UNITY Biotechnology Announces Results from Phase 2 ENVISION Study of UBX1325 in Patients with Wet Age-Related Macular Degeneration

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UBX1325 monotherapy did not achieve non-inferiority through 24 weeks due, in part, to an unexpected 3.5 letter gain in the anti-VEGF control arm

UBX1325 maintained visual acuity in patients with ongoing active disease through 24 weeks with less than one letter mean decrease from baseline

52% of UBX1325-treated patients did not require anti-VEGF treatment through 24 weeks

Company to share 48-week BEHOLD DME data in April and intends to initiate Phase 2b study in DME in second half of 2023

UNITY to host investor call today, March 27, at 8:00 a.m. ET

SOUTH SAN FRANCISCO, Calif., March 27, 2023 (GLOBE NEWSWIRE) -- UNITY Biotechnology, Inc. ("UNITY") [Nasdaq: UBX], a biotechnology company developing therapeutics to slow, halt, or reverse diseases of aging, today announced results from Part A of the Phase 2 ENVISION study of UBX1325 in patients with wet age-related macular degeneration (AMD) who were not achieving optimum benefit with their ongoing anti-VEGF therapy. UBX1325 treatment generally maintained visual acuity for 6 months (change of -0.8 ETDRS letters from baseline), with a majority of patients not requiring any anti-VEGF rescue. Patients in the every 8-week aflibercept arm had an early and unexpected gain of 3.5 letters at week 2 which was mostly maintained for the duration of the study. As a result of the strength on the control arm, the study did not meet the non-inferiority threshold compared to aflibercept through 24 weeks.

"Maintenance of visual acuity in hard-to-treat patients with active disease after withdrawal of their anti-VEGF therapy suggests that UBX1325 had an active treatment effect in wet AMD. We continue to be impressed with the durability of effect of UBX1325 in this patient population," said Anirvan Ghosh, Ph.D., chief executive officer of UNITY. "Following a full analysis of ENVISION results, we will assess and optimize our resource allocation for future development of UBX1325. In the weeks ahead we will provide an update on Part B of the ENVISION study, and importantly, share 48-week data from the Phase 2 BEHOLD DME study. In DME, UBX1325 showed strong evidence of biologic activity and improvement in visual acuity – and, as a result, we plan to initiate a Phase 2b study in the second half of this year."

The ENVISION study enrolled 51 patients with an average baseline visual acuity of 60.2 ETDRS letters who had ongoing active disease with a baseline CST of approximately 370 µm and had been on anti-VEGF treatment for at least 6 months. On average, patients received approximately 4 anti-VEGF injections in the 6 months prior to enrollment. At enrollment, all patients received a single run-in injection of aflibercept. Within 4-8 weeks following the run-in injection, patients were randomized to receive either (a) an injection of UBX1325 at week 0 and at week 4, or (b) an injection of aflibercept at week 0 and every 8 weeks thereafter, and followed for 24 weeks.

Phase 2 ENVISION data through 24 weeks:

- UBX1325 demonstrated a favorable safety and tolerability profile with no cases of intraocular inflammation, retinal artery occlusion, endophthalmitis, or vasculitis
- Patients treated with UBX1325 had a mean change from baseline in BCVA of -0.8 ETDRS letters at 24 weeks compared to +3.1 ETDRS letters in the aflibercept control arm
- Patients treated with UBX1325 had a mean change from baseline in CST of +87.3 µm at 24 weeks compared to +30.5 µm in the aflibercept control arm
- 52% of UBX1325-treated patients went at least 24 weeks without receiving anti-VEGF treatment; 92% of UBX1325-treated patients achieved a maximal anti-VEGF treatment-free interval of 12 weeks or longer

The ENVISION study did not meet the non-inferiority margin of -4.5 letters compared to aflibercept with an 85% confidence interval.

