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Ocuphire Initiates ZETA-1 Phase 2 Clinical Trial Investigating APX3330 in Diabetic Retinopathy

APX3330 has the Potential to be a Novel Oral Treatment Option with Dual Mechanism of Anti-VEGF and Anti-Inflammatory for Diabetic Retinopathy

Top Line Data from ZETA-1 Expected by Early 2022

FARMINGTON HILLS, Mich., April 08, 2021 (GLOBE NEWSWIRE) -- Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of several eye disorders, announced today that it has screened the first patient in ZETA-1, a Phase 2 trial to evaluate APX3330 in non-proliferative diabetic retinopathy (NPDR) and mild proliferative diabetic retinopathy (mild PDR). Effects on diabetic macular edema will be explored as a secondary outcome. A number of retinal centers across the US are active and recruiting eligible diabetic retinopathy patients.

Diabetes is the leading cause of blindness among adults aged 20 – 74. In the United States alone, over 7 million patients suffer from diabetic retinopathy (DR), a complication of diabetes in which chronically elevated blood sugar levels cause damage to blood vessels in the retina. An additional 750,000 patients suffer from diabetic macular edema (DME), one of the most common complications of diabetic retinopathy where the macula swells from fluid leaked from damaged blood vessels. The disease progression of both DR and DME involves abnormal vessel proliferation and inflammation. Thus, current approved treatments for DR and DME encompass an over $10 billion global market and involve administering anti-VEGF injections (such as EYLEA® by Regeneron, Lucentis® by Genentech, and Avastin® by Genentech) to decrease vessel formation or steroids (such as OZURDEX® by Allergan) to decrease inflammation into eyes with advanced retinal disease. ZETA-1 is investigating the potential of APX3330 to offer an innovative and conveniently administered oral treatment for diabetic retinopathy that addresses both of these disease pathways.

Dr. Peter K. Kaiser, Professor of Ophthalmology at the Cole Eye Institute of the Cleveland Clinic Foundation commented, “There remains a strong need to develop a non-injectable alternative treatment option for patients with DR as these injectables—although approved for this indication— are not widely used. If successfully developed, APX3330 could lead to the first oral option for DR as well as an adjunct therapy that may improve dosing convenience and compliance by alleviating some of the burden of chronic anti-VEGF injection treatments for DME and other retinal diseases.”

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 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 diabetic retinopathy (DR), diabetic macular edema (DME), and age-related macular degeneration (AMD).

Dr. Mark R. Kelley, Professor in the Department of Pediatrics and Glick Eye Center at Indiana University School of Medicine, co-founder of the APX3330 program, and member of Ocuphire's Medical Advisory Board stated, "APX3330, a potential first oral therapy for DR, is not only novel in its oral route of administration, but it builds on decades of studies targeting Ref-1 as an impactful way to block both angiogenesis and inflammation using a single drug candidate. It is rewarding to see APX3330 begin this Phase 2 trial in ophthalmology with the potential to offer a new treatment option for patients with retinal diseases, particularly diabetics."

The ZETA-1 trial is a randomized, placebo-controlled, double-masked study designed to evaluate the efficacy of APX3330 to improve diabetic retinopathy over 24 weeks. The study will be conducted in up to 20 U.S. sites and is expected to enroll approximately 100 subjects with moderately-severe to severe NPDR or mild PDR in the study eye. 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. The primary endpoint of the study will evaluate the percentage of subjects with a ≥ 2 step improvement on the Diabetic Retinopathy Severity Scale (DRSS) score. Secondary endpoints include evaluation of central subfield thickness to assess effects on diabetic macular edema, BCVA, safety and tolerability. For more information, refer to www.ClinicalTrials.gov Identifier: NCT04692688.

Mina Sooch, MBA, President and CEO of Ocuphire Pharma commented, "We are very excited to advance APX3330 in the ZETA-1 Phase 2 clinical trial. Building off of 11 prior trials that have demonstrated a favorable safety and tolerability profile in over 300 oncology and hepatic patients, APX3330 has the potential to become the first oral therapy used for diabetic retinopathy. Due to its highly differentiated mechanism of action, we believe that APX3330 could also emerge as an important add-on therapy with the currently approved anti-VEGF treatments and extend the time between injections. The team at Ocuphire has now initiated all 4 clinical trials planned since its public listing last November, and we look forward to continuing enrollment and data readouts over the next 12 months."

About Diabetic Retinopathy

Diabetes, a worldwide epidemic, is the leading cause of blindness among adults age 20 to 74. 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 the 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 scarring and retinal detachment. Despite the approval of intravitreal injection therapies for DR, patients with DR are not widely treated.

About Ocuphire Pharma

Ocuphire is a publicly traded (NASDAQ: OCUP), 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 front and back of the eye indications. The company's lead product candidate, Nyxol® (0.75% phentolamine ophthalmic solution) Eye Drops, 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 dim light or night vision disturbances (NVD), reversal of pharmacologically-induced mydriasis (RM), and presbyopia, and has been studied in 8 clinical trials including the recently completed Phase 3 trial in RM. Ocuphire reported positive topline data on March 15, 2021 for MIRA-2 Phase 3 FDA registration study for treatment of RM. Nyxol is also currently in Phase 3 clinical development for NVD and in Phase 2 for presbyopia. 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. APX3330 is entering Phase 2 clinical development for DR/DME. 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. Please visit www.clinicaltrials.gov to learn more about Ocuphire's completed Phase 2 trials, recently completed Phase 3 registration trial (NCT04620213), ongoing Phase 3 registration trial (NCT04638660) and Phase 2 trial in presbyopia (NCT04675151), and Phase 2 trial in DR/DME (NCT04692688). For more information, please 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 Ocuphire's product candidates, results of ongoing and future clinical trials, and commercialization and market opportunities. 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, and (ix) the success and timing of commercialization of any of Ocuphire's product candidates. 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.

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