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Ocuphire Pharma Announces In-License of Phase 2 Oral Small Molecule Drug Candidate for Diabetic Retinopathy and Diabetic Macular Edema from Apexian Pharmaceuticals

APX3330, a First-in-Class Ref-1 Inhibitor for Diabetic Ocular Diseases Affecting the Retina, Added to Ocuphire Portfolio of Ophthalmic Drug Candidates

Data from Two Recently Completed Nyxol® Phase 2b Studies Accepted for Presentation at ARVO 2020 Conference

FARMINGTON HILLS, Michigan--(BUSINESS WIRE)-- Ocuphire Pharma, Inc., a clinical-stage pharmaceutical company focused on the development and commercialization of therapies to treat patients with a variety of ophthalmic disorders, today announced that it has entered into an agreement with Apexian Pharmaceuticals, Inc., granting Ocuphire an exclusive worldwide sublicense to Apexian's Ref-1 Inhibitor program, including its lead drug candidate APX3330, for all ophthalmic and diabetic indications.

APX3330 is a first-in-class, orally-administered, small molecule drug candidate that selectively targets and inhibits the Ref-1 (reduction-oxidation effector factor-1) protein, a novel upstream regulator of critical transcription factors controlling inflammatory and angiogenesis pathways that are implicated in diabetic retinopathy (DR) and diabetic macular edema (DME). DR and DME are common diabetic complications that arise due to damage to small blood vessels within the eye, causing leakage, oxygen starvation and abnormal vessel growth that progressively obstructs vision, leading to blindness. APX3330 may improve eye health in diabetics by reducing inflammation, hypoxia signaling, and abnormal angiogenesis.

With nearly 8 million DR patients and another 750,000 DME patients in the U.S., there is a large unmet market opportunity for new treatments to complement existing therapies. The primary therapies today are intravitreal anti-VEGF antibodies (Lucentis® and Eylea®) with sales over $10 billion worldwide, which are given as injections into the white (sclera) of the eye every one to three months. Earlier treatment options to prevent or delay vision loss for patients with diabetic eye disease are important. APX3330's safety profile, pharmacokinetic properties, and molecular target engagement data observed in clinical trials and its drug exposure in the retina seen in mouse models, combined with a unique oral tablet formulation, suggest its potential to reduce the frequency of anti-VEGF treatments and increase compliance for better outcomes.

APX3330 has been dosed twice-a-day in over 400 subjects across 11 Phase 1 and Phase 2 trials, with few systemic adverse events reported and clinical data that supports chronic administration. Dr. Mark R. Kelley, Associate Director of Basic Science, Indiana University Simon Cancer Center, discovered and characterized the Ref-1 target and its mechanisms and led the team that identified APX3330 as an effective Ref-1 inhibitor. Dr. Kelley co-founded Apexian, which initially explored APX3330's utility in advanced solid tumors, with recent presentations at ASCO and AACR, and then ophthalmic and other clinical indications. Based on APX3330's clinical and pre-clinical data, Ocuphire plans to begin a Phase 2 proof-of-concept study in non-proliferative DR and DME in 2020.

"We are very pleased to enter into this licensing agreement and partnership with Ocuphire to advance APX3330 into Phase 2 clinical ophthalmology trials for DR and DME. The expertise, experience and leadership of the Ocuphire team is a major factor for our entering into this partnership," said Dr. Mark R. Kelley, Chief Scientific Officer of Apexian. "APX3330 is an oral drug that has demonstrated a promising safety profile, predicted PK and target engagement on APE1/Ref-1 in previous clinical trials. The partnership with Ocuphire will also allow us to develop the extensive pipeline of Ref-1 inhibitors including APX2009 for future ophthalmology therapeutic interventions including in Age-Related Macular Degeneration".

