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Opus Genetics Announces Presentation of OPGX-LCA5 Gene Therapy Data at ARVO; 12 Month Phase 1/2 Results Support Potential to Restore to Meaningful Vision

Improvements in subjective and objective measures of efficacy observed at six months persisted for one year in patients with severe vision impairment from inherited retinal degeneration due to mutations in the LCA5 gene

Administration of OPGx-LCA5 by subretinal injection was well tolerated by study participants

RESEARCH TRIANGLE PARK, N.C., May 05, 2025 (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 other treatments for ophthalmic disorders ("Opus" or the "Company"), today announced one-year results from adult patients treated in the ongoing Phase 1/2 Study of its lead gene therapy candidate OPGx-LCA5. These results were presented yesterday at the 2025 annual meeting of the Association for Research in Vision and Ophthalmology (ARVO), taking place May 4 – 7, 2025 in Salt Lake City, Utah. The presentation, entitled "Recovery of Cone-Mediated Vision in a Severe Ciliopathy after Gene Augmentation: One Year Results of a Phase I/II Trial for LCA5-LCA," was delivered by Dr. Tomas Aleman of the Scheie Eye Institute, University of Pennsylvania.

"The preliminary data emerging from this Phase 1/2 study of OPGx-LCA5 are very encouraging. We are pleased to see evidence of durable efficacy, with the treatment benefits observed at six months being sustained out to one year," said Dr. Aleman. "Unquestionable gains in cone-mediated vision (daytime) confirmed one year after treatment have been associated with improvements in patients' reading vision and ability to recognize objects, which are meaningful to these patients with severely impaired visual function. These findings support continued development of this gene therapy, which offers potentially groundbreaking opportunities, as we look forward to enrolling additional patients into the study."

George Magrath, M.D., Chief Executive Officer of Opus Genetics, added, "Presentation of the 12-month data at ARVO underscores the growing interest in this program, and if approved, OPGx-LCA5 could potentially offer a life changing treatment for these patients. The new data, while in a limited number of adults patients, give us even more conviction that our initial success with OPGx-LCA5 has the potential to translate to the rest of our pipeline, which contains gene therapy treatments for six additional inherited retinal diseases, as we plan to enter Phase 1/2 with our BEST-1 program later this year. Additionally, we have been in discussions with the U.S. Food and Drug Administration (FDA) regarding the registration

trial design for OPGx-LCA5, with the goal of initiating the study in 2026.

Highlights of 12-month Phase 1/2 Study Results

- The goal of this clinical trial is to evaluate the safety and preliminary efficacy results of subretinal gene therapy with OPGx-LCA5 in patients with inherited retinal degeneration due to biallelic mutations in the LCA5 gene.
- The results presented comprised three adult patients (ages 19, 26 and 34 years old), all of whom received subretinal (SR) injections in a single eye of up to 300 µl of low dose ($1x10^{10}$ vector genome (vg) per eye) OPGx-LCA5. Each patient had severe disease at baseline, with limited but detectable photoreceptors and disease that had progressed to the central retina.
- A further two adolescent patients have now also been treated with promising preliminary data that were not included in this presentation.

Efficacy and functional endpoints

- **Multi-Luminance orientation and Mobility Test (MLoMT)**: This is a virtual reality-based test designed to measure changes in functional vision. Similar to 6 months, the results at 12 months showed that all treated subjects identified more objects compared to baseline. Two out of the three participants showed a clinically meaningful improvement in the MLoMT with a three-object recognition threshold (ORT) or more improvement and with the last participant going from being unable to complete the MLoMT course to being able to complete it (although without an increase in the ORT).
- **Visual Acuity (VA):** Continued VA improvements out to 12 months (averaging 0.35 logMAR, equivalent to a 3.5 line improvement across the three participants).
- **Full-field Stimulus Testing (FST):** FST is a measure of retinal sensitivity. Improvements were seen at multiple time points post treatment. Study eyes showed larger improvements in sensitivity from baseline, with a 0.86 log improvement being observed at 12 months vs 0.16 log units for the control eyes. For interocular difference, there was an average of 0.7 log units better sensitivity when compared to the control eyes.
- **Pupillary Light Reflex (PLR) :** PLR is a natural reflex that controls the diameter of the pupil, in response to the intensity (luminance) of light. Pupil responses increased at 12 months in the study eyes compared to both control eyes and baseline. The treated eyes demonstrated a shift in response toward dimmer intensities compared to baseline. These results are supportive of improved cone-mediated vision through 12 months.
- **Microperimetry:** Microperimetry is a visual field test that incorporates perimetry and retinal imaging. It allows for the direct mapping of a stimulus in specific parts of the retina, thereby correlating functional information (visual field testing) with structural/anatomical data (retinal imaging). Data were collected from one patient (not possible in the other two participants at the baseline visit due to poor fixation), who saw substantial improvements in macular sensitivity. At 12 months, fixation in this patient stabilized and shifted toward the foveal center, suggesting improved central vision with improved fixation.

Safety

- The results provided evidence that OPGx-LCA5 was well tolerated with no reports of dose-limiting toxicities or serious adverse events out to 12 months. Anticipated adverse events were mild and unrelated to treatment, mostly related to the use of systemic steroids or with the surgical procedure. No major changes in the retinal structure of treated eyes were observed. All early adverse events resolved within 30 days of the procedure.

