Ocuphire Announces MIRA-2 Phase 3 Registration Trial for the Reversal of Mydriasis Meets Primary Endpoint

Nyxol Meets Its Primary and Multiple Secondary Endpoints Including Statistically Significant Efficacy Returning Subjects More Rapidly to Normal Pupil Size Across a Breadth of Dilating Agents and Iris Colors

Nyxol has Potential to be a New Treatment Option for Reversal of Pharmacologically-Induced Pupil Dilation

Conference Call and Webcast Today @ 8:30am ET

Farmington Hills, Mich., March 15, 2021 - 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 positive top line results in the MIRA-2 Phase 3 registration trial investigating its product candidate Nyxol® for reversal of pharmacologically induced mydriasis (dilation of pupil for eye exams). Nyxol is a proprietary, preservative-free, stable, investigational eye drop formulation of phentolamine mesylate designed to reduce pupil size by inhibiting contraction of the iris dilator muscle. MIRA-2 was designed as a multi-center, randomized, double-masked, placebo-controlled, parallel, 24-hour Phase 3 trial that planned 168 healthy study participants, and ultimately enrolled 185 study participants.

These topline results indicate that the MIRA-2 trial met its primary endpoint with 49% percent of subjects (study eye) treated with Nyxol returning to ≤ 0.2 mm of their baseline pupil diameter at 90 minutes compared to 7% of subjects (study eye) treated with placebo ($p < 0.0001$). The study population was comprised of subjects who had received one of three mydriatic (dilating) agents in the modified Intent to Treat population (mITT). The three mydriatic agents used in this trial were phenylephrine 2.5% (alpha 1 agonist works on the iris dilator muscle), tropicamide 1% (cholinergic blocker works on the iris sphincter muscle), and Paremyd® (a combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25%), which are all commonly used in optometry and ophthalmology offices to dilate patients' pupils for annual or special exams.

"The successful outcome of this Phase 3 MIRA-2 FDA registration trial is a major milestone for Ocuphire and we are thrilled to announce these positive and clinically meaningful results. Nyxol showed a statistically significant improvement on the primary as well as multiple secondary endpoints, demonstrating its ability to more rapidly return pupil diameter back to normal baselines over multiple timepoints, breadth of iris colors, and dilating agents that work on one or both iris muscles that control pupil size," said Mina Sooch, MBA, President and CEO of Ocuphire Pharma. "These Phase 3 results build on a growing body of evidence to establish Nyxol's therapeutic product profile including the positive results seen in our recently published MIRA-1 Phase 2b trial. This

further validates the mechanism of action, therapeutic effect, and safety profile of the Nyxol platform for potential additional refractive indications - presbyopia and night vision disturbance. We are very grateful to the study participants and investigators who participated in this U.S. study."

Highlights of MIRA-2 Topline Efficacy and Safety Results

MIRA-2 (NCT04620213) is a Phase 3 registration trial evaluating the product candidate Nyxol to expedite the reversal of pharmacologically induced mydriasis. In the trial 185 study participants (171 adults and 14 adolescents at or over age 12) were randomized 1:1 to receive Nyxol (0.75% phentolamine ophthalmic solution) or vehicle control (placebo) 1 hour after receiving one of 3 mydriatic agents.

- The primary endpoint was met with 49% percent of subjects (study eye) treated with Nyxol returning to ≤ 0.2 mm of their baseline pupil diameter at 90 minutes compared to 7% of placebo treated subjects ($p < 0.0001$) across three mydriatic agents (phenylephrine, tropicamide, and Paremyd®).
- Multiple secondary efficacy endpoints also met statistical significance.
    - A clinically meaningful higher number of Nyxol treated subjects (study eye and non-study eye) returned to baseline pupil diameter at 60 minutes compared to placebo, and every subsequent timepoint through 6 hours post-dosing.
    - Nyxol treated subjects had mean pupil diameters that were 1 to 2.5 mm smaller than placebo treated subjects at all timepoints from 1 to 6 hours post-dosing.
    - Nyxol treated subjects returned to baseline pupil diameter more quickly than placebo treated subjects with:
        (i) all three dilating agents;
        (ii) both light and dark irides; and
        (iii) with one and two drops of Nyxol.
- Nyxol demonstrated a favorable safety profile.
    - Nyxol was well-tolerated in the study population with no serious adverse events or withdrawals due to adverse events.
    - A mild transient increase in conjunctival hyperemia was observed in Nyxol treated subjects which peaked at one hour post-dose and decreased steadily thereafter.

