Ocular Therapeutix™ Highlights Exceptional AXPAXLI™ SOL-1 Enrollment and Plans for Repea Dosing Study (SOL-R) in wet AMD at Investor Day, Along with Positive 48-week Data from HELIOS NPDR Study

June 13, 2024

151 subjects enrolled in various stages of loading and randomization in SOL-1 pivotal study of AXPAXLI in wet AMD as of June 7, 2024

Announces plans for SOL-R study to evaluate repeat doses of AXPAXLI in wet AMD

48-week HELIOS NPDR results show 23.1% of patients in AXPAXLI arm experienced ≥2-step DRSS improvement with no patients experiencing worsening of DRSS or vision threatening complications

BEDFORD, Mass., June 13, 2024 (GLOBE NEWSWIRE) -- Ocular Therapeutix, Inc. (NASDAQ: OCUL, “Ocular”, the “Company”), a biopharmaceutical company committed to enhancing people’s vision and quality of life through the development and commercialization of innovative therapies for wet age-related macular degeneration (wet AMD), diabetic retinopathy, and other diseases and conditions of the eye, today hosted an Investor Day where it highlighted excellent clinical development progress with AXPAXLI for wet age-related macular degeneration (wet AMD) and non-proliferative diabetic retinopathy (NPDR) and updated its corporate strategy.

“2024 has been a time of significant accomplishment for Ocular. To support our mission to become a leader in retinal care, we successfully assembled a 'Retina Dream Team' of recognized leaders in the field, fortified our balance sheet with additional capital and streamlined the organization. We are already seeing the positive impact of these efforts, based on exceptional enrollment in the pivotal SOL-1 AXPAXLI study for wet AMD, coupled with plans for a new SOL-R repeat dosing study and the report of positive 48-week topline data from the Phase 1 HELIOS NPDR study,” **said Pravin U. Dugel, MD, Executive Chairman, President and Chief Executive Officer of Ocular Therapeutix.** “Our transformation into a retina-focused company is built on three pillars: convincing data from three clinical studies with AXPAXLI, de-risking the regulatory pathway in wet AMD, and a focus on expansive, retinal vascular disease markets. We are more confident today than ever before that AXPAXLI has demonstrated monotherapy activity, with potential best-in-class durability and a favorable safety profile that is well positioned to disrupt today’s treatment paradigm which includes frequent, burdensome regimens.”

Investor Day Highlights

- **Excellent enrollment in AXPAXLI SOL-1 study (Phase 3, wet AMD)** with 60 study sites active and 151 subjects enrolled in various stages of loading and randomization as of June 7, 2024, reflecting strong investigator engagement. The pivotal SOL-1 study is designed for regulatory approval and is being conducted under a Special Protocol Assessment (SPA) with the US FDA. The Company intends to randomize 300 treatment naïve patients in the SOL-1 study, comparing a single AXPAXLI implant (450µg) to a single aflibercept injection (2mg) after all patients have received two loading doses of aflibercept.

- **Company plans to initiate SOL-R AXPAXLI repeat dosing study (Phase 3, wet AMD)** to evaluate repeat dosing of AXPAXLI (450µg) at six months (Q6M) compared to aflibercept (2mg) dosed every eight weeks (Q8W) and a comparator arm dosed Q6M in 825 wet AMD patients. This trial is designed for commercial impact and is being initiated at regulatory risk. Ocular has requested a Type C meeting to seek FDA guidance regarding the SOL-R protocol. Patients enrolled in SOL-R are initially expected to include patients that constitute loading or randomization failures from the SOL-1 study. The SOL-R protocol requires that all patients enrolled in SOL-R be enriched through multiple aflibercept (2mg) loading doses and monitored to ensure limited retinal fluid fluctuations prior to randomization. After the completion of enrollment and randomization of SOL-1, patients will be enrolled directly into the SOL-R study.

- **Positive HELIOS 48-week data (Phase 1, NPDR)** improves on previously reported 40-week data with all signals of diabetic retinopathy severity scale (DRSS) improvement coming from AXPAXLI-treated patients while any vision threatening complications (VTCs) that developed were in sham-treated patients. The HELIOS study compares a single AXPAXLI implant (600µg) to a single sham injection with neither arm receiving a loading treatment. The Company plans to discuss these results with the FDA to determine a path forward for the development of AXPAXLI in NPDR.
    - 23.1% of patients (N=3) demonstrated a ≥2-step DRSS improvement in the AXPAXLI arm at week 48 compared to 0% in the sham arm; an additional 23.1% of patients (N=3) demonstrated a 1-step DRSS improvement in the AXPAXLI arm compared to 0% in the sham arm.

