# OpRegen® (RG6501) Phase 1/2a Clinical Study 24-Month Visual Acuity Results Featured at 2024 Retinal Cell & Gene Therapy Innovation Summit

May 6, 2024

- **BCVA gains of +5.5 letters at 24 months in Cohort 4 patients (n=10)**
- **BCVA gains of +7.4 letters among Cohort 4 patients with extensive OpRegen bleb coverage of the GA lesion (n=5)**
- **Maintenance or increases in external limiting membrane (ELM) and retinal pigment epithelium (RPE) layers observed by optical coherence tomography (OCT) in patients with extensive bleb coverage of the GA lesion**
- **Data suggests OpRegen may counteract RPE cell dysfunction and cell loss in GA by providing support to remaining retinal cells, with effects observed through at least 2 years following a single administration**

CARLSBAD, Calif.--(BUSINESS WIRE)--May 6, 2024-- 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 24 month visual acuity results from patients enrolled in a Phase 1/2a clinical study (ClinicalTrials.gov Identifier: NCT02286089) of RG6501 (OpRegen) in patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD), were presented at the 2024 Retinal Cell & Gene Therapy Innovation Summit. The meeting was jointly organized by the Foundation Fighting Blindness and the Oregon Health & Science University Casey Eye Institute. The presentation, *"OpRegen® Retinal Pigment Epithelium (RPE) Cell Therapy for Patients with Geographic Atrophy (GA): Month 24 Results from the Phase 1/2a Trial,"* was presented by David Telander, MD, PhD, Retinal Consultants Medical Group, on behalf of Roche and Genentech, a member of the Roche Group.

RG6501 (OpRegen) is a suspension of human allogeneic retinal pigment epithelial (RPE) cells currently in development for the treatment of GA secondary to 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).

"The products approved recently for the treatment of GA secondary to AMD have not demonstrated a compelling functional benefit, so there remains a need for treatments that can positively affect patient vision," stated Brian M. Culley, Lineage CEO. "We are encouraged by the apparent durability of visual performance being achieved by patients in this study, notably in the 5 patients who received a thorough coverage of OpRegen cells across the majority of their atrophic areas and who had experienced a cessation or reversal of their areas of atrophy, evidenced by outer retinal structural improvements on optical coherence tomography (OCT). Dry AMD has traditionally been considered to be an irreversible and progressively degenerative disease leading to vision loss. However, these data suggest that OpRegen RPE cells may provide a one-time treatment which could slow or even reverse this damage by way of direct support to the patients' remaining retinal cells, including those near or within atrophic areas. We look forward to additional, future clinical data updates on the OpRegen program from our partners, Roche and Genentech."

**2024 Retinal Cell & Gene Therapy Innovation Summit Highlights**

- Improvement in visual acuity and outer retinal structure in patients with extensive OpRegen bleb coverage of their GA area was present at 12 months (primary endpoint) and persisted through 24 months

- BCVA gains in Cohort 4 patients (less advanced GA than in other cohorts) measured at 12 months were sustained at 24 months following a single subretinal administration of OpRegen

- Mean change in BCVA among treated eyes for patients (n=10) completing 2-year follow up was +5.5 letters (Early Treatment Diabetic Retinopathy Study [ETDRS] assessment)

- Effects were greater on average in the five (5) patients with extensive OpRegen coverage of atrophic areas at the time of surgical delivery

    - In these patients' treated eyes, the mean change in BCVA was +7.4 ETDRS letters for those completing 2-year follow-up (n=5)

- Maintenance or improvements in external limiting membrane (ELM) and RPE drusen complex (RPEDC) structure on OCT were observed in five patients in Cohort 4 with extensive OpRegen coverage of atrophic areas at the time of surgical delivery

