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Opus Genetics Receives FDA Agreement Under Special Protocol Assessment for Phase 3 Trial of APX3330 in Diabetic Retinopathy

Agreement Reached on Primary Endpoint and Phase 3 Trial Design

Oral APX3330 is a Late-Stage Clinical Asset Available for Partnering

FARMINGTON HILLS, Mich., Dec. 19, 2024 (GLOBE NEWSWIRE) -- Opus Genetics, Inc. (Nasdaq: IRD), a clinical-stage ophthalmic biotechnology company developing gene therapies for the treatment of inherited retinal diseases (IRDs) and small-molecule drugs to treat other ophthalmologic disorders, today announced that it has reached agreement with the U.S. Food and Drug Administration (FDA) on a Special Protocol Assessment (SPA) for a Phase 3 clinical trial evaluating oral APX3330 for the treatment of moderate to severe non-proliferative diabetic retinopathy (NPDR).

The SPA agreement reflects that the proposed Phase 3 trial design, endpoints, and planned analyses will be adequate to support a New Drug Application (NDA) submission for treatment of NPDR, subject to a successful outcome of the trial and review of all data in the NDA. The agreed primary endpoint is a reduction in 3-step or greater worsening on the binocular diabetic retinopathy severity scale (DRSS) score, compared to placebo. In the previous Phase 2 ZETA-1 trial, oral APX3330 showed the potential to slow or prevent clinically meaningful progression of DR and demonstrated a favorable safety profile.

“This SPA agreement reflects our alignment with the FDA on the design of a Phase 3 trial for APX3330 and is a testament to the team’s developmental and regulatory acumen,” said George Magrath, M.D., Chief Executive Officer of Opus Genetics. "If successful in Phase 3 and subsequently approved, APX3330 has the potential to be a transformative treatment option for patients with NPDR. We believe that having this SPA in place will help de-risk certain regulatory aspects of this program. Our intention is to seek a partner for APX3330 to fund further development, as we focus our resources on advancing our gene therapy candidates for IRDs.”

Diabetic retinopathy is a progressive eye disease which results in vision impairment and blindness among adults with diabetes. It is the leading cause of blindness in working age adults and impacts approximately 10 million patients in the US.

About APX3330
APX3330 is a first-in-class, small molecule, oral inhibitor of the transcription factor regulator

Ref-1 (reduction-oxidation effector factor-1). With a novel, multimodal mechanism of action, APX3330 modulates the downstream pathways regulated by Ref-1 – which involve angiogenesis (VEGF), oxidative stress (Nrf2) and inflammation (NFkB) – to restore homeostatic levels of angiogenenic, oxidative stress and inflammatory factors that are implicated across several ocular diseases, including DR, diabetic macular edema (DME), and age-related macular degeneration (AMD). APX3330 has shown a favorable tolerability profile in 12 clinical trials conducted in healthy, hepatitis, cancer, and diabetic subjects.

About Opus Genetics

Opus Genetics is a clinical-stage ophthalmic biotechnology company developing gene therapies to treat patients with inherited retinal diseases (IRDs) and other ophthalmologic disorders. The pipeline includes adeno-associated virus (AAV)-based investigational gene therapies that address mutations in genes that cause different forms of bestrophinopathy, Leber congenital amaurosis (LCA) and retinitis pigmentosa. The company's most advanced gene therapy program is designed to address mutations in the LCA5 gene, which encodes the lebercilin protein and is currently being evaluated in a Phase 1/2 open-label, dose-escalation trial, with encouraging early data. BEST1 investigational gene therapy is designed to address mutations in the BEST1 gene, which is associated with retinal degeneration; a Phase 1/2 study is expected to be initiated in 2025. The pipeline also includes Phentolamine Ophthalmic Solution 0.75%, a non-selective alpha-1 and alpha-2 adrenergic antagonist being investigated to reduce pupil size, and APX3330, a novel small-molecule inhibitor of Ref-1 being investigated to slow the progression of non-proliferative diabetic retinopathy. Phentolamine Ophthalmic Solution 0.75% is currently being evaluated in Phase 3 trials for treatment of presbyopia and reduced dim (mesopic) light vision following keratorefractive surgery. The company has reached agreement with the FDA on an SPA for a Phase 3 trial to evaluate oral APX3330 for the treatment on NPDR. For more information, please visit www.opusgtx.com.

Forward Looking Statements

This press release contains 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 expectations regarding the potential of APX3330 to be a treatment option for patients with DR and future development of APX3330 with a partner.

