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Ocuphire Completes Enrollment of Over 100 Subjects in 24-Week ZETA-1 Phase 2b Trial of Oral APX3330 for the Treatment of Diabetic Retinopathy

Successful Execution and Completion of Enrollment in Four Late-Stage Clinical Trials Across Nyxol and APX3330 Programs in First Quarter of 2022

APX3330 as an Oral Therapy Has the Potential to Treat Over 7 MillionDiabetic Retinopathy Patients With Limited Treatment Options

Rapid Enrollment for 24-Week Phase 2b Retina Trial with Top-line Results Expected in Second Half of 2022

FARMINGTON HILLS, Mich., March 16, 2022 (GLOBE NEWSWIRE) -- Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of refractive and retinal eye disorders, today announced that it has completed enrollment of 103 diabetic patients with moderately severe-to-severe non-proliferative diabetic retinopathy (NPDR) or mild proliferative diabetic retinopathy (mild PDR) in ZETA-1, a Phase 2b trial evaluating the efficacy and safety of APX3330 for the treatment of diabetic retinopathy (DR) at 25 investigational sites across the U.S. in less than a year.

Diabetes is the leading cause of blindness among adults aged 20 to 74 years. In the United States alone, over 7 million patients suffer from diabetic retinopathy. The progression of DR involves abnormal vascular leakage and proliferation caused by increased levels of VEGF and inflammation. Currently approved treatments for DR consist mainly of anti-VEGF injections (EYLEA® by Regeneron, Lucentis® by Genentech) to improve retinal vascular integrity. Despite their approval for the treatment of DR, intravitreal injection therapies are not widely used in patients at an early stage without macular edema or proliferative diseases because of the asymptomatic nature before progression and patients' resistance to adhere to invasive and frequent VEGF therapies.

"APX3330 is a potential first oral therapy for DR/DME. It has a highly differentiated dual mechanism of action supported by an extensive body of evidence suggesting that targeting Ref-1 can block both angiogenesis and inflammation," said David Boyer, MD, practicing ophthalmologist at Retina-Vitreous Associates Medical Group, Medical Adviser to Ocuphire, and Investigator in the ZETA-1 trial. "If approved, APX3330 as an oral, systemic therapy has the potential to address the large unmet need in diabetic retinopathy patients and other diabetes-related complications such as diabetic nephropathy and neuropathy. Importantly, it

could also be used as an oral adjunct therapy in patients with PDR or DME that may improve dosing convenience and compliance by alleviating the burden associated with chronic anti-VEGF intravitreal injection treatments."

The ZETA-1 trial is a multi-center, randomized, placebo-controlled, double-masked Phase 2b trial designed to evaluate the safety and efficacy of APX3330 in DR. A total of 103 subjects (target of 80-100) with moderately severe-to-severe NPDR or mild PDR with a Diabetic Retinopathy Severity Scale (DRSS) score between 47 and 61 have been enrolled. Subjects are randomized to receive 600mg APX3300 or placebo daily over 24 weeks. The primary endpoint is a responder analysis that evaluates the percentage of subjects with a ≥ 2 step improvement on the DRSS score. If patients who are enrolled also have DME in their non-study eye, this eye will also be followed during the trial for potential improvement. Secondary endpoints include evaluation of central subfield thickness to assess effects on diabetic macular edema, BCVA, safety, and tolerability. For more information about the ZETA-1 Phase 2b trial design and its US clinical sites, refer to www.ClinicalTrials.gov Identifier: NCT04692688.

Jeffrey Heier, MD, Medical Advisor to Ocuphire added, "As an investigator in many retinal clinical trials, historically, we have faced challenges with patient enrollment and retention. This trial enrolled remarkably well, and we would like to thank the ZETA-1 investigators, their site staff, and especially the patients electing to participate in a 6-month trial with multiple site visits during a global pandemic. It speaks to the unmet need and patient willingness to adopt and continue self-administering a convenient oral treatment option. An oral treatment has the potential to minimize the need for frequent office visits and intraocular injections, thereby making treatment more accessible to patients for whom such visits are difficult, including those in rural areas in the U.S. and globally."

Mina Sooch, MBA, CEO and Founder, Ocuphire Pharma commented, "Completion of enrollment in ZETA-1 in under a year is impressive relative to competitive DR trials over the last few years. In addition, this trial marks the completion of enrollment of four late-stage clinical trials in the first few months of 2022. We are very pleased to have exceeded enrollment with more than 100 DR patients in ZETA-1 Phase 2b trial and we look forward to the 24-week primary endpoint data in the second half of 2022. The team at Ocuphire is excited to be advancing APX3330 as the first small molecule, dual action, oral treatment option with the potential to address the high unmet need for early intervention for progressive vision-threatening diabetic eye disease."

About APX3330

APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of the transcription factor regulator Ref-1 (reduction-oxidation effector factor-1). With its novel dual mechanism of action, APX3330 blocks the downstream pathways regulated by Ref-1, including those involving angiogenesis (VEGF) and inflammation (NF-kB), to decrease abnormal activation of both angiogenesis and inflammatory pathways that are implicated across several ocular diseases, including DR, DME, and age-related macular degeneration (AMD).

