequate and well-controlled trials to support a potential New Drug Application (NDA) and label for AXPAXLI in wet AMD.
- **SOL-1 (Phase 3, wet AMD) randomization complete in December 2024.** In total, more than 300 subjects were randomized across greater than 100 clinical trial sites located in the U.S. and Argentina. SOL-1 is a superiority trial comparing a single AXPAXLI injection to a single aflibercept (2 mg) injection in treatment naïve wet AMD subjects with a nine-month primary endpoint and up to two-year follow-up. SOL-1 is the first registrational trial for AXPAXLI in wet AMD and was designed to establish AXPAXLI's durability, and potentially enable a superiority claim on a potential future label. The Company expects topline results for SOL-1 to be available in the fourth quarter of 2025.
- **SOL-R (Phase 3, wet AMD) outstanding enrollment progress to date.** 311 subjects enrolled across various stages of loading and randomization in the U.S. and South America as of January 10, 2024. SOL-R is a non-inferiority trial comparing repeat AXPAXLI injections every six months to repeat aflibercept (2 mg) injections every eight weeks, with a 56-week primary endpoint. SOL-R is the second registrational trial for AXPAXLI in wet AMD and was designed to inform real world treatment decisions, establish AXPAXLI's safety and efficacy with repeat dosing, and provide commercially relevant data.
- **Ocular plans to seek FDA feedback in H1 2025 on the clinical trial design for AXPAXLI in NPDR.** Following positive results from the Phase 1 HELIOS trial of AXPAXLI shared in 2024, Ocular plans to continue clinical development in NPDR. In the HELIOS trial, after a single AXPAXLI injection, no patients receiving AXPAXLI (N=13) developed a vision threatening

complication (VTC) at 48 weeks compared to nearly 40% in the sham-treated patients (N= 8). Further, all patients in the AXPAXLI arm who presented with non-center-involved diabetic macular edema (non-CI-DME) at baseline (N=8) had improvement in their DME based on Optical Coherence Tomography (OCT) image analysis at week 48 compared to none of the sham-treated subjects (N=3). All subjects who received AXPAXLI showed diabetic retinopathy severity scale (DRSS) improvement or stability, while any worsening of DRSS occurred only in sham-treated subjects.

Arshad M. Khanani, MD, MA, FASRS, Director of Clinic Research at Sierra Eye Associates, Reno, Nevada noted, "Real-world evidence shows that 40 to 50% of patients with wet AMD discontinue their injections due to the high treatment burden, putting them at increased risk of blindness. This issue is even more pronounced in patients with diabetic retinopathy. My team, our patients, and I are excited to support the SOL studies, and delighted that Ocular will soon target diabetic retinopathy, a huge unmet need in our space. If approved, I believe AXPAXLI will be rapidly adopted, as it has the potential to significantly reduce treatment burden with a durability of 6-12 months."

Patricio G. Schlottmann, MD, Director of the Research Department at the Charles Ophthalmic Center and Ophthalmology Department Director at Organización Médica de Investigación in Buenos Aires, Argentina, commented, "Wet AMD and diabetic retinopathy are global diseases in which millions of patients around the world lose vision because we have an unsustainable treatment regimen. I continue to enthusiastically support the SOL programs in wet AMD and am particularly happy that Ocular will also target diabetic retinopathy. If approved, I believe Axpaxli will be enthusiastically adopted and has the potential to positively impact millions of patients around the world."

About AXPAXLI
AXPAXLI™ (axitinib intravitreal injection, also known as OTX-TKI) is an investigational, bioresorbable, hydrogel incorporating axitinib, a small molecule, multi-target, tyrosine kinase inhibitor with anti-angiogenic properties, being evaluated for the treatment of wet AMD, diabetic retinopathy, and other retinal diseases.

About the SOL-1 Study
The registrational Phase 3 SOL-1 trial (NCT06223958) is designed to evaluate the safety and efficacy of AXPAXLI in a multi-center, double-masked, randomized (1:1), parallel group study that involves more than 100 clinical trial sites located in the U.S. and Argentina. In December 2024, the trial completed randomization of more than 300 evaluable treatment-naïve subjects with a diagnosis of wet AMD in the study eye.

The superiority study has an eight-week loading segment prior to randomization, a 9-month treatment segment, and a safety follow-up. During the loading segment, subjects who have 20/80 vision or better and who satisfy other enrollment criteria receive two doses of aflibercept (2 mg) at Week -8 and Week -4. Eligible subjects who achieve best corrected visual acuity (BCVA) of 20/20 at Day 1 or gain at least 10 early treatment diabetic retinopathy (ETDRS) letters at Day 1 are then randomized to receive a single dose of AXPAXLI or a single dose of aflibercept (2 mg) and assessed monthly for the duration of the study. The clinical trial protocol requires that, during the study, subjects in any arm meeting pre-specified rescue criteria will receive a supplemental dose of aflibercept (2 mg).

The primary endpoint of SOL-1 is the proportion of subjects who maintain visual acuity, defined as a loss of <15 ETDRS letters of BCVA, at Week 36. The study is being conducted under a Special Protocol Agreement (SPA) with the FDA.