- 0% of patients in the AXPAXLI arm showed worsening in DRSS by week 48 compared to 25% of patients (N=2) in the sham arm.
- 0% of patients in the AXPAXLI arm developed proliferative diabetic retinopathy (PDR) or center-involved diabetic macular edema (CI-DME) by week 48 compared to 37.5% of patients (N=3) in the sham arm.
- On average, patients in the AXPAXLI arm showed improvement in central subfield thickness compared to the sham arm, which showed worsening over the 48-week follow up.
- AXPAXLI was generally well-tolerated and did not result in any reported incidence of intraocular inflammation, iritis, vitritis, or vasculitis.

- **Cash runway remains into 2028** with a prioritization of resources on the clinical development of AXPAXLI for wet AMD**.** Based on the Company's current operating plan, which includes the completion of the SOL-1 and SOL-R clinical trials, the assessment of AXPAXLI for NPDR and PAXTRAVA™ for ocular hypertension and glaucoma, the cessation of substantive development activities for other clinical programs, the recent personnel changes in research and technical operations, the anticipated revenues from DEXTENZA® product sales, and the Company's observance of its minimum liquidity covenant, the Company believes its current cash and cash equivalents continue to enable it to fund its planned operating expenses, its debt service obligations and its capital expenditure requirements into 2028.

Dilsher S. Dhoot, MD, of California Retina Consultants commented, "While SOL-1 enrollment has exceeded our expectations, perhaps we should not have been surprised. We are recruiting treatment naïve wet AMD patients with good vision, the largest de novo patient population we see, and there is no competing clinical trial for these patients. Many patients know someone with wet AMD and understand how burdensome treatment is. When I talk to my patients about the SOL-1 study, they are excited about the potential durability of AXPAXLI. In addition, they like the study design because if they are randomized, they are guaranteed to receive an active agent, not a sham. They find it comforting to know that I will see them monthly, at a minimum, and if the drug they are receiving appears to be losing strength, they can be rescued with aflibercept, as needed, for the remainder of the study."

Baruch D. Kuppermann, MD, PhD, Chair of the Department of Ophthalmology, and Director of the Gavin Herbert Eye Institute at the University of California, Irvine noted, "I believe the start of the SOL-R study will be good news for patients and the retina community. Clearly, SOL-1 was designed as a regulatory study. It is exactly what the FDA is asking for in their latest guidance documents and is being conducted under an SPA, which has become increasingly important in today's regulatory landscape. SOL-R is different because it is a large, 'real-world' repeat-dosing study designed to provide physicians with data on how we may ultimately use AXPAXLI, if approved. I believe having the results of this study will be important for the retina community and so I am enthusiastic about the clinical trial. Further, I expect the SOL-R design feature to initially enroll patients who failed loading or randomization in SOL-1 to enhance enrollment in both studies by giving patients twice the opportunity to participate in a study."

Dr. Dhoot added, "After reviewing the expanded HELIOS Phase 1 data set in NPDR, I am even more comfortable that AXPAXLI has the potential to be safe and effective, with durable activity in the back of the eye. The current approved anti-VEGF agents for DR necessitate frequent injections, and for that reason I have very few patients receiving treatment. In the HELIOS study, patients receiving AXPAXLI sustained or improved DRSS to week 48 without the development of a single vision threatening complication, unlike patients in the sham control arm. In NPDR, I care about maintaining or improving my patients' vision, and if I can do this with a 6 to 12-month treatment, I believe many of my patients would be very excited. This is a differentiated result compared to other benchmark agents and it fortifies my confidence in the potential use of AXPAXLI in both wet AMD and NPDR."

A replay of the webcast and presentation can be accessed through the "Events and Presentations" section of the Company's investor website at investors.ocutx.com. A replay of the webcast will be archived for at least 30 days.

About the SOL-1 Study
The pivotal Phase 3 SOL-1 trial is designed to evaluate the safety and efficacy of AXPAXLI in a multi-center, double-masked, randomized (1:1), parallel group study that involves sites primarily located in the U.S. The trial is intended to randomize approximately 300 evaluable treatment-naïve patients with a diagnosis of wet AMD in the study eye.

