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# Ocuphire Announces Positive Topline Results from MIRA-3 Phase 3 FDA Registration Trial for Nyxol® in the Reversal of Mydriasis

*Meets Primary Endpoint With 58% Of Nyxol treated Subjects Returning to Baseline Pupil Diameter at 90 Minutes Compared to 6% of Placebo Subjects ( $p < 0.0001$ )*

*MIRA-3 Confirms Prior MIRA-2 Phase 3 Registration Trial Showing Substantial Benefit in Accelerating Reversal of Mydriasis (RM)*

*NDA Filing for Nyxol in RM Planned for Late 2022*

*Potential Launch as Only Dilation Reversal Drop in 2H 2023*

*Conference Call and Webcast Today at 8.30am ET*

FARMINGTON HILLS, Mich., March 29, 2022 (GLOBE NEWSWIRE) -- 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 positive topline results in the MIRA-3 trial, the company's second Phase 3 registration trial investigating its product candidate Nyxol® for the reversal of pharmacologically-induced mydriasis (dilation of pupil). Ocuphire announced positive results from its first Phase 3 trial, MIRA-2, in March 2021.

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-3 was designed as a multi-center, randomized, parallel arm, double-masked, placebo-controlled Phase 3 trial evaluating the safety and efficacy of Nyxol in subjects with pharmacologically-induced mydriasis. MIRA-3 enrolled 368 subjects from November 2021 to February 2022 at 16 sites in the U.S.

These topline results demonstrated that the MIRA-3 trial met its primary endpoint with 58% of subjects (study eye) treated with Nyxol returning to  $\leq 0.2$  mm of their baseline pupil diameter (PD) at 90 minutes compared to only 6% of subjects (study eye) treated with placebo ( $p < 0.0001$ ). The effect was also significant at 60 minutes (Nyxol 42% vs. placebo 2%,  $p < 0.0001$ ). In comparison, only 36% of placebo treated subjects returned back to baseline PD at 6 hours. These results showed clinically meaningful differences between Nyxol and placebo for accelerating reversal of pharmacologically-induced mydriasis.

"The successful completion of the MIRA-3 Phase 3 trial is a major milestone in our

development program for Nyxol in RM,” said Mina Sooch, MBA, President and CEO of Ocuphire Pharma. “We are delighted with the positive efficacy and safety outcomes which confirm the results from our prior MIRA-2 Phase 3 trial. We now have over 900 subjects studied across 10 clinical trials of which over 550 have been exposed to Nyxol. Importantly, today’s announcement means that that we have two FDA registration trials to support potential approval for the RM indication. We intend to file an NDA with the U.S. FDA in late 2022, which, if approved, would position Ocuphire for commercial launch of Nyxol in RM in the second half of 2023. We want to thank the study participants, physicians, study site personnel, and everyone who was involved in the MIRA-2 and MIRA-3 trials for their contribution in advancing this program and bringing us closer to potentially delivering an FDA-approved treatment for RM.”

### **Highlights of MIRA-3 Efficacy and Safety Results**

MIRA-3 ([NCT05134974](#)) is a Phase 3 registration trial evaluating the product candidate Nyxol to expedite the reversal of pharmacologically induced mydriasis. In the trial 368 study participants (336 adults and 32 adolescents at or over age 12) were randomized 2:1 to receive Nyxol (0.75% phentolamine ophthalmic solution) or vehicle control (placebo) 1 hour after receiving one of 3 mydriatic agents. The three mydriatic agents used in this trial were phenylephrine 2.5% (alpha 1 agonist targeting the iris dilator muscle), tropicamide 1% (cholinergic blocker targeting 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 as well as surgical procedures. The study population was comprised of subjects in the modified Intent to Treat population (mITT).

#### *Summary of MIRA-3 Topline Data*

- The primary endpoint was met with 58% of subjects (study eye) treated with Nyxol returning to  $\leq 0.2$  mm of their baseline pupil diameter at 90 minutes compared to only 6% of placebo treated subjects ( $p < 0.0001$ ) across the three mydriatic agents.
- Key secondary efficacy endpoints also met statistical significance:
  - Early onset of action with 42% of subjects at baseline PD by 60 minutes post-dose (vs. 2% placebo,  $p < 0.001$ )
  - Significantly more Nyxol-treated subjects returned to normal PD or smaller than placebo-treated subjects at all time points from 1 hour to 24 hours
  - Similar efficacy was seen with one or two drops of Nyxol (as the study eye was treated with 2 drops and the fellow eye with one)
  - Nyxol was effective regardless of iris color or mydriatic agent used
  - Approximately 4 hours were gained in time to return to normal pupil diameter overall and across mydriatic agents and iris colors
  - Nyxol restored normal distance corrected near vision significantly faster than placebo
- Nyxol demonstrated a favorable safety and tolerability profile.
  - Nyxol was well tolerated with no serious adverse events or withdrawals due to adverse events

- The only AE occurring in greater than 5% subjects was mild, transient conjunctival hyperemia (11%)

Jay S. Pepose, MD, PhD, Director of the Pepose Vision Institute, Professor of Clinical Ophthalmology at Washington University School of Medicine, and Ocuphire Medical Advisory Board member and Board member commented, “Nyxol’s unique MOA makes it an ideal agent for reversal of mydriasis, as it does not have the potential safety risks of retinal tears, accommodative spasm and angle closure associated with cholinergic agents like pilocarpine. The MIRA-3 and MIRA-2 trials confirm the favorable safety profile and efficacy, showing rapid reversal of mydriasis following dilation with all mydriatic agents tested and in both light and dark iris colors. In addition, the pupil reduction of 1 to 1.5 mm from baseline through 24 hours is a potential read through for our other clinical indications for Nyxol including presbyopia and night vision disturbances.”