APX330 has shown a favorable safety and tolerability profile over 11 clinical trials conducted in healthy, hepatitis, and cancer subjects prior to ZETA-1. The overall incidence of adverse events in these trials was low, with less than 5% drug-related events being diarrhea and skin

rash (all mild). There was no significant organ toxicity in liver, heart, kidneys, brain, or lungs. An analysis of masked safety data from ZETA-1, conducted when the trial was approximately 70% fully enrolled, announced at Ocuphire's R&D Day on January 31, 2022, demonstrated a favorable safety profile consistent with these prior studies. There have been over 5,800 subject-days of exposure at doses of 600 mg/day or higher across previous 11 trials and current ZETA-1 trial.

About Diabetic Retinopathy

Diabetes, a worldwide epidemic, is the leading cause of blindness among adults aged 20 to 74 years. DR is the most common diabetic complication that affects the eyes and is manifested when chronically elevated blood sugar levels cause damage to blood vessels in the retina. DR affects over 7 million patients in the U.S. and 93 million patients worldwide. This problem is projected to worsen as the number of individuals at risk of developing diabetes increases by 55% by 2035 to a worldwide total of 592 million people.

There are two major types of DR: (1) non-proliferative DR (NPDR) and (2) proliferative DR (PDR). NPDR is an earlier, more typical stage of DR that can progress to more severe forms of DR if untreated and if underlying diabetes remains uncontrolled. PDR is a more advanced stage of DR that is characterized by retinal neovascularization that, if left untreated, can lead to permanent damage and blindness. When DR is in its early stages, blood vessels in the retina are damaged and can leak fluid into the retina, a complication called diabetic macular edema (DME). Fluid from DME and hemorrhage of the abnormal blood vessels formed in PDR can interfere with vision and can cause irreversible visual impairment due to retinal ischemia, scarring and detachment.

About Ocuphire Pharma

Ocuphire is a publicly-traded (NASDAQ: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of several eye disorders. Ocuphire's pipeline currently includes two small-molecule product candidates targeting refractive and retinal indications. The company's lead product candidate, Nyxol® eye drops (0.75% phentolamine ophthalmic solution) is a once-daily, preservative-free eye drop formulation of phentolamine mesylate, a non-selective alpha-1 and alpha-2 adrenergic antagonist designed to reduce pupil size, and is being developed for several indications, including reversal of pharmacologically-induced mydriasis (RM), presbyopia and dim light or night vision disturbances (NVD), and has been studied in 9 completed clinical trials. Ocuphire reported positive top-line data for MIRA-2, the first Phase 3 registration trial for the treatment of RM, and recently initiated and completed enrollment in the second Phase 3 registration trial (MIRA-3) and pediatric safety trial in RM. Ocuphire also reported positive top-line data from a Phase 2 trial of Nyxol for treatment of presbyopia, both alone and with low dose pilocarpine ("LDP") 0.4% as adjunctive therapy. The company recently completed enrollment in its Phase 3 study of Nyxol for NVD. Ocuphire's second product candidate, APX3330, is an oral tablet designed to inhibit angiogenesis and inflammation pathways relevant to retinal and choroidal vascular diseases, such as diabetic retinopathy (DR) and diabetic macular edema (DME) and has been studied in 11 Phase 1 and 2 trials. The company announced the completion of enrollment in a Phase 2b clinical trial of APX3330 to treat DR/DME (ZETA-1). Please visit www.clinicaltrials.gov to learn more about Ocuphire's recently enrolled second Phase 3 registration trial in RM (NCT05134974),

MIRA-4 pediatric safety study in RM (NCT05223478), Phase 3 registration trial in NVD (NCT04638660), and Phase 2b trial in DR/DME (NCT04692688). Ocuphire previously completed the first Phase 3 registration trial in RM (NCT04620213) and Phase 2 trial in presbyopia (NCT04675151). As part of its strategy, Ocuphire will continue to explore opportunities to acquire additional ophthalmic assets and to seek strategic partners for late-stage development, regulatory preparation, and commercialization of drugs in key global markets. For more information, visit www.ocuphire.com.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning the timing and results of the ZETA-1 trial, additional regulatory timelines, commercial timelines, and future clinical trials in RM, presbyopia, NVD, and DR/DME. These forward-looking statements are based upon Ocuphire's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) the success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; (ii) regulatory requirements or developments; (iii) changes to clinical trial designs and regulatory pathways; (iv) changes in capital resource requirements; (v) risks related to the inability of Ocuphire to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vi) legislative, regulatory, political and economic developments, (vii) changes in market opportunities, (viii) the effects of COVID-19 on clinical programs and business operations, (ix) the success and timing of commercialization of any of Ocuphire's product candidates and (x) the maintenance of Ocuphire's intellectual property rights. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by Ocuphire from time to time with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Ocuphire undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Ocuphire Contacts

Mina Sooch, President & CEO
Ocuphire Pharma, Inc.
ir@ocuphire.com
www.ocuphire.com

Corey Davis, Ph.D.
LifeSci Advisors
cdavis@lifesciadvisors.com

Source: Ocuphire Pharma