Data From Ongoing Clinical Trial Continues to Demonstrate a Single Administration of OpRegen® Can Provide Anatomical and Functional Improvements in Patients With Dry AMD With Geographic Atrophy

September 15, 2021

- **First Reported Case of Retinal Tissue Restoration Showed Zero Growth of Atrophy at 33 Months**
- **Second Case of Retinal Tissue Restoration Exhibited a 10% Reduction in Atrophy Size at 8 Months**
- **Third Case of Retinal Restoration is 18 Letters Above Baseline at Last Available Time Point**
- **Average Difference in BCVA Between Treated and Untreated Eyes Was More Than Two ETDRS Lines (10.8 Letters Read) in Cohort 4 Patients at 9-12 Months Post-Treatment**

CARLSBAD, Calif.--(BUSINESS WIRE)--Sep. 15, 2021-- Lineage Cell Therapeutics, Inc. (NYSE American and TASE: LCTX), a clinical-stage biotechnology company developing allogeneic cell therapies for unmet medical needs, today reported updated interim results from its ongoing, 24-patient Phase 1/2a clinical study of its lead product candidate, OpRegen. OpRegen is an investigational cell therapy consisting of allogeneic retinal pigment epithelium (RPE) cells, administered in a single surgery to the subretinal space, for the treatment of dry age-related macular degeneration (AMD) with geographic atrophy (GA). These updated results include a minimum of 9 months of follow-up in all 12 patients treated in Cohort 4, which as a group had better baseline vision and smaller areas of GA at baseline than earlier cohorts. Overall, in the study (N=24), OpRegen has been well tolerated to date and there have been no new, unexpected ocular or systemic adverse events or serious adverse events not previously reported.

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“I am particularly encouraged by the OCT findings in the second retinal restoration patient. Based on historical growth patterns, we knew this patient was a slower progressor than many other patients enrolled, and therefore less likely to benefit from treatment. Despite this, we have been able to demonstrate a reduction in the atrophic area as quickly as 2 months post-treatment and a marked slowing of disease progression,” stated Jordi Monés, M.D., Ph.D., Director of the Institut de la Màcula and Barcelona Macula Foundation. “Further, even in patients with an incomplete coverage of OpRegen over the primary area of atrophy, we have observed resolution of not only lesions of iRORA (incomplete retinal pigment epithelial and outer retinal atrophy), but also resolution of areas with features of cRORA, which is a state of complete loss of the RPE and outer retinal tissue. Additionally, the structural benefits may help explain the improvement in visual acuity. I eagerly look forward to new data as they are collected.”

“While competing efforts are focused on reducing the growth rate of geographic atrophy, Lineage has reported several patients whose areas of atrophy have stabilized or reduced in size. These observations, which are present across clinically-meaningful periods, indicate a reversal of the degeneration of critical retinal tissue layers which support vision, consistent with the proposed mechanism of an RPE cell transplant. Importantly, all three of the patients exhibiting restoration had confirmed historic growth rate in these areas and these data have been collected using multiple imaging modalities. The durability of the improvements to visual acuity, when coupled with the clear structural improvements we’ve seen in patients which received fuller coverage of OpRegen across their GA, strongly suggest that cell therapy may be able to achieve therapeutic benefits that are beyond the reach of targeted drugs or antibodies," added Brian M. Culley, Lineage CEO. “We are extremely pleased that our data is moving in a positive direction with each interim update we provide. We will continue to collect follow up data and work towards a meeting with FDA to discuss key aspects of our program. Our objective with OpRegen is to demonstrate the potential for allogeneic cell therapy to deliver the best available clinical outcomes and apply our technology to additional areas such as cancer, spinal cord injury, and other attractive opportunities.”

OpRegen Phase 1/2a Interim Clinical Results

- Overall, 8/12 (67%) of the Cohort 4 patients’ treated eyes were at or above baseline visual acuity at their last assessment, based on per protocol scheduled visits ranging from 9 months to over 3 years post-transplant. Conversely, 9/12 (75%) of the patients’ untreated eyes were below baseline visual acuity at that assessment.
- Improvement in best corrected visual acuity (BCVA) reached up to +24 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart for a Cohort 4 patient.
- Comparing all treated eyes to all fellow (untreated) eyes showed an average difference of 10.8 letters read in Cohort 4 patients at their last assessment.
- In those Cohort 4 patients with a benefit in treated as compared with fellow eye (10/12), the average difference between treated and untreated eyes was 13.6 letters read at the last assessment, which exceeded 3 years post-transplant for some patients.
- Among the six Cohort 4 patients treated between September and November 2020, three (50%) continue to exhibit marked improvements in BCVA, ranging from +5 to +18 to +24 letters read at the patient’s last scheduled assessment, which was at least 9 months post-transplant.
- Among the other three Cohort 4 patients treated in the Fall of 2020, one patient showed a gain of +1 letter read and two patients measured -2 and -6 letters below baseline at their last assessment.
- Across the study, in patients with previously reported structural improvements in the retina, decreases in drusen density, and a trend toward slower GA progression in treated compared to untreated eyes have continued to be present.
- Evidence of durable engraftment of OpRegen RPE cells has extended to more than 5 years in the earliest treated patients,

supporting the potential for OpRegen to be a one-time treatment.

