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Ocuphire Pharma Receives FDA Agreement Under Special Protocol Assessment for LYNX-2 Phase 3 Trial of Phentolamine Ophthalmic Solution for the Treatment of Decreased Visual Acuity under Dim (mesopic) Light Conditions

Phase 3 Startup Activities are Underway, with Trial Initiation Expected in Q1 2024

FARMINGTON HILLS, Mich., Jan. 04, 2024 (GLOBE NEWSWIRE) -- Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of retinal and refractive eye disorders, today announced it has received agreement from the U.S. Food and Drug Administration (FDA) under a Special Protocol Assessment (SPA) for the clinical trial protocol and planned statistical analysis of the LYNX-2 Phase 3 trial to evaluate phentolamine ophthalmic solution for the proposed indication for the treatment of decreased visual acuity under dim (mesopic) light conditions.

“The SPA agreement with the FDA provides a clear regulatory path for phentolamine ophthalmic solution in patients with poor night vision after keratorefractive surgery,” said George Magrath, M.D., M.B.A, M.S, CEO of Ocuphire. “Preparations for the LYNX-2 Phase 3 trial have begun, and we anticipate patient enrollment to begin in the first quarter of 2024.”

“Patients with night vision disturbances face a range of symptoms including glare, halos, starbursts and reduced contrast which affect the quality of vision especially while driving at night,” said Marguerite McDonald, M.D., F.A.C.S. Clinical Professor of Ophthalmology at New York University’s Langone Medical Center and Tulane University Health Sciences Center. “Currently, there are no FDA-approved pharmacologic therapies to treat this condition that is routinely presented in our clinics. As someone who has been involved with the development of phentolamine for over 15 years, I am hopeful that we might be closer to a treatment than ever and applaud Ocuphire for their commitment to developing a treatment for the keratorefractive patients using phentolamine ophthalmic solution 0.75% to reduce the pupil diameter without engaging the ciliary muscle. A distinct attribute of phentolamine ophthalmic solution compared to other miotics in the class is that it does not make the pupil too small, which can decrease contrast and degrade vision.”

Ocuphire received written agreement from the FDA that the clinical trial protocol and planned

statistical analysis of the LYNX-2 Phase 3 trial of phentolamine ophthalmic solution could adequately address objectives supporting regulatory submission and a potential future marketing application in this indication. LYNX-2 will be a multi-center, randomized, double-masked, placebo-controlled Phase 3 trial designed to evaluate the safety and efficacy of phentolamine ophthalmic solution in up to 200 patients in the U.S. The agreed primary endpoint will be a gain of 3 lines (or 15 letters) or more of distance vision improvement on a low contrast chart in dim light conditions after 15 days of dosing.

Under the terms of the November 2022 license agreement, Viatris will fund the development of phentolamine ophthalmic solution for the treatment of decreased visual acuity under dim (mesopic) light conditions and presbyopia. Ocuphire is eligible to receive a milestone payment upon FDA approvals in these indications.

About Ocuphire Pharma

Ocuphire Pharma, Inc. is a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of retinal and refractive eye disorders.

Ocuphire's lead retinal product candidate, APX3330, is a first-in-class small-molecule inhibitor of Ref-1 (reduction oxidation effector factor-1 protein). Ref-1 is a regulator of the transcription factors HIF-1a and NF-kB. Inhibiting REF-1 reduces levels of vascular endothelial growth factor ("VEGF") and inflammatory cytokines which are known to play key roles in ocular angiogenesis and inflammation. Through inhibition of Ref-1, APX3330 normalizes the levels of VEGF to physiologic levels, unlike biologics that deplete VEGF below the levels required for normal function. APX3330 is an oral tablet to be administered twice per day for the treatment of diabetic retinopathy ("DR"). A Phase 2 study in subjects with DR and an End-of-Phase 2 meeting have recently been completed, and a Special Protocol Assessment is planned to be submitted with the FDA.

DR affects approximately 10 million people with diabetes and is projected to impact over 14 million Americans by 2050. DR is classified as Non-Proliferative Diabetic Retinopathy ("NPDR"), the early stage of the disease in which symptoms may be mild or non-existent or Proliferative Diabetic Retinopathy ("PDR") which is the more advanced stage of diabetic eye disease that can be highly symptomatic with loss of vision. Approximately 80% of DR patients have NPDR that will progress to PDR if left untreated. Despite the risk for visual loss associated with this disease, over 90% of NPDR patients currently receive no course of treatment apart from observation by their eye care specialist until they develop sight-threatening complications. This is due to the treatment burden of the frequent eye injections required with currently approved therapies for this disease. APX3330 as an oral tablet has the potential to be an early, non-invasive treatment for the 8 million NPDR patients in the U.S. Treatment with APX3330 is expected to delay or prevent progression of NPDR, thereby reducing the need for expensive intravitreal injections with anti-VEGF therapies and reducing the likelihood of vision loss due to DR.

Ocuphire has also in-licensed APX2009 and APX2014, which are second-generation analogs of APX3330. The unique dual mechanism of action of these Ref-1 inhibitors that reduces both angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as age-related macular degeneration and geographic atrophy. Ocuphire is currently evaluating local delivery routes in addition to the systemic (oral) route

as part of its pipeline expansion in retinal therapies.

Ocuphire has a partnership with Viatris, Inc. to develop and commercialize phentolamine ophthalmic solution 0.75%. Phentolamine is a non-selective alpha-1 and alpha-2 adrenergic antagonist designed to reduce pupil size by uniquely blocking the alpha-1 receptors found on the iris dilator muscle without affecting the ciliary muscle. In September 2023, the FDA approved RYZUMVI™ (phentolamine ophthalmic solution 0.75%) to treat pharmacologically induced mydriasis produced by adrenergic agonists (e.g., phenylephrine) or parasympatholytic agents (e.g., tropicamide). Phentolamine ophthalmic solution 0.75% is also in Phase 3 clinical development for the treatment of presbyopia and for the treatment of decreased visual acuity in dim light conditions.

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, statements concerning the timing of the LYNX-2 Phase 3 trial, the potential for FDA approval of phentolamine ophthalmic solution for the proposed indication for the treatment of decreased visual acuity under dim (mesopic) light conditions, and the potential receipt of a milestone payment from Viatris upon such FDA approval. 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) risks that the phentolamine ophthalmic solution partnership may not facilitate the commercialization or market acceptance of Ocuphire's product candidates; (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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