About the SOL-R Study
The registrational Phase 3 SOL-R trial (NCT06495918) is designed to evaluate the safety and efficacy of AXPAXLI in a multi-center, double-masked, randomized (2:2:1), three-arm study that will involve sites located in the U.S. and the rest of the world. The trial is intended to randomize approximately 825 subjects who are treatment-naïve or were diagnosed with wet AMD in the study eye within three months prior to enrollment.

The non-inferiority study reflects a patient enrichment strategy that includes multiple loading doses of aflibercept (2 mg) and monitoring to exclude subjects with significant retinal fluid fluctuations. Subjects in the first arm receive a single dose of AXPAXLI at Day 1 and are re-dosed at Week 24. Subjects in the second arm receive aflibercept (2 mg) on-label every 8 weeks. Subjects in the third arm receive a single dose of aflibercept (8 mg) at Day 1 and are re-dosed at Week 24, aligned with the AXPAXLI treatment arm for adequate masking. Subjects in any arm that meet pre-specified rescue criteria will receive a supplemental dose of aflibercept (2 mg).

The primary endpoint of SOL-R is non-inferiority in mean BCVA change from baseline between the AXPAXLI and on-label aflibercept (2 mg) arms at one year. In a written Type C response received in August 2024, the FDA agreed that the SOL-R repeat dosing wet AMD study should be appropriate as an adequate and well-controlled study in support of a potential New Drug Application and product label.

About Wet AMD
Wet age-related macular degeneration (wet AMD) is a leading cause of severe, irreversible vision loss affecting approximately 14 million individuals globally and 1.65 million in the United States alone (2023 Market Scope® Retinal Pharmaceuticals Market Report). Wet AMD causes vision loss due to abnormal new blood vessel growth and hyperpermeability and associated retinal vascularity in the macula, which is primarily stimulated by local upregulation of vascular endothelial growth factor (VEGF). Without prompt and continuous treatment to control this exudative activity, patients develop irreversible vision loss. With proper treatment, patients may maintain visual function for a period of time and may temporarily regain lost vision. Challenges with current therapies include pulsatile, repeated intraocular injections, treatment-related adverse events and up to 40% patient discontinuation within

one year of initiating treatment with continued disease progression. Taken together, these factors lead to undertreatment and a lack of long-term vision improvement for patients.

About Ocular Therapeutix, Inc.
Ocular Therapeutix, Inc. is a biopharmaceutical company committed to redefining the retina experience. AXPAXLI™ (axitinib intravitreal injection, also known as OTX-TKI), Ocular's product candidate for retinal disease, is based on its ELUTYX™ proprietary bioresorbable hydrogel-based formulation technology. AXPAXLI is currently in Phase 3 clinical trials for wet age-related macular degeneration (wet AMD).

Ocular's pipeline also leverages the ELUTYX technology in its commercial product DEXTENZA®, an FDA-approved corticosteroid for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis, and in its product candidate PAXTRAVA™ (travoprost intracameral injection or OTX-TIC), which is currently in a Phase 2 clinical trial for the treatment of open-angle glaucoma or ocular hypertension.

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Forward-Looking Statements
Any statements in this press release about future expectations, plans, and prospects for the Company, including the development and regulatory status of the Company's product candidates; the design of, and the timing of the enrollment and randomization of patients in and the availability of data from the Company's SOL-1 and SOL-R Phase 3 clinical trials of AXPAXLI (also called OTX-TKI) for the treatment of wet AMD; the Company's plans to advance the development of AXPAXLI and its other product candidates, including in additional indications such as NPDR; the potential utility or adoption, if approved, of any of the Company's product candidates; and other statements containing the words "anticipate", "believe", "estimate", "expect", "intend", "designed", "goal", "may", "might", "plan", "predict", "project", "target", "potential", "will", "would", "could", "should", "continue", and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the timing and costs involved in commercializing any product or product candidate that receives regulatory approval; the ability to retain regulatory approval of any product or product candidate that receives regulatory approval; the initiation, design, timing, conduct and outcomes of ongoing and planned clinical trials; the risk that the FDA will not agree with the Company's interpretation of the written agreement under the Special Protocol Assessment for the SOL-1 trial; the risk that the FDA may not agree that the protocol and statistical analysis plan of SOL-R or the data generated by the SOL-1 and SOL-R trials support marketing approval, even if the trials are successful; the risk that the Company and the FDA may not agree on the registrational pathway for AXPAXLI for NPDR or any other indication; uncertainty as to whether the data from earlier clinical trials will be predictive of the data of later clinical trials, particularly later clinical trials that have a different design or utilize a different formulation than the earlier trials, whether preliminary or interim data from a clinical trial will be predictive of final data from such trial, or whether data from a clinical trial assessing a product candidate for one indication will be predictive of results in other indications; availability of data from clinical trials and expectations for regulatory submissions and approvals; the Company's scientific approach and general development progress; uncertainties inherent in estimating the Company's cash runway, future expenses and other financial results, including its ability to fund future operations, including clinical trials; the Company's existing indebtedness and the ability of the Company's creditors to accelerate the maturity of such indebtedness upon the occurrence of certain events of default; and other factors discussed in the "Risk Factors" section contained in the Company's quarterly and annual reports on file with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views as of the date of this press release. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, whether as a result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this press release.

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