June 29, 2022

Ocuphire Granted New U.S. Patent for Late-Stage Oral Drug Candidate APX3330 for Use in Diabetics and Announces New Peer-Reviewed APX3330 Publication

Newly Issued Patent Broadens Medical Uses of Oral APX3330 Therapy in Patients with Diabetes and Extends Expiry Thru 2038

Peer-Reviewed Publication Highlights the Critical Role of Inflammation RegulatorNFkB as a Target for Ref-1 inhibition Using APX3330 and APX Pipeline Compounds

Topline Results from ZETA-1, a Multi-Center, Masked, Placebo-Controlled Phase 2b Trial of APX3330 in Diabetic Retinopathy with 100+ Patients, Expected in 2H 2022

FARMINGTON HILLS, Mich., June 29, 2022 - 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 the United States Patent and Trademark Office (USPTO) has issued a new patent extending expiry and broadening coverage of the company's late-stage oral product candidate, APX3330. In addition, a new publication supporting the novel mechanism of action inhibiting NFkB and the inflammation pathway for APX3330 and the APX pipeline candidates has been published in a peer-reviewed journal.

"We are pleased to announce the issuance of a new U.S. patent that further strengthens our patent estate for APX3330," said Mina Sooch, MBA, Founder and CEO of Ocuphire Pharma. "If approved, oral APX3330 has the potential to address the high unmet need for early intervention for progressive vision-threatening diabetic eye disease, including diabetic retinopathy (DR) and diabetic macular edema (DME). The timing is ideal as we continue to advance our fully enrolled clinical program investigating APX3330 in DR/DME where we have reported interim masked safety results at multiple medical meetings throughout this year demonstrating a consistent and favorable safety profile for a first-in-class oral treatment option. Top-line results from the Phase 2b ZETA-1 trial are expected in the second half of 2022."

U.S. Patent No. 11,351,130 has claims directed to methods of treatment using APX3330, which makes it eligible for listing in the U.S. FDA Orange Book. It was issued on June 7, 2022 and has a term that expires in year 2038. Claims in this patent include methods of treating inflammation and chronic pain in a subject suffering from diabetes. This patent complements the company's patent estate relating to APX3330 and the company's pipeline products including APX2009 and APX2014, together the subject of over 40 cases that are a

combination of patents and pending patent applications directed to ophthalmic and other uses in the U.S., Europe, Japan, and other foreign countries.

Ocuphire also announced the publication of a preclinical study outlining the pivotal role of NFkB (RelA) in Ref-1 inhibition in a pancreatic ductal adenocarcinoma (PDAC) cell model with a Kras genotype and offers evidence of anti-inflammatory benefits of APX3330 in PDAC.

The publication entitled, "*RelA is an Essential Target for Enhancing Cellular Responses to the DNA Repair/Ref-1 Redox Signaling Protein and Restoring Perturbated Cellular Redox Homeostasis in Mouse PDAC Cells*" had several key findings such as NFkB being a key target driving pancreatic cell sensitivity to Ref-1 redox inhibition, and confirmed small molecules APX33330, APX2009, and APX2014 suppresses inflammatory process mediated by NFkB pathway.

The full online publication in *Frontiers in Oncology* can be accessed here: https://doi.org/10.3389/fonc.2022.826617

Mark Kelley, PhD, member of Ocuphire's Medical Advisory Board Professor of Pediatric Oncology Research, and Professor of Ophthalmology at Indiana University, commented, "The results from this preclinical study continue to support the underlying mechanism of action of Ref-1 inhibitors in the reduction of inflammation and highlight the potential broad utility of APX3330 in diseases implicated by Ref-1 signaling, including in diabetic and retinal eye diseases. It is very rewarding to be involved in the advancement of APX3330 especially as we approach a data read-out this year from the Phase 2b trial in diabetic patients with retinopathy. This clinical study represents a significant milestone that is a result of years of research and translational medicine by many of us."

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 (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 over 11 clinical trials conducted in healthy, hepatitis, and cancer subjects prior to ZETA-1 trial. APX3330 is currently in a Phase 2 clinical trial in diabetic retinopathy patients. The most recent interim analysis of masked safety data from ZETA-1 trial was presented by Dr. David Boyer at the Annual Macula Society Meeting in June 2022 and oral APX3330 continued to demonstrate a favorable safety profile consistent with the prior trials. Across all the trials, the safety findings represent over 7,700 subject-days of exposure at the target dose of 600 mg/day of APX3330.

About Ocuphire Pharma

Ocuphire is a publicly-traded (NASDAQ: OCUP), clinical-stage ophthalmic

biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of refractive and retinal eye disorders. 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 12 completed clinical trials. Ocuphire has reported positive data from MIRA-2 and MIRA-3 registration trials and MIRA-4 pediatric safety trial for the treatment of RM. Ocuphire also reported positive topline data from the VEGA-1 Phase 2 trial of Nyxol for treatment of presbyopia, both Nyxol as a single agent and Nyxol with low dose pilocarpine ("LDP") 0.4% as adjunctive therapy. The Company recently reported positive topline results from LYNX-1 Phase 3 trial 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 in March the completion of enrollment in the ZETA-1 Phase 2b clinical trial of APX3330 to treat DR/DME. Please visit www.clinicaltrials.gov to learn more about Ocuphire's ongoing APX3330 Phase 2b trial in DR/DME ZETA-1 (NCT04692688) and completed Nyxol trials: Phase 3 registration trial in NVD LYNX-1 (NCT04638660), Phase 3 registration trials in RM MIRA-2 (NCT04620213) and MIRA-3 (NCT05134974), MIRA-4 Phase 3 pediatric safety study (NCT05223478), and Phase 2 trial in presbyopia VEGA-1 (NCT04675151). As part of its strategy, Ocuphire will continue to explore opportunities to acquire additional ophthalmic assets and 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, the success and timing of planned regulatory filings, the results of the ZETA-1 Phase 2b trial, and the market for Ocuphire's indications, business strategy, pre-commercialization activities, and commercialization of Ocuphire's product candidates. 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.

Contacts

Corporate

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

Investors

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

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