"The acquisition of APX3330 further expands our late-clinical stage small molecule ophthalmic pipeline to now include potential blockbuster retina indications," said Mina Sooch, President, and Chief Executive Officer of Ocuphire. "Diabetic retinopathy and diabetic macular edema are a leading cause of vision loss worldwide, and we believe that there is an unmet need for an efficacious, first oral medication that can increase compliance and alleviate the burden of intravitreal injections. We are excited to work with our new partners at Apexian to develop and commercialize APX3330. We are also pleased to share that our positive Phase 2b trial results for Nyxol in 2019 have been accepted for presentation at the upcoming ARVO industry conference."

The Association for Research in Vision and Ophthalmology (ARVO) 2020 Conference will be held in Baltimore, MD on May 3-7, 2020. The two recently completed multi-center, double-masked, randomized, placebo-controlled Phase 2b clinical trials for Nyxol Eye Drops have been accepted for presentation. Dr. Jay Pepose, MD, Medical Director of the Pepose Vision Institute, will present results from the ORION-1 trial (NCT03960866), "Phentolamine mesylate ophthalmic solution provides long lasting pupil modulation and improves visual acuity". Dr. Paul Karpecki, D.O., FAAO, Clinical Director of Advanced Ocular Surface Disease at Kentucky Eye Institute, will present the accepted abstract for the MIRA-1 trial (NCT04024891), "Phentolamine ophthalmic solution reduces time to recovery of medically-induced mydriasis in a Phase 2 trial".

About APX3330

APX3330 is a first-in-class, oral small molecule drug candidate that inhibits the Ref-1 target (known also as APE1/Ref-1 or APE1), with an opportunity to treat multiple retina (back-of-the-eye) disorders. APX3330 is initially targeting diabetic retinopathy and diabetic macular edema, and future indications for APX3330 may include wet age-related macular degeneration and retinal vascular occlusion. APX3330 has a dual mechanism of action in validated pathways for these retinal diseases. It uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1, specifically HIF-1a to reduce VEGF signaling and NF-kB to modulate VEGF, TNF-α and other inflammatory

cytokines. APX3330 has been dosed twice-a-day in over 400 subjects across 11 Phase 1 and Phase 2 trials, with few systemic adverse events reported and clinical data that supports chronic administration. APX3330 was originally developed by Eisai Co., Ltd. for use in multiple hepatic inflammatory indications through Phase 2 development, and then further developed by Apexian Pharmaceuticals, Inc. to explore clinical utility in advanced solid tumors.

About Nyxol

Nyxol is a novel eye drop drug candidate for multiple front-of-the-eye disorders, including night vision disturbances (NVD), reversal of mydriasis (RM), presbyopia, and normal-tension glaucoma. Nyxol is a proprietary ophthalmic formulation of phentolamine mesylate, an approved alpha-1 and alpha-2 inhibitor, allowing a more efficient 505(b)(2) development pathway for approval. With safety and efficacy data from seven Phase 1 and Phase 2 trials, Nyxol has demonstrated a differentiated target product profile that includes moderately reducing pupil size (which leads to improved vision night and day at both far and near distances), lowering intraocular pressure in normal range, and convenient once-daily evening dosing with durable >24 hour effects. Use of the active ingredient in Nyxol in improving certain types of visual performance was originally developed by Dr. Gerald Horn, an ophthalmologist and laser vision specialist in Chicago, who later also invented the recently-approved redness reliever eye drop Lumify®.

About Ocuphire

Ocuphire is a clinical-stage biopharmaceutical company engaged in the development and commercialization of drugs to treat important ophthalmic disorders. The company's lead drug candidate, preservative-free Nyxol Eye Drops, is being developed for multiple front-of-the-eye (pupil/cornea) indications. Ocuphire's second drug candidate, APX3330, is a novel oral small molecule targeting multiple back-of-the-eye (retina) indications. Please visit www.clinicaltrials.gov to learn more about our past clinical trials. For more information, please visit www.ocuphire.com.

Forward-looking statements are made in this press release and you are cautioned not to put any undue reliance on such statements. There are a number of risks and uncertainties that could cause actual events to differ from the expectations indicated in these forward-looking statements. This press release shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

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