The superiority study begins with an eight-week loading segment, a 9-month treatment segment followed by 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 (at week -8 and week -4). Subjects that achieve visual acuity 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 and assessed monthly for the entire 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.

The primary endpoint of SOL-1 is the proportion of subjects who maintain visual acuity, defined as <15 ETDRS letters of BCVA loss, at Week 36.

About the SOL-R Study
The Phase 3 SOL-R trial 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 patients diagnosed with wet AMD within three months prior to enrollment in the study eye.

The one-year, non-inferiority study reflects a patient enrichment strategy that includes multiple loading doses of aflibercept and monitoring to exclude those with significant retinal fluid fluctuations. In the first arm, patients will be randomized to receive a single dose of AXPAXLI at Day 1 and re-dosed at Week 24. In the second arm, patients will receive aflibercept (2mg) on label every 8 weeks. In a third arm, patients will receive a single dose of the comparator at Day 1 and re-dosed at Week 24, similar to the first arm. 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.

The primary endpoint is non-inferiority in mean best corrected visual acuity (BCVA) change from baseline between the AXPAXLI and on-label aflibercept (2mg) arms at one year.

About the HELIOS study

The Phase 1 HELIOS trial is a multi-center, double-masked, randomized (2:1), parallel group study conducted in the U.S. The study was designed to evaluate the safety, tolerability, and efficacy of AXPAXLI compared to a sham control in subjects with moderately severe to severe non-proliferative diabetic retinopathy (NPDR) without center-involved diabetic macular edema (CI-DME). The data set reported here is based on 21 evaluable subjects (one patient of the 22 enrolled subjects died from an unrelated event). The primary endpoint of the study is frequency of treatment emergent adverse events (TEAEs). Secondary study endpoints include changes in the diabetic retinopathy severity score (DRSS), changes in best corrected visual acuity (BCVA) compared to baseline, changes in central subfield thickness (CSFT) compared to baseline, and the portion of subjects receiving rescue therapy.

About AXPAXLI™
AXPAXLI is an investigational bioresorbable, hydrogel implant incorporating axitinib, a small molecule, multi-target, tyrosine kinase inhibitor with anti-angiogenic properties, being evaluated for the treatment of wet AMD, DR, and other retinal diseases.

About Ocular Therapeutix, Inc.
Ocular Therapeutix, Inc. is a biopharmaceutical company committed to enhancing people's vision and quality of life through the development and commercialization of innovative therapies for wet age-related macular degeneration (wet AMD), diabetic retinopathy (DR), and other diseases and conditions of the eye. AXPAXLI™ (axitinib intravitreal implant, 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 a Phase 3 clinical trial for wet AMD. The clinical portfolio also includes PAXTRAVA™ (travoprost intracameral implant, also known as OTX-TIC), currently in a Phase 2 clinical trial for the treatment of open-angle glaucoma or ocular hypertension.

Ocular's expertise in the formulation, development, and commercialization of innovative therapies of the eye and the ELUTYX platform supported the development and launch of its first commercial drug product, DEXTENZA®, an FDA-approved corticosteroid for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis.

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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 timing, design, and enrollment of the Company's SOL-1 Phase 3 clinical trial of AXPAXLI (also called OTX-TKI) for the treatment of wet AMD; the timing, design, and initiation of the Company's SOL-R Phase 3 clinical trial of AXPAXLI; the Company's plans to advance the development of AXPAXLI and its other product candidates; the potential utility of any of the Company's product candidates; the Company's objective to become a leader in retinal care; the Company's cash runway and the sufficiency of the Company's cash resources; and other statements containing the words "anticipate", "believe", "estimate", "expect", "intend", "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 preclinical and clinical 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 DEXTENZA or any product or product candidate that receives regulatory approval; the ability to retain regulatory approval of DEXTENZA or 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 Special Protocol Assessment for the SOL-1 trial; the risk that even though the FDA has agreed with the overall design of the SOL-1 trial, the FDA may not agree that the data generated by the SOL-1 trial supports potential marketing approval; uncertainty as to the FDA's view of the Company's proposed design for the SOL-R trial; 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, or whether preliminary or interim data from a clinical trial will be predictive of final data from such trial; 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; the Company's ability to enter into strategic alliances or generate additional funding on a timely basis, on favorable terms, or at all; 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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