RG6501 (OpRegen®) Phase 1/2a Results Show Evidence of Rapid Improvement of Outer Retinal Structure in Patients With Geographic Atrophy Secondary to Age-Related Macular Degeneration

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CARLSBAD, Calif.--(BUSINESS WIRE)--Oct. 5, 2023-- Lineage Cell Therapeutics, Inc. (NYSE American and TASE: LCTX), a clinical-stage biotechnology company developing allogeneic cell therapies for unmet medical needs, today announced that the results of imaging analyses demonstrating rapid improvement in outer retinal structure from patients enrolled in a Phase 1/2a clinical study of RG6501 (OpRegen) (ClinicalTrials.gov Identifier: NCT02286089), which were reviewed by multiple, independent reviewers, were presented at the 23rd EURETINA Congress. The presentation, *"Time to retinal structure improvements following OpRegen subretinal delivery in patients with geographic atrophy (GA),"* was presented by Adiel Barak, M.D., Professor of Ophthalmology, Vitreoretinal Unit Director, Tel Aviv Medical Center, on behalf of Roche and Genentech, a member of the Roche Group.

RG6501 (OpRegen) is a suspension of human allogeneic retinal pigmented epithelial (RPE) cells currently in development for the treatment of GA secondary to age-related macular degeneration (AMD). OpRegen subretinal delivery has the potential to counteract RPE cell loss in areas of GA lesions by supporting retinal cell health and improving retinal structure and function. It is being developed under an exclusive worldwide collaboration between Lineage, Roche, and Genentech, a member of the Roche Group, and is currently being evaluated in a Phase 2a clinical study in patients with GA secondary to AMD (ClinicalTrials.gov Identifier: NCT05626114).

"We are extremely pleased to see these additional observations of rapid improvements to outer retinal structure in the initial clinical study of OpRegen. These data suggest that OpRegen RPE cells may provide direct support to the patients' remaining retinal cells within atrophic areas, and that the improvements to retinal structure can be detected within the first three months following a single administration. We look forward to additional, future clinical data updates on the OpRegen program from our partners, Roche and Genentech," stated Brian Culley, CEO of Lineage.

23rd EURETINA Congress Highlights:

- All 5 patients enrolled in cohort 4 who had extensive coverage of the GA lesion with the surgical bleb containing OpRegen in suspension, demonstrated evidence of improvement in outer retinal structure as assessed by optical coherence tomography (OCT) within the first 3 months after treatment.

  - Retinal structural improvement in the patients described above were initially observed on day 1 (n=1), day 14 (n=1), month 1 (n=2), and month 3 (n=1).
  - Maintenance and/or greater improvements in retinal structure were observed over time.
  - Structural improvement (as defined below) was only observed within GA lesions with extensive coverage with the surgical bleb suggesting that OpRegen RPE cells provide support to the remaining retinal cells within atrophic areas.
  - These 5 patients had an average of 4.4 letter BCVA gain by 3 months and 12.8 letter BCVA gain by 1 year compared to baseline.
  - OCT images were reviewed by three independent graders from the day after surgery to the start of structural improvement and subsequent follow-up visits.
  - Structural improvement on OCT was qualitatively defined as meeting all pre-specified criteria including: 1) reduction in outer plexiform layer (OPL) and/or inner nuclear layer (INL) subsidence; 2) reappearance of external limiting membrane (ELM); and 3) increased hyperreflectivity and/or thickness of RPE and/or Bruch's membrane or reduction of hypertransmission on at least two non-adjacent B scans.
  - The patient who demonstrated retinal structure improvement as early as day 1 following OpRegen subretinal delivery exhibited persistence of structural improvement as measured by OCT, with resolution of areas of complete RPE and outer retinal atrophy (cRORA) features at 24 months following treatment. Durability of retinal structure improvements beyond the 12-month primary endpoint is still being evaluated in other patients.

- A Phase 2a study evaluating the success of OpRegen delivery to target areas of GA is currently enrolling patients (ClinicalTrials.gov: NCT05626114).

Dr. Barak's presentation is now available on the Events and Presentations section of Lineage's website.

About EURETINA

EURETINA started life as the European Retina, Macula and Vitreous Society in June 2000. Since then, the organization has grown to over 4,500 members and its annual Congress attracts thousands of delegates. Its goal is to enable access to the same cutting-edge retina science worldwide. Through membership, annual Congress, Winter Meeting and always-on digital resource, the organization and its members share robust scientific and educational resources relating to retina. For more information, please visit https://euretina.org or follow the association on Twitter @EURetina.

