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Ocuphire Pharma Announces Successful End-of-Phase 2 Meeting with FDA for Oral APX3330 in Diabetic Retinopathy

Agreement on Phase 3 Primary Endpoint of 3-step Worsening on Binocular Diabetic Retinopathy Severity Scale (DRSS) Score

Company Plans to Submit a Special Protocol Assessment (SPA)

APX3330 has the Potential to be the First Oral Option for 8M Non-Proliferative Diabetic Retinopathy (NPDR) Patients in the US

FARMINGTON HILLS, Mich., Nov. 02, 2023 (GLOBE NEWSWIRE) -- Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of retinal and refractive eye disorders, today announced the successful outcome of an End-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA), supporting the advancement of oral APX3330 for the treatment of diabetic retinopathy (DR) into Phase 3 studies based on the recently completed Phase 2 ZETA-1 trial.

“We are pleased to have FDA agreement on the primary endpoint for Phase 3 pivotal trials of APX3330 which we believe is the most advanced oral therapy currently in development for diabetic retinopathy,” said George Magrath, M.D, MBA., M.S., Chief Executive Officer of Ocuphire. “Results from our Phase 2 ZETA-1 results demonstrate that oral APX3330 has the potential to slow or prevent clinically meaningful progression of diabetic retinopathy, as measured by the percentage of subjects with ≥ 3-step worsening on a binocular diabetic retinopathy severity scale (DRSS), which will be the Phase 3 primary endpoint. As recommended by the FDA, Ocuphire plans to submit a Special Protocol Assessment to agree on the clinical trial protocol and statistical analysis plan for the Phase 3 trials and will share specifics on the study design parameters and anticipated timing once agreed with the FDA. We are grateful for the FDA’s support and guidance and look forward to continued collaboration as we advance APX3330 into Phase 3 development.”

The EOP2 meeting was supported by results from the previously completed Phase 2 ZETA-1 trial. The randomized, double-masked, placebo-controlled Phase 2 trial was designed to evaluate the efficacy and safety of oral APX3330 in diabetic retinopathy patients. A higher percentage of placebo-treated patients had ≥ 3-step worsening on binocular DRSS from baseline compared to APX3330-treated patients at 24 weeks. APX3330 demonstrated favorable safety and tolerability in diabetic patients.

David Brown, M.D., F.A.C.S., co-chairman of the medical leadership board at Retina

Consultants of America (RCA) said, “Given the increasing number of DR patients and current treatment options, I am encouraged by the results of the ZETA-1 trial showing that APX3330 can potentially slow or prevent progression to vision threatening diseases such as Proliferative Diabetic Retinopathy. The current treatment paradigm for NPDR patients is for physicians to monitor progression every 4-6 months depending on DR severity. Approved anti-VEGF therapies are not widely utilized in NPDR patients because of the necessity for consistent intravitreal injections in asymptomatic patients. A safe convenient oral medication that could slow or prevent diabetic retinopathy would be a major advance in our fight against diabetic blindness.”

About APX3330

APX3330 is a first-in-class, small molecule, oral inhibitor of the transcription factor regulator Ref-1 (reduction-oxidation effector factor-1). With a novel dual mechanism of action, APX3330 blocks the downstream pathways regulated by Ref-1 – which involve angiogenesis (VEGF) and inflammation (NFkB) – 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). APX3330 has shown a favorable safety and tolerability profile in 12 clinical trials conducted in healthy, hepatitis, cancer, and diabetic subjects.

About Ocuphire Pharma

Ocuphire Pharma, Inc. is a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of retinal and refractive eye disorders.

Ocuphire’s lead retinal product candidate, APX3330, is a first-in-class small-molecule inhibitor of Ref-1 (reduction oxidation effector factor-1 protein). Ref-1 is a regulator of transcription factors such as HIF-1a and NF-kB. Inhibiting REF-1 reduces levels of vascular endothelial growth factor (“VEGF”) and inflammatory cytokines which are known to play key roles in ocular angiogenesis and inflammation. Through inhibition of Ref-1, APX3330 normalizes the levels of VEGF to physiologic levels, unlike biologics that deplete VEGF below the levels required for normal function. APX3330 is an oral tablet administered twice per day for the treatment of diabetic retinopathy (“DR”). A Phase 2 study in subjects with DR and an End-of-Phase 2 meeting have recently been completed, and a Special Protocol Assessment is planned to be submitted with the U.S. Food and Drug Administration (FDA).

DR affects approximately 10 million people with diabetes and is projected to impact over 14 million Americans by 2050. DR is classified as Non-Proliferative Diabetic Retinopathy (“NPDR”), the early stage of the disease in which symptoms may be mild or non-existent or Proliferative Diabetic Retinopathy (“PDR”) which is the more advanced stage of diabetic eye disease that can be highly symptomatic with loss of vision. Approximately 80% of DR patients have NPDR that will progress to PDR if left untreated. Despite the risk for visual loss associated with this disease, over 90% of NPDR patients currently receive no course of treatment apart from observation by their eye care specialist until they develop sight-threatening complications. This is due to the treatment burden of the frequent eye injections required with currently approved therapies for this disease. APX3330 as an oral tablet has the potential to be an early, non-invasive treatment for the 8 million NPDR patients in the US. Treatment with APX3330 is expected to delay or prevent progression of NPDR, thereby

reducing the need for expensive intravitreal injections with anti-VEGF therapies and reducing the likelihood of vision loss due to DR.

Ocuphire has also in-licensed APX2009 and APX2014, which are second-generation analogs of APX3330. The unique dual mechanism of action of these Ref-1 inhibitors of reducing angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as age-related macular degeneration, and geographic atrophy. Ocuphire is currently evaluating local delivery routes in addition to the systemic (oral) route as part of its pipeline expansion in retinal therapies.

Ocuphire has a partnership with Viatris, Inc. to develop and commercialize phentolamine ophthalmic solution 0.75%. Phentolamine is a non-selective alpha-1 and alpha-2 adrenergic antagonist designed to reduce pupil size by uniquely blocking the alpha-1 receptors found on the iris dilator muscle without affecting the ciliary muscle. In September 2023, the FDA approved RYZUMVI™ (phentolamine ophthalmic solution 0.75%) to treat pharmacologically induced mydriasis produced by adrenergic agonists (e.g., phenylephrine) or parasympatholytic agents (e.g., tropicamide). Phentolamine ophthalmic solution 0.75% is also in Phase 3 clinical development for the treatment of presbyopia and dim light (night) vision disturbances.

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 End-of-Phase 2 meeting with the FDA to confirm Phase 3 registration endpoints, study parameters for Phase 3 pivotal studies, and FDA agreement on Special Protocol Assessment. 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) risks that the Viatris partnership may not facilitate the commercialization or market acceptance of Ocuphire's product candidates; (x) the success and timing of commercialization of any of Ocuphire's product candidates and (xi) 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.

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