    - Mean improvement of RPEDC area compared with baseline was maintained in treated eyes from 12 months (+2.6 $mm^2$; n=5) to 24 months (+2.6 $mm^2$; n=4)
        - In comparison, mean change in RPEDC area decreased in untreated fellow eyes from 12 months (-1.1 $mm^2$; n=5) to 24 months (-2.8 $mm^2$; n=4)
    - Mean change in ELM area increased in treated eyes from 12 months (+0.4 $mm^2$; n=5) to 24 months (+0.8 $mm^2$; n=4)
        - In comparison, mean change in ELM area decreased in untreated fellow eyes from 12 months (-1.3 $mm^2$; n=5) to 24 months (-1.9 $mm^2$; n=4)

- Overall, these data suggest that OpRegen RPE cells may counteract RPE cell dysfunction and loss in GA by providing support to the remaining retinal cells within atrophic areas and such effects are durable through at least 24 months after a single administration

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

**About the Innovation Summit**

The annual Retinal Cell and Gene Therapy Innovation Summit 2024 is jointly organized by the Foundation Fighting Blindness and the Oregon Health & Science University Casey Eye Institute. Representatives from the biotech and pharma industries will come together with members of the medical and research communities to discuss rapidly emerging ocular gene and cell therapies and strategize how to move the most advanced retinal diseases therapies toward clinical utility. The Summit features presentations by leading retinal disease experts on potential gene and cell-based therapies and how best to deliver them to patients. For more information visit: https://give.fightingblindness.org/event/retinal-cell-and-gene-therapy-innovation-summit-2024/e529485.

**About the OpRegen 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 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 include evaluating the preliminary activity of OpRegen treatment by assessing the changes in ophthalmological parameters measured by various methods of primary clinical relevance.

**About Geographic Atrophy**

GA is an advanced form of 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 or "off-the-shelf," cell therapies to address unmet medical needs. Lineage's programs are based on its proprietary cell-based technology platform and associated development and manufacturing capabilities. From this platform, Lineage designs, develops, manufactures, and tests specialized human cells with anatomical and physiological functions similar or identical to cells found naturally in the human body. These cells are created by applying directed differentiation protocols to established, well-characterized, and self-renewing pluripotent cell lines. These protocols generate cells with characteristics associated with specific and desired developmental lineages. Cells derived from such lineages are transplanted into patients in an effort to replace or support cells that are absent or dysfunctional due to degenerative disease, aging, or traumatic injury, and to restore or augment the patient's functional activity. Lineage's neuroscience focused pipeline currently includes: (i) OpRegen, a retinal pigment epithelial cell therapy in Phase 2a development under a worldwide collaboration with Roche and Genentech, a member of the Roche Group, for the treatment of geographic atrophy secondary to age-related macular degeneration; (ii) OPC1, an oligodendrocyte progenitor cell therapy in Phase 1/2a development for the treatment of spinal cord injuries; (iii) ANP1, an auditory neuronal progenitor cell therapy for the potential treatment of auditory neuropathy; (iv) PNC1, a photoreceptor neural cell therapy for the potential treatment of vision loss due to photoreceptor dysfunction or damage; and (v) RND1, a novel hypoimmune induced pluripotent stem cell line being developed in collaboration with Eterna Therapeutics Inc. For more information, please visit www.lineagecell.com or follow the company on X/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 of 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, durability and visual function improvements; and the timing and availability of clinical data updates on the OpRegen program. 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 studies of a product candidate may not be predictive of success in subsequent clinical studies of that candidate; 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 competing alternative therapies may adversely impact the commercial potential of OpRegen; that the ongoing Israel-Hamas war may materially and adversely impact our manufacturing processes, which are conducted by our subsidiary in Jerusalem, Israel; 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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**Lineage Cell Therapeutics, Inc. IR**
Ioana C. Hone
(ir@lineagecell.com)
(442) 287-8963

**LifeSci Advisors**
Daniel Ferry
(daniel@lifesciadvisors.com)
(617) 430-7576

**Russo Partners – Media Relations**
Nic Johnson or David Schull
(Nic.johnson@russopartnersllc.com)
(David.schull@russopartnersllc.com)
(212) 845-4242

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