About the Phase 1/2a Study

The Phase 1/2a study is an open-label, single-arm, multi-center, dose-escalation trial evaluating a single administration of OpRegen delivered subretinally in patients with bilateral GA secondary to dry-form AMD. Twenty-four patients were enrolled into 4 cohorts. The first 3 cohorts enrolled only legally blind patients with a best corrected visual acuity (BCVA) of 20/200 or worse. The fourth cohort enrolled 12 patients with impaired vision (BCVA

from 20/65 to 20/250 with smaller mean areas of GA). Cohort 4 also included patients treated with a new “thaw-and-inject” formulation of OpRegen, which can be shipped directly to sites and used immediately upon thawing, removing the complications and logistics of having to use a dose preparation facility. The primary objective of the study was to evaluate the safety and tolerability of OpRegen as assessed by the incidence and frequency of treatment-emergent adverse events. Secondary objectives are to evaluate the preliminary activity of OpRegen treatment by assessing the changes in ophthalmological parameters measured by various methods of primary clinical relevance.

About Geographic Atrophy

Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD) characterized by severe loss of visual function. GA is a leading cause of adult blindness in the developed world, affecting at least 5 million people globally. There are two forms of advanced AMD: neovascular AMD and GA. GA and neovascular AMD can occur simultaneously in the same eye, and patients treated for neovascular AMD may still go on to develop GA. GA typically affects both eyes.

About Lineage Cell Therapeutics, Inc.

Lineage Cell Therapeutics is a clinical-stage biotechnology company developing novel cell therapies for unmet medical needs. Lineage’s programs are based on its robust proprietary cell-based therapy platform and associated in-house development and manufacturing capabilities. With this platform Lineage develops and manufactures specialized, terminally differentiated human cells from its pluripotent and progenitor cell starting materials. These differentiated cells are developed to either replace or support cells that are dysfunctional or absent due to degenerative disease or traumatic injury or administered as a means of helping the body mount an effective immune response to cancer. Lineage’s clinical and preclinical programs are in markets with billion dollar opportunities and include five allogeneic (“off-the-shelf”) product candidates: (i) OpRegen, a retinal pigment epithelial cell therapy in Phase 2a development for the treatment of geographic atrophy secondary to age-related macular degeneration, is being developed under a worldwide collaboration with Roche and Genentech, a member of the Roche Group; (ii) OPC1, an oligodendrocyte progenitor cell therapy in Phase 1/2a development for the treatment of acute spinal cord injuries; (iii) VAC2, a dendritic cell therapy produced from Lineage’s VAC technology platform for immuno-oncology and infectious disease, currently in Phase 1 clinical development for the treatment of non-small cell lung cancer; (iv) ANP1, an auditory neuronal progenitor cell therapy for the potential treatment of auditory neuropathy; and (v) PNC1, a photoreceptor neural cell therapy for the potential treatment of vision loss due to photoreceptor dysfunction or damage. For more information, please visit www.lineagecell.com or follow the company on Twitter @LineageCell.

Forward-Looking Statements

Lineage cautions you that all statements, other than statements of historical facts, contained in this press release, are forward-looking statements. Forward-looking statements, in some cases, can be identified by terms such as “believe,” “aim,” “may,” “will,” “estimate,” “continue,” “anticipate,” “design,” “intend,” “expect,” “could,” “can,” “plan,” “potential,” “predict,” “seek,” “should,” “would,” “contemplate,” “project,” “target,” “tend to,” or the negative version of these words and similar expressions. Such statements include, but are not limited to, statements relating to: the potential therapeutic benefits OpRegen in patients with GA secondary to AMD; the significance of clinical data reported to date from the Phase 1/2a study of OpRegen, including the findings of retinal tissue restoration and visual function improvements; and the potential utilization of OCT imaging to measure efficacy in a pivotal clinical trial of OpRegen. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause Lineage’s actual results, performance or achievements to be materially different from future results, performance or achievements expressed or implied by the forward-looking statements in this press release, including, but not limited to, the following risks: that positive findings in early clinical and/or nonclinical studies of a product candidate may not be predictive of success in subsequent clinical and/or nonclinical studies of that candidate; that competing alternative therapies may adversely impact the commercial potential of OpRegen; that Roche and Genentech may not successfully advance OpRegen or be successful in completing further clinical trials for OpRegen and/or obtaining regulatory approval for OpRegen in any particular jurisdiction; that Lineage may not be able to manufacture sufficient clinical quantities of its product candidates in accordance with current good manufacturing practice; and those risks and uncertainties inherent in Lineage’s business and other risks discussed in Lineage’s filings with the Securities and Exchange Commission (SEC). Lineage’s forward-looking statements are based upon its current expectations and involve assumptions that may never materialize or may prove to be incorrect. All forward-looking statements are expressly qualified in their entirety by these cautionary statements. Further information regarding these and other risks is included under the heading “Risk Factors” in Lineage’s periodic reports with the SEC, including Lineage’s most recent Annual Report on Form 10-K filed with the SEC and its other reports, which are available from the SEC’s website. You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date on which they were made. Lineage undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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