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Ocuphire Pharma Announces Two Publications Supporting the APX3330 Program

Emerging data on the benefits of Ref-1 inhibition via APX3330 have shown its potential to treat multiple inflammatory and angiogenic disease processes

FARMINGTON HILLS, Mich., Nov. 12, 2020 (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, today announced the publication of two seminal papers supporting its APX3330 program. The first is a review paper on the Ref-1 protein, a novel molecular target involved in multiple inflammatory and angiogenic disease processes, focusing on ocular, gastrointestinal, and cancer disorders in *Drug Discovery Today*, a journal dedicated to all aspects of preclinical drug discovery. The second publication covers a preclinical study outlining the benefits of APX3330 that were shown in mouse models of chronic colitis, an inflammatory condition, in the peer-reviewed journal *Inflammatory Bowel Disease*.

The publication entitled, **“The multifunctional APE1 DNA repair–redox signaling protein as a drug target in human disease,”** reported the following:

- Ref-1 has emerged as a novel therapeutic target developed for treating ocular diseases
- Findings in other indications, such as in preclinical models of cancer and IBD, support the targeting of Ref-1 to interfere with angiogenesis and inflammation in ocular disease such as diabetic retinopathy (DR), diabetic macular edema (DME), and age-related macular degeneration (AMD) with APX3330, APX2009, and APX2014
- Findings from a solid tumor Phase-1 trial, where doses up to 600 mg per day of APX3330 demonstrated chronic tolerability, for some patients up to a year
- Use of Ref-1 inhibitors has also promoted prevention of neuropathy in preclinical studies

The full online publication can be accessed at the following link: [sciencedirect.com](https://www.sciencedirect.com)

The second publication entitled, **“Inhibition of APE1/Ref-1 Redox Signaling Alleviates Intestinal Dysfunction and Damage to Myenteric Neurons in a Mouse Model of Spontaneous Chronic Colitis,”** reported the following:

- Inflammation-induced oxidative stress is implicated in the pathophysiology of GI dysfunction in IBD
- When given systemically to mice with chronic colitis, APX3330 reduced mitochondrial superoxide production, oxidative DNA damage, leading to neuroprotective effects of the enteric nervous system
- APX3330 improved disease severity, reduced immune cell infiltration, restored GI function, and demonstrated Ref-1 target inhibition

The full online publication can be accessed at the following link: academic.oup.com

Mark Kelley, PhD, member of Ocuphire's Ocular Medical Advisory Board, commented, "The results presented in both publications support the underlying mechanism of action of Ref-1 inhibitors in the prevention of inflammation and angiogenesis as well as the potential chronic daily use of APX3330 for ocular diseases."

These publications offer evidence on the anti-inflammatory and anti-angiogenesis benefits of APX3330, and with the increasing implications of inflammatory pathways in diabetic eye disease, there is significant promise for its success in treating diabetic retinopathy, macular edema, and wet age-related macular degeneration.

APX3330 to be Investigated in the ZETA-1 Phase 2 Trial in Diabetic Retinopathy

The planned multi-center, randomized, placebo-controlled, double-masked Phase 2 study is designed to evaluate the efficacy of daily oral dosing of APX3330 to improve Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) score in patients with moderately severe to severe non-proliferative diabetic retinopathy (NPDR) or mild proliferative diabetic retinopathy (PDR). The trial is expected to enroll 100 patients in early 2021 over multiple sites in the US and will evaluate a 600mg daily dosage of APX3330 over the course of 24 weeks. The primary endpoint will be the percentage of patients with a ≥ 2 -step improvement in DRSS score in the study eye at week 24. Please refer to ocuphire.com for more information.

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[®] 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, pharmacologically-induced mydriasis, and presbyopia. Ocuphire's second product candidate, APX3330, is a twice-a-day oral tablet, designed to inhibit angiogenesis and inflammation pathways relevant to retinal and choroidal vascular diseases, such as diabetic retinopathy and diabetic macular edema. 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 recent Phase 2 clinical trials. 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 and potential. 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; (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, and (vii) the effects of COVID-19 on clinical programs and business operations. 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 (including the proxy statement/prospectus included in that certain Registration Statement on Form S-4 (File No. 333-239702) initially filed with the SEC on July 6, 2020 and declared effective by the SEC on October 2, 2020. 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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