Study Design
This clinical trial was designed to evaluate the safety and preliminary efficacy of subretinal gene therapy with OPGx-LCA5 in patients with inherited retinal degeneration due to biallelic mutations in the LCA5 gene. It is an open-label, Phase 1/2 trial evaluating OPGx-LCA5. The trial has been enrolling both adult and pediatric patients. Dosing of the first pediatric patients began in February 2025. Efficacy endpoints include measurement of functional vision using: 1) the Multi-Luminance orientation and Mobility Test (MLoMT); 2) Full-Field Stimulus Testing (FST), which measures the retina's sensitivity to light; and 3) microperimetry, which measures point-wise sensitivity to light. For more information, visit clinicaltrials.gov (NCT05616793). The six-month results on adult patients treated with OPGx-LCA5 were presented in a Key Opinion Leader (KOL) webinar, hosted by Opus on December 11, 2024. A copy of the presentation from the webinar can be accessed here.

About Opus Genetics
Opus Genetics is a clinical-stage ophthalmic biopharmaceutical company developing therapies to treat patients with inherited retinal diseases (IRDs) and other treatments for ophthalmic disorders. Our pipeline includes adeno-associated virus (AAV)-based investigational gene therapies that address gene mutations responsible for different forms of Leber congenital amaurosis (LCA), bestrophinopathy and retinitis pigmentosa. Our most advanced investigational 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. Our pipeline also includes BEST1 investigational gene therapy, designed to address mutations in the BEST1 gene, which is associated with retinal degeneration. 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 that is currently being evaluated in Phase 3 trials for presbyopia and mesopic (dim) light vision disturbances. For additional 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, expectations regarding data from and future enrollment for our clinical trials and our pipeline of additional indications.

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 Annual Report on Form 10-K for the fiscal year

ended December 31, 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:

- Data reported in this press release is preliminary and related to a relatively small group of patients, and, as a result, data that initially appears promising may be revised, updated, or invalidated at a later data readout and/or may ultimately not be capable of duplication in additional patients;

- Failure to successfully integrate our businesses following our acquisition of former Opus Genetics Inc. (the “Opus Acquisition”) could have a material adverse effect on our business, financial condition and results of operations;

- The Opus Acquisition significantly expanded our product pipeline and business operations and shifted our business strategies, which may not improve the value of our common stock;

- Our gene therapy product candidates are based on a novel technology that is difficult to develop and manufacture, which may result in delays and difficulties in obtaining regulatory approval;

- Our planned clinical trials may face substantial delays, result in failure, or provide inconclusive or adverse results that may not satisfy FDA requirements to further develop our therapeutic products;

- Delays or difficulties associated with patient enrollment in clinical trials may affect our ability to conduct and complete those clinical trials and obtain necessary regulatory approvals;

- Changes in regulatory requirements could result in increased costs or delays in development timelines;

- We depend heavily on the success of our product pipeline; if we fail to find strategic partners or fail to adequately develop or commercialize our pipeline products, our business will be materially harmed;

- Others may discover, develop, or commercialize products similar to those in our pipeline before or more successfully than we do or develop generic variants of our products even while our product patents remain active, thereby reducing our market

share and potential revenue from product sales;

- We do not currently have any sales or marketing infrastructure in place, and we have limited drug research and discovery capabilities;
- The future commercial success of our products could significantly depend upon several uncertain factors, including third-party reimbursement practices and the existence of competitors with similar products;
- Product liability lawsuits against us or our suppliers or manufacturers could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop;
- Failure to comply with health and safety laws and regulations could lead to material fines;
- We have not generated significant revenue from sales of any products and expect to incur losses for the foreseeable future;
- Our future viability is difficult to assess due to our short operating history and our future need for substantial additional capital, access to which could be limited by any adverse developments that affect the financial services market;
- Raising additional capital may cause our stockholders to be diluted, among other adverse effects;
- We operate in a highly regulated industry and face many challenges adapting to sudden changes in legislative reform or the regulatory environment, which affects our pipeline stability and could impair our ability to compete in international markets;
- We may not receive regulatory approval to market our developed product candidates within or outside of the U.S.;
- With respect to any of our product candidates that receive marketing approval, we may be subject to substantial penalties if we fail to comply with applicable regulatory requirements;
- Our potential relationships with healthcare providers and third-party payors will be subject to certain healthcare laws and regulations, which could expose us to extensive potential liabilities;
- We rely on third parties for material aspects of our business, such as conducting our nonclinical and clinical trials and supplying and manufacturing bulk drug substances, which exposes us to certain risks;
- We may be unsuccessful in entering into or maintaining licensing arrangements (such as the Viatris License Agreement) or establishing strategic alliances on favorable terms, which could harm our business;
- Our current focus on the cash-pay utilization for future sales of RYZUMVI may limit our ability to increase sales or achieve profitability with this product;

- Inadequate patent protection for our product candidates may result in our competitors developing similar or identical products or technology, which would adversely affect our ability to successfully commercialize;
- We may be unable to obtain full protection for our intellectual property rights under U.S. or foreign laws;
- We may become involved in lawsuits for a variety of reasons associated with our intellectual property rights, including alleged infringement suits initiated by third parties;
- We are dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy;
- As we grow, we may not be able to operate internationally or adequately develop and expand our sales, marketing, distribution, and other corporate functions, which could disrupt our operations;
- The market price of our common stock is expected to be volatile ; and
- Factors out of our control related to our securities, such as securities litigation or actions of activist stockholders, could adversely affect our business and stock price and cause us to incur significant expenses.

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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