New Publication in Nature Medicine Supports Therapeutic Potential of Senolytics to Provide Long-lasting, Disease-modifying Intervention in Vision Loss

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SOUTH SAN FRANCISCO, Calif., Feb. 06, 2024 (GLOBE NEWSWIRE) -- UNITY Biotechnology, Inc. (“UNITY”) [NASDAQ: UBX], a biotechnology company developing therapeutics to slow, halt or reverse diseases of aging, today announced new research published in the peer-reviewed journal *Nature Medicine* that supports the clearance of senescent cells in the retina as a therapeutic approach that can lead to long-term improvements in vision in patients with diabetic macular edema (DME). Sustained hyperglycemia from diabetes induces cellular senescence which damages the retina, including the delicate vasculature in the eye. This can lead to fluid accumulation and retinal thickening – a key feature of DME. The study shows that the therapeutic clearance of senescent cells can potentially remove an underlying source of pathogenesis and thus allow healthy cells to regenerate and remodel retinal vasculature, ultimately leading to long-term disease modification.

Multiple studies have demonstrated that cells enter a state of senescence, in which they remain viable and metabolically active in the body, yet generate various inflammatory factors and metalloproteases. These senescent cells can modify the surrounding environment and contribute to different cellular dysfunction and tissue degeneration. A team of scientists at University of Montreal and UNITY Biotechnology revealed that cellular senescent pathways are triggered in the diabetic retina and are specifically activated in endothelial cells. They demonstrated that these senescent cells contribute to loss of barrier function, which can cause leaky blood vessels.

Researchers showed that senolysis through BCL-xL inhibition improved retinal barrier function in diabetic mice, modifying the retinal microenvironment and reestablishing tissue homeostasis. In addition, in clinical trials BCL-xL inhibition led to improvements in visual acuity and retinal structure stabilization in patients with advanced disease.

“This research provides compelling mechanistic evidence of the therapeutic approach of eliminating senescent cells to reduce diabetes-induced retinal vascular leakage and preserve retinal function,” Anirvan Ghosh, Ph.D., chief executive officer of UNITY and an author of the paper. “As senescent cell burden is observed in many other diseases, this study highlights the potential benefit of senolytic drugs for various age-related and metabolic diseases.”

The BCL-xL inhibitor UBX1325 has been evaluated in a Phase 2 study as well, as previously announced, which demonstrated that a single injection led to statistically significant and clinically meaningful improvements in visual acuity through 48 weeks in patients with DME, while reducing anti-VEGF treatment burden. UNITY is actively enrolling patients for a Phase 2b clinical trial where UBX1325 is being evaluated head-to-head versus aflibercept, with 16-week results expected in Q4 2024.

“Most therapeutic options available and in development for DME target the VEGF pathway. As a BCL-xL inhibitor, the senolytic UBX1325 targets an alternative mechanism and holds the potential to not only address the limitations of but also compliment anti-VEGF agents,” said Przemyslaw (Mike) Sapieha, Ph.D., chief scientist at UNITY and the lead author of the paper. “A new long-lasting and disease-modifying therapy for DME would be transformative for patients. This research further supports the potential for senolytic medicines to address the significant unmet need with current standard of care.”

About UBX1325
UBX1325 is an investigational compound being studied in retinal diseases, including DME and wet AMD, and is not approved for any use in any country. UBX1325 is a potent small molecule inhibitor of BCL-xL, a member of the BCL-2 family of apoptosis regulating proteins. UBX1325 is designed to inhibit the function of proteins that senescent cells rely on for survival. The Phase 2 BEHOLD study in patients with DME demonstrated that a single injection of UBX1325 resulted in a statistically significant and clinically meaningful improvement in mean Best Corrected Visual Acuity (BCVA) through 48 weeks compared to sham treatment. In preclinical studies, UNITY has demonstrated that targeting Bcl-xL with UBX1325 preferentially eliminated senescent cells from diseased tissue while sparing cells in healthy tissue. UNITY’s goal with UBX1325 is to transformationally improve real-world outcomes for patients with retinal disease.

About UNITY
UNITY is developing a new class of therapeutics to slow, halt, or reverse diseases of aging. UNITY’s current focus is on creating medicines to selectively eliminate or modulate senescent cells and thereby provide transformative benefit in age-related ophthalmologic and neurologic diseases. More information is available at www.unitybiotechnology.com or follow us on X (Formerly Twitter) and LinkedIn.

Forward-Looking Statements
This press release contains forward-looking statements including statements related to UNITY’s understanding of cellular senescence and the role it plays in diseases of aging, the potential for UNITY to develop therapeutics to slow, halt, or reverse diseases of aging, including for ophthalmologic and neurologic diseases, the potential for UNITY to successfully commence and complete clinical studies of UBX1325 for DME, AMD, and other ophthalmologic diseases, the expected timing of enrollment and results of the clinical trials in UBX1325, and UNITY’s expectations regarding the sufficiency of its cash runway. These statements involve substantial known and unknown risks, uncertainties, and other factors that may cause our actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements, including the risk that the COVID-19 worldwide pandemic may continue to negatively impact the development of preclinical and clinical drug candidates, including delaying or disrupting the enrollment of patients in clinical trials, risks relating to the uncertainties inherent in the

drug development process, and risks relating to UNITY's understanding of senescence biology. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this press release represent our views as of the date of this release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this release. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see UNITY's most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, filed with the Securities and Exchange Commission on November 13, 2023, as well as other documents that may be filed by UNITY from time to time with the Securities and Exchange Commission.

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