"Despite anti-VEGF therapies remaining the standard of care for neovascular AMD for the past two decades, there is an unmet need for treatments with new mechanisms of action to optimize vision outcomes and reduce the treatment burden associated with frequent injections," said Arshad M. Khanani, MD, MA, FASRS, Director of Clinical Research, Sierra Eye Associates. "The ENVISION study results show that treatment with UBX1325 in nAMD patients with active disease maintained visual acuity with reduced injection burden over six months. The data from the ENVISION AMD and BEHOLD DME studies suggest that UBX1325, with its novel mechanism of action, could lead to a potential treatment option for patients."

Jamie Dananberg, M.D., chief medical officer of UNITY, added: "Whereas today's results from the ENVISION study and our Phase 2 BEHOLD study both show encouraging signs of biological activity of UBX1325, the relatively stronger efficacy we observed in DME may be related to the distinct underlying pathophysiologies of the two diseases. We look forward to sharing 48-week data in our BEHOLD DME study in the coming weeks."

Conference Call at 8:00 a.m. ET Today
UNITY will host a video conference call and webcast for investors and analysts today at 8:00 a.m. ET to discuss the most recent UBX1325 clinical data. Members of the UNITY senior management team will lead the discussion on the 24-week ENVISION study results. The live webcast can be accessed in the "Investors and Media" section of our website, www.unitybiotechnology.com, under "Events & Presentations" or by clicking here. A replay will be available two hours after the completion of the call and can be accessed in the "Investors & Media" section of our website, under "Events and Presentations."

About the ENVISION Study
The proof-of-concept Phase 2 ENVISION study is a multi-center, randomized, double-masked, active-controlled study designed to evaluate the safety, tolerability, efficacy and durability of a repeat intravitreal injection of UBX1325 in patients with neovascular AMD evaluated though 24 weeks. The study enrolled 51 patients being actively treated with anti-VEGF who had a visual acuity deficit (73 ETDRS letters, approximately 20/40, or worse) and residual retinal fluid (CST ≥300 microns). Patients were randomized into two groups to receive either two 10 mcg doses of UBX1325 at a week 0 and at week 4 or aflibercept 2 mg every 8 weeks. Patients have the option of continuing in the long-term extension (Part B) portion of the study through 48-weeks. To date, a majority of patients have opted to remain in the study. More information about the study is available here (NCT05275205).

About the BEHOLD Study
The proof-of-concept Phase 2 BEHOLD study is a multi-center, randomized, double-masked, sham-controlled study designed to evaluate the safety, tolerability, efficacy and durability of a single 10 mcg dose of UBX1325 in patients with DME evaluated though 24 weeks. The study enrolled 65 patients being actively treated with anti-VEGF who had a visual acuity deficit (73 ETDRS letters, approximately 20/40, or worse) and residual retinal fluid (CST ≥300 microns). Patients have the option of continuing in the long-term extension portion of the study through 48-weeks. To date, a majority of patients have opted to remain in the study. More information about the study is available here (NCT04857996).

About UBX1325
UBX1325 is an investigational compound being studied for age-related diseases of the eye, including diabetic macular edema (DME), age-related macular degeneration (AMD), and diabetic retinopathy (DR) that 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. In the 24-week data of the Phase 2 BEHOLD study in patients with DME, a single injection of UBX1325 led to a statistically significant and clinically meaningful improvement in mean Best Corrected Visual Acuity (BCVA) at 24 weeks compared to sham treatment. In a Phase 1 clinical study in advanced wet AMD and DME, UBX1325 showed a favorable safety profile and improvements in visual acuity sustained through 24 weeks following a single intravitreal injection. 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 DME, AMD, and DR.

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 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, UNITY's expectations regarding potential benefits, activity, effectiveness, and safety of UBX1325, the potential for UNITY to successfully commence and complete clinical studies of UBX1325 for DME, AMD, and other ophthalmologic diseases, the expected timing of the 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 UNITY in general, see UNITY's most recent Annual Report on Form 10-K for the year ended December 31, 2022, filed with the Securities and Exchange Commission on March 15, 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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