Jay S. Pepose, MD, PhD, Director of the Pepose Vision Institute, Professor of Clinical Ophthalmology at the Washington University School of Medicine, and Ocuphire Medical Advisory Board member commented, "I am excited to see robust effects of Nyxol in reversing pharmacologically induced mydriasis with a favorable safety profile. The Phase 3 trial results exceeded my expectations with statistical and clinical significance on the primary endpoint at 90 minutes, as well as at the earlier 60 minute timepoint. In addition, Nyxol demonstrated significant benefit through 6 hours across the range of commonly

used mydriatic agents, light and dark iris colors, and age cohorts. Nyxol is unique as the only alpha-1/2 antagonist in clinical trials. Nyxol has the potential to address an unmet medical need as there are no commercial treatments currently available for reversal of mydriasis. If approved for marketing by the FDA, Nyxol may provide substantial benefit to patients after dilation, and may even increase the compliance with standard of care guidance for dilated examinations during visits to eye care specialists and thereby improve overall eye health."

A more detailed presentation of the topline MIRA-2 results will be discussed on a conference call this morning and posted shortly thereafter to the Investors section of Ocuphire's corporate website in the Events section. For more information about the MIRA-2 Phase 3 trial design and its 12 U.S. clinical sites, please visit www.clinicaltrials.gov (NCT04620213). Ocuphire collaborated closely with Oculos Development Services, a Tampa, Florida based clinical research organization and subsidiary of Iuvo BioScience, on the execution of the MIRA-2 trial.

Building on the positive results of this first completed Phase 3 registration trial for Nyxol (MIRA-2), a second Phase 3 registration trial (MIRA-3) is planned to initiate in the second half of this year. A New Drug Application (NDA) to obtain approval to market Nyxol for this pharmacologically induced mydriasis indication is expected to be submitted to the FDA in early 2023.

Full results from the MIRA-2 Phase 3 trial will be presented at an upcoming industry conference - 2021 ASCRS Annual Meeting July 23–27 in Las Vegas, Nevada. Ocuphire also plans to submit these Phase 3 results to a peer-reviewed journal for publication later this year.

Reversal of Mydriasis Market Opportunity

Every year in the U.S., approximately 100 million eye exams are performed that require dilation of the pupil (mydriasis) to examine the back of the eye either for routine check-ups, disease monitoring or surgical procedures. Depending on the individual and the color of their eyes, the pharmacologically-induced dilation can last anywhere from 6 to 24 hours. Dilated eyes have heightened sensitivity to light and an inability to focus on near objects, causing difficulty with reading, working, and driving.

Market research conducted by GlobalData surveyed several hundred patients and eye care providers (optometrists and ophthalmologists) about Reversal of Mydriasis (as well as Night Vision Disturbances and Presbyopia). Over 65% of surveyed patients reported moderate to severe negative impact of a dilated exam. This underscores the potential value of the role of the investigational product candidate Nyxol in improving comfort and daily function after pupil dilation. Additionally, an estimated 45% of patients responded that they would be very likely to request a dilation reversal drop, and more than 40% of eye care providers would be likely to use a reversal drop if such a treatment were commercially available.

Conference Call and Webcast (with slides)

Ocuphire management will host a conference call and webcast with slides, today at 8.30am ET. Details for the call are as follows:

Toll free (U.S.)	877-407-4018
International:	201-689-8471
Conference ID	13717533
Webcast:	http://public.viavid.com/index.php?id=143904

The webcast will also be available on the "Investors" tab of the Ocuphire corporate website tab, under News & Events and will be archived for 90 days.

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. 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 soon to recruit 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; (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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