These forward-looking statements relate to us, our business prospects and our results of operations and are subject to certain risks and uncertainties posed by many factors and events that could cause our actual business, prospects and results of operations to differ materially from those anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described under the heading "Risk Factors" included in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 and in our other filings with the U.S. Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "aim," "may," "ongoing," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. We undertake no obligation to revise any forward-looking statements in order to reflect events or

circumstances that might subsequently arise.

These forward-looking statements are based upon our 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:

- Our ability to successfully integrate the business of former Opus Genetics Inc. and manage our expanded combined product pipeline;
- Our ability to develop and obtain regulatory approval for newly acquired gene therapies to treat inherited retinal diseases;
- Our ability to obtain and maintain orphan drug designation or rare pediatric disease designation for our current and future product candidates;
- The success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts;
- Regulatory requirements or developments;
- Changes to or unanticipated events in connection with clinical trial designs and regulatory pathways;
- Delays or difficulties in the enrollment of patients in clinical trials;
- Substantial competition;
- Rapid technological change;
- Our development of sales and marketing infrastructure;
- Future revenue losses and profitability;
- Changes in capital resource requirements;
- Risks related to our inability to obtain sufficient additional capital to continue to advance our product candidates and our preclinical programs;
- Domestic and worldwide legislative, regulatory, political and economic developments;
- Our dependency on key personnel;
- Changes in market opportunities and acceptance;
- Reliance on third parties to conduct our clinical trials and supply and manufacture drug supplies;
- Future, potential product liability and securities litigation;
- System failures, unplanned events, or cyber incidents;
- The substantial number of shares subject to potential issuance associated with our equity line of credit arrangement;
- Risks that our licensing or partnership arrangements may not facilitate the commercialization or market acceptance of our product candidates;
- Future fluctuations in the market price of our common stock;
- The success and timing of commercialization of any of our product candidates;

- Obtaining and maintaining our intellectual property rights; and
- The success of mergers and acquisitions.

The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive. Readers are urged to carefully review and consider the various disclosures made by us in this report and in our other reports filed with the Securities and Exchange Commission that advise interested parties of the risks and factors that may affect our business. All forward-looking statements contained in this press release speak only as of the date on which they were made. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

This press release contains 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 expectations regarding our cash runway, data from and future enrollment for our clinical trials, our pipeline of additional indications, expectations of potential growth, and our expectations regarding integration following the acquisition of Opus Genetics, including with respect to the combination of their portfolio of clinical assets into our existing portfolio and our combined focus on gene therapy treatment.

These forward-looking statements relate to us, our business prospects and our results of operations and are subject to certain risks and uncertainties posed by many factors and events that could cause our actual business, prospects and results of operations to differ materially from those anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described under the heading “Risk Factors” included in Ocuphire’s Annual Report on Form 10-K. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. In some cases, you can identify forward-looking statements by the following words: “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “aim,” “may,” “ongoing,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. We undertake no obligation to revise any forward-looking statements in order to reflect events or circumstances that might subsequently arise.

These forward-looking statements are based upon our 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:

- The success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts;
- Regulatory requirements or developments;
- Changes to or unanticipated events in connection with clinical trial designs and regulatory pathways;
- Delays or difficulties in the enrollment of patients in clinical trials;
- Substantial competition and rapid technological change;

- Our development of sales and marketing infrastructure;
- Future revenue losses and profitability;
- Our relatively short operating history;
- Changes in capital resource requirements;
- Risks related to our inability to obtain sufficient additional capital to continue to advance our product candidates and our preclinical programs;
- Domestic and worldwide legislative, regulatory, political and economic developments;
- Employee misconduct;
- Reliance on third parties;
- Future, potential product liability and securities litigation;
- System failures, unplanned events, or cyber incidents;
- The substantial number of shares subject to potential issuance associated with our equity line of credit arrangement;
- Risks that our partnership or other licensing arrangements, may not facilitate the commercialization or market acceptance of our product candidates;
- Future fluctuations in the market price of our common stock;
- Our ability to realize the expected benefits of the acquisition of Opus Genetics;
- Our ability to execute clinical programs for gene therapies successfully and changes in expected commercial value we predict from the development of gene therapies;
- The success and timing of commercialization of any of our product candidates; and
- Obtaining and maintaining our intellectual property rights.

The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive. Readers are urged to carefully review and consider the various disclosures made by us in this report and in our other reports filed with the Securities and Exchange Commission that advise interested parties of the risks and factors that may affect our business. All forward-looking statements contained in this press release speak only as of the date on which they were made. We undertake 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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Source: Opus Genetics, Inc.