Retinal Tissue Restoration Update

- Three patients with evidence of retinal restoration and confirmed history of GA growth continue to demonstrate areas of retinal restoration as of their last per protocol assessments, ranging from 9 months to 33 months following treatment.
- The first Cohort 4 patient with evidence of retinal restoration and confirmed history of GA growth, demonstrated zero growth in atrophy (GA) 33 months following treatment with OpRegen.
- The second patient with evidence of restoration of critical retinal structures showed a 10% reduction at approximately 8 months after treatment, as assessed by square root transformation (SQRT).
    - Based on historical images of the patient's treated eye taken ~2 years prior to treatment, the area of GA had increased from approximately 2.39 mm to approximately 2.81 mm at baseline.
    - Following OpRegen transplantation, the atrophic lesion measured approximately 2.28 mm at the patient's month 2 per protocol assessment visit, which was ***smaller*** than the historical size of 2.39 mm from the image taken ~2 years prior to treatment.
    - Additional follow-up showed the lesion size calculated as approximately 2.53 mm at the patient's month 8 per protocol assessment visit, which continued to be ***smaller*** than baseline.
- The third case of restoration demonstrated clinically meaningful improvements in visual acuity, having gained +18 letters on the ETDRS chart since OpRegen transplantation, supporting the view that the changes in retinal structure observable on Optical Coherence Tomography (OCT) can result in functional benefit.

As previously described, outer retinal layer restoration was observed using clinical high-resolution OCT. To be considered as suggestive of retinal restoration, new areas of RPE monolayer with overlying ellipsoid zone, external limiting membrane, and outer nuclear layer, which were not present at the time of baseline assessment, had to be present post-treatment with OpRegen. These findings, observed in 3 Cohort 4 patients, suggest integration of the new RPE cells with functional photoreceptors in areas that previously showed no presence of these cells. These effects were most prominent in the transitional areas around the primary area of atrophy. The use of OCT allows for a more precise determination of changes in retinal thickness, organization, and overall health of the retina in areas of potential atrophy, benefits which are possible with cell transplant therapy.

The loss of RPE cells over time creates progressively larger areas of atrophy in the adult retina, leading to impaired vision or complete blindness, a condition known as atrophic AMD. Humans lack the innate ability to regenerate retinal tissue and replace lost retina cells, which led to a presumption that progression of GA may someday be slowed or halted but could not be reversed. The unique findings from the ongoing OpRegen clinical study support a different view, in which an RPE cell transplant can potentially replace or rescue retinal cells in patients who suffer from retinal lesions or degeneration. The totality of these findings supports the view that atrophic AMD is not an irreversible, degenerative condition and that some portion of diseased retinal tissue may be recoverable.

About OpRegen
OpRegen is currently being evaluated in a Phase 1/2a open-label, dose escalation safety and efficacy study of a single injection of human retinal pigment epithelium cells derived from an established pluripotent cell line and transplanted subretinally in patients with advanced dry AMD with GA. The study enrolled 24 patients into 4 cohorts. The first 3 cohorts enrolled only legally blind patients with BCVA of 20/200 or worse. The fourth cohort enrolled 12 better vision patients (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 is 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 efficacy of OpRegen treatment by assessing the changes in ophthalmological parameters measured by various methods of primary clinical relevance. OpRegen has been well tolerated to date and there have been no new, unexpected ocular or systemic adverse events or serious adverse events that have not been previously reported. OpRegen is a registered trademark of Cell Cure Neurosciences Ltd., a majority-owned subsidiary of Lineage Cell Therapeutics, Inc.

About Age-Related Macular Degeneration
Age-related macular degeneration (AMD) is an eye disease that can blur the sharp, central vision in patients and is the leading cause of vision loss in people over the age of 60. There are two forms of AMD: dry (atrophic) AMD and wet (neovascular) AMD. Dry (atrophic) AMD is the more common of the two forms, accounting for approximately 85-90% of all cases. In atrophic AMD, parts of the macula get thinner with age and accumulations of extracellular material between Bruch's membrane and the RPE, known as drusen, increase in number and volume, leading to a progressive loss of central vision, typically in both eyes. Global sales of the two leading wet AMD therapies were in excess of $10 billion in 2019. Nearly all cases of wet AMD eventually will develop the underlying atrophic AMD if the newly formed blood vessels are treated correctly. There are currently no U.S. Food and Drug Administration (FDA), or European Medicines Agency, approved treatment options available for patients with atrophic AMD.

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 programs are in markets with billion dollar opportunities and include three allogeneic ("off-the-shelf") product candidates: (i) OpRegen ®, a retinal pigment epithelium transplant therapy in Phase 1/2a development for the treatment of dry age-related macular degeneration, a leading cause of blindness in the developed world; (ii) OPC1, an oligodendrocyte progenitor cell therapy in Phase 1/2a development for the treatment of acute spinal cord injuries; and (iii) VAC2, an allogeneic 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. 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,” “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 benefits of treatment with OpRegen in dry AMD patients with GA, the significance of clinical data reported to date from the ongoing Phase 1/2a study of OpRegen, including the findings of retinal tissue restoration, Lineage plans to meet with the FDA to discuss OpRegen’s clinical development, the potential utilization of OCT imaging to measure efficacy in a pivotal clinical trial of OpRegen for the treatment of dry AMD with GA, and the potential for Lineage’s investigational allogeneic cell therapies to provide safe and effective treatment for multiple, diverse serious or life threatening conditions. 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 risks and uncertainties inherent in Lineage’s business and other risks 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 and Quarterly Report on Form 10-Q 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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