RG6501 (OpRegen®) Phase 1/2a Clinical Results Support the Potential for OpRegen to Slow, Stop or Reverse Disease Progression in Geographic Atrophy Secondary to Age-Related Macular Degeneration

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- **Preliminary Evidence of Durable Anatomical and Functional Improvements Following Administration of OpRegen Cells**
- **Extensive OpRegen Surgical Bleb Coverage of Areas of GA May Be Critical for Optimizing Patient Outcomes**
- **OCT Imaging With Segmentation Analysis is Advantageous in Assessment of Retinal Integrity Post-Treatment**

CARLSBAD, Calif.--(BUSINESS WIRE)--Apr. 26, 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 results from imaging analyses of structural changes and visual data from a Phase 1/2a clinical study of RG6501 (OpRegen), were presented at the 2023 Association for Research in Vision and Ophthalmology Annual Meeting (ARVO 2023). The presentation, *"Exploratory optical coherence tomography (OCT) analysis in patients with geographic atrophy (GA) treated by OpRegen: Results from the Phase 1/2a trial"* was presented by Eyal Banin, M.D., Ph.D., Director, Center for Retinal and Macular Degenerations, Department of Ophthalmology at Hadassah-Hebrew University Medical Center, on behalf of Roche and Genentech, a member of the Roche Group.

RG6501 (OpRegen) is an allogeneic retinal pigment epithelial (RPE) cell therapy currently in development for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). It is being developed under an exclusive worldwide collaboration between Lineage, Roche and Genentech, 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 our observations of improved retinal structure in the initial clinical study of OpRegen are being reinforced by additional external and independent analyses of the images performed by Genentech and Roche. Looking ahead, we are excited to collaborate with Genentech and Roche on the ongoing Phase 2a study of OpRegen, which is currently enrolling patients and open at multiple sites in the US, with more sites expected to come online this year," stated Brian Culley, CEO of Lineage.

Dr. Banin added, "I have been closely involved with the OpRegen program since its beginning and I continue to be excited about the potential therapeutic benefit for patients afflicted with dry AMD and geographic atrophy, a progressive and debilitating disease that significantly affects the quality of life of many. These data further highlight the potential for a single dose of OpRegen to provide significant clinical outcomes for patients in a disease with a tremendous unmet need."

2023 ARVO Presentation Highlights

- Preliminary evidence of outer retinal structure and visual function improvements with OpRegen was observed in patients with GA and impaired vision (Cohort 4 [n=12]):
  - Patients in Cohort 4 had an average 7.6 letter gain in visual acuity at 12 months in the study eye;
  - Three patients in Cohort 4 (25%) had a 15 letter or greater gain in visual acuity at 12 months in the study eye.
- Long term vision preservation with outer retinal structure improvement observed in the OpRegen treated eye persisted for up to 4 years of follow-up.
- The extent of OpRegen bleb coverage over the area of atrophy may be important to optimize patient outcomes:
  - In patients with extensive OpRegen bleb coverage, maintenance or improvement of outer retina structure was observed in treated eyes compared to worsening in fellow eyes:
    - Five patients in Cohort 4 who had a surgically delivered bleb containing OpRegen that extensively covered their atrophic areas and the foveal center, experienced an average 12.8 letter gain in their study eye.
  - Improvement in outer retinal layers also correlated with the extent of OpRegen bleb coverage:
    - Slower rates of RPE and external limiting membrane (ELM) loss were observed in OpRegen treated eyes compared to fellow untreated eyes;
    - Patients with extensive OpRegen bleb coverage of the atrophic area had maintenance or improvement of RPE and ELM layers compared to patients with limited OpRegen bleb coverage.
  - Resolution of complete RPE and outer retinal atrophy (cRORA) near borders of baseline GA were observed in cases with extensive coverage:
    - Signs of improvement in areas of cRORA included: greater hyperreflectivity at the level of RPE/ Bruch's membrane (BM); less choroidal hypertransmission; reduction of retinal subsidence, and greater continuity of outer retinal layers.
  - OCT imaging with segmentation analysis may be advantageous in assessment of retinal integrity following OpRegen treatment:
    - OCT enables quantitation of changes in RPE and outer retinal structure (such as ELM loss) not possible

with FAF imaging following OpRegen subretinal delivery.

- One patient in Cohort 4 maintained improvement in visual acuity at 4 years post-treatment in the study eye (+3 letters read), compared to losing 30 letters in the untreated eye.
- Overall, these data suggest that OpRegen RPE cells may provide support to the remaining retinal cells within atrophic areas by counteracting host RPE cell dysfunction and loss.
- Further assessment of the optimal disease stage for intervention and target delivery location of OpRegen in a larger clinical study is needed to confirm these preliminary findings.
- A Phase 2a study evaluating the success of OpRegen delivery to target areas of GA is currently enrolling patients (ClinicalTrials.gov: NCT05626114).

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

The Association for Research in Vision and Ophthalmology, Inc. (ARVO) was founded in 1928 in Washington, DC by a group of 73 ophthalmologists. ARVO is the largest and most respected eye and vision research organization in the world. ARVO members include nearly 11,000 researchers from over 75 countries. ARVO advances research worldwide into understanding the visual system and preventing, treating and curing its disorders. For more information, please visit https://www.arvo.org/ or follow the association on Twitter @ARVOInfo.

About OpRegen®

OpRegen is a retinal pigment epithelial cell therapy in development for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration. Following subretinal delivery, OpRegen has the potential to counteract RPE cell loss in areas of GA lesions by supporting retinal structure and function. OpRegen is being developed under a worldwide collaboration between Lineage, Roche and Genentech, a member of the Roche Group.

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. 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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