Edward Holland, MD, Director of Cornea Services at Cincinnati Eye Institute and Ocuphire Medical Advisory Board member commented, “Pupil dilation is a necessary tool for ophthalmologists and optometrists to screen for and monitor diseases of the eye. However, patients often find dilation problematic, citing unwanted symptoms including inability to read, photophobia, loss of accommodation, and inability to work effectively. Many patients complain about or refuse dilation for these reasons. There are no approved treatments currently available for reversal of mydriasis, and with the announcement today of positive results from MIRA-3, I am very pleased to see the continued progress in advancing Nyxol toward potential FDA approval. If approved, I believe that Nyxol would be widely used in clinical practice, which could increase the overall number of dilated exams as well as improve patient experience, and lead to better eye health for our patients.”

For more information about the MIRA-3 Phase 3 trial design, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT05134974). Ocuphire collaborated closely with Oculos Development Services, a Rush, NY based clinical research organization and subsidiary of Iuvo BioScience, on the execution of the MIRA-3 trial.

## **Nyxol Development Plan and Next Steps in RM**

Ocuphire recently completed enrollment of 23 pediatric subjects in the MIRA-4 trial evaluating the safety and efficacy of Nyxol eye drops to reverse pharmacologically-induced mydriasis. Top line results are expected in the second quarter of 2022. If MIRA-4 meets its endpoints, the results would potentially support a broader label for Nyxol in RM to include children as young as age 3. Ocuphire is also on track to complete the Chemistry, Manufacturing and Controls (CMC) section of the NDA as three registration batches of Nyxol have been completed and on stability. The company plans to file an NDA that includes the results of MIRA-1, MIRA-2, MIRA-3, and MIRA-4 with the U.S. FDA in late 2022.

## **Reversal of Mydriasis Market Opportunity**

Every year in the U.S., an estimated 100 million eyes dilations are conducted to examine the back of the eye, either for routine check-ups, disease monitoring or surgical procedures, across all eye care practice groups. 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 a decreased ability to focus on near objects, causing difficulty reading, working, and driving. Currently, there are no approved or available options

to safely reverse mydriasis. Nyxol has the potential to be the first and only FDA-approved agent for RM.

Market research conducted by GlobalData surveyed several hundred patients and eye care providers (optometrists and ophthalmologists) about Reversal of Mydriasis. Over 65% of surveyed patients reported moderate to severe negative impact of a dilated pupil. These data underscore the potential value of the role of the investigational product candidate Nyxol in improving comfort and daily function after pupil dilation. Furthermore, approximately 80% of patients responded that they would be likely to request a dilation reversal drop, and more than 70% of eye care providers would be likely to use a reversal drop. The market research confirmed patients' willingness to pay out-of-pocket to reverse their dilations, supporting a market size estimate of over \$500M. Ocuphire is currently evaluating partnering options for an effective and cost-efficient commercial launch of Nyxol targeted for the second half of 2023.

### **Conference Call and Webcast (with slides)**

A more detailed presentation of the topline MIRA-3 results will be discussed on a conference call and webcast at 8.30am EDT this morning and will be posted shortly thereafter to the Investors section of Ocuphire's corporate website under the [Events](#) heading, where it will be archived and available for 90 days.

Details for the call are as follows:

Toll free: 1-877-407-4018

International: 1-201-689-8472

Conference ID: 13728061

Webcast: [Link](#)

### **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 refractive and retinal indications. The company's lead product candidate, Nyxol<sup>®</sup> 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 10 completed clinical trials. Ocuphire has reported positive topline data from MIRA-2 and MIRA-3, two registration trials for the treatment of RM, and recently completed enrollment in a pediatric safety trial (MIRA-4) in RM. Ocuphire also reported positive top-line data from a 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 completed enrollment in its Phase 3 study of Nyxol for NVD (LYNX-1). 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 recently announced the completion of enrollment in a Phase 2b clinical trial of APX3330 to treat DR/DME (ZETA-1). Please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) to learn more about Ocuphire's Phase 3 registration trial in RM discussed herein ([NCT05134974](https://clinicaltrials.gov/ct2/show/study/NCT05134974)), pediatric safety study in RM ([NCT05223478](https://clinicaltrials.gov/ct2/show/study/NCT05223478)), Phase 3 registration trial in NVD ([NCT04638660](https://clinicaltrials.gov/ct2/show/study/NCT04638660)), and Phase 2b trial in DR/DME ([NCT04692688](https://clinicaltrials.gov/ct2/show/study/NCT04692688)). Ocuphire previously completed the first Phase 3 registration trial in RM ([NCT04620213](https://clinicaltrials.gov/ct2/show/study/NCT04620213)) and Phase 2 trial in presbyopia ([NCT04675151](https://clinicaltrials.gov/ct2/show/study/NCT04675151)). 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. For more information, visit [www.ocuphire.com](http://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, timing and results in RM, presbyopia, NVD and DR/DME future clinical trials, potential market size of RM, as well as statements concerning the success and timing of planned regulatory filings and commercialization. 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.

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