UNITY Biotechnology Reports Promising Topline Data from Phase 1 First-in-human Study of UBX0101 in Patients with Osteoarthritis of the Knee

June 18, 2019

Clinical results support senescent cell elimination with UBX0101 as a potential treatment for osteoarthritis

Topline results demonstrate a dose-dependent and clinically meaningful impact on pain

Call with management scheduled for today at 8:00 a.m. EDT

SAN FRANCISCO, June 18, 2019 (GLOBE NEWSWIRE) -- UNITY Biotechnology, Inc. (UNITY) [NASDAQ: UBX], a biotechnology company developing therapeutics to extend healthspan by slowing, halting or reversing diseases of aging, today announced promising results from its first-in-human Phase 1 study of UBX0101 in patients with moderate to severe osteoarthritis (OA) of the knee. The study demonstrated that UBX0101 was safe and well-tolerated. Improvement in several clinical measures, including pain, function, as well as modulation of certain senescence-associated secretory phenotype (SASP) factors and disease-related biomarkers was observed after a single dose of UBX0101.

"This Phase 1 study of UBX0101 is an important first step in exploring the potential of a senolytic approach in the treatment of a range of age-related diseases," said Keith Leonard, chairman and chief executive officer of UNITY. “We believe our novel approach to eliminating senescent cells has the potential to meaningfully impact healthspan.”

“New treatments for OA are desperately needed, especially an intervention that targets the biology of the condition that includes cell senescence,” said Richard F. Loeser, Jr., M.D., Director, UNC Thurston Arthritis Research Center Herman and Louise Smith Distinguished Professor of Medicine, Division of Rheumatology, Allergy & Immunology. “These exciting data are supportive of this very promising new approach for this chronic painful condition.”

Phase 1 Trial Design and Results

Trial Design

The Phase 1 clinical trial of UBX0101 is a randomized, double-blind, placebo-controlled study evaluating the safety, tolerability and pharmacokinetics of a single intra-articular injection of UBX0101 in patients diagnosed with moderate to severe painful OA of the knee. UBX0101 is a p53/MDM2 interaction inhibitor that targets selective elimination of senescent cells.

In Part A, 48 patients were randomly assigned to receive one of six dose levels of UBX0101 (between 0.1 mg to 4 mg) or placebo in a 3:1 randomization. Primary endpoints were safety and tolerability. Secondary and exploratory endpoints included plasma pharmacokinetics, synovitis as measured by MRI, pain, and measurement of SASP factors and disease-related biomarkers present in synovial fluid and plasma.

In Part B, 30 patients were randomized to receive UBX0101 (4 mg dose) or placebo in a 2:1 randomization. Primary endpoints were safety and tolerability. Secondary and exploratory endpoints included changes in the levels of SASP factors and disease-related biomarkers present in synovial fluid and plasma, and pain. Synovial fluid samples were obtained at baseline and four weeks post-treatment.

Safety, Tolerability and PK
In Part A, UBX0101 was well tolerated up to the maximum administered dose of 4 mg. There were no serious adverse events and no patients discontinued because of an adverse event. There were no dose-dependent adverse events or relevant clinical laboratory findings. The majority (66%) of adverse events were mild.

In Part B, UBX0101 was well tolerated at the 4 mg dose. There were no serious adverse events and no patients discontinued because of an adverse event. The majority (75%) of adverse events were mild and there were no relevant clinical laboratory findings.

UBX0101 demonstrated dose-proportional plasma pharmacokinetics. Model-based predicitons of concentrations within the knee suggested that doses at or above 1 mg may be pharmacologically active. This informed the prospectively defined low dose (0.1, 0.2, and 0.4 mg) and high dose (1, 2, and 4 mg) groupings for analyses.

Pain Measures

Numerical Rating Scale (NRS):

In Part A, evaluation of pain by NRS (0-10 point scale) measured at 12 weeks demonstrated a dose-dependent and clinically meaningful reduction. The range of mean baseline values was between 5.90 to 6.76.

	NRS	
	CFBL	**Pbo-Adj**

Placebo (n=14)	-1.96	NA
Low doses (n=16)	-2.66	-0.65 (p = 0.42)
High doses (n=18)	-3.95	-1.98 (p < 0.01)

CFBL=change from baseline; Pbo-Adj=placebo adjusted; low doses=0.1, 0.2, and 0.4 mg; high doses=1, 2, and 4 mg

WOMAC-A:

In Part A, evaluation of pain by WOMAC-A mean item score (0-4 point scale) measured at 12 weeks demonstrated a dose-dependent and clinically meaningful reduction. The range of mean baseline values was between 1.80 to 2.36.

	WOMAC-A	
	CFBL	**Pbo-Adj**
Placebo (n=14)	-0.74	NA
Low doses (n=16)	-0.49	+0.23 (p = 0.43)
High doses (n=18)	-1.09	-0.41 (p = 0.07)

CFBL=change from baseline; Pbo-Adj=placebo adjusted; low doses=0.1, 0.2, and 0.4 mg; high doses=1, 2, and 4 mg

In Part B, WOMAC-A, measured at 4 weeks, showed a numerical reduction that was not significantly different from placebo.

Function

WOMAC-C:

In Part A, evaluation of function by WOMAC-C mean item score (0-4 point scale) demonstrated a dose-dependent and clinically meaningful improvement. The range of mean baseline values was between 1.40 to 2.47.

	WOMAC-C	
	CFBL	**Pbo-Adj**
Placebo (n=14)	-0.72	NA
Low doses (n=16)	-0.49	+0.22 (p = 0.43)
High doses (n=18)	-1.05	-0.35 (p = 0.13)

CFBL=change from baseline; Pbo-Adj=placebo adjusted; low doses=0.1, 0.2, and 0.4 mg; high doses=1, 2, and 4 mg

Other Measures
There were no observed changes in stiffness as measured by WOMAC-B. Evaluation of Patient Global Impression of Change with treatment demonstrated a higher proportion of patients being “much improved” or “very much improved” versus placebo (placebo = 42.9%, low doses = 50.0%, high doses = 61.1%).

Exploratory Measures

Synovial Inflammation by MRI:

Evaluation of synovial inflammation by MRI detected no significant placebo adjusted change at any dose level.

SASP Factors and Biomarkers:
In Part A, an insufficient number of matched samples were collected due to a lack of adequate levels of synovial fluid in patients for sampling. Therefore, an analysis of change in biomarkers from baseline to 12 weeks was not performed. In Part B, 19 biomarkers were analyzed across 20 matched pair samples. In approximately half the biomarkers measured in synovial fluid (treatment versus placebo) modulation was observed consistent with elimination of senescent cells and potential improvement in the tissue environment. Changes were observed in MMPs, tissue remodeling factors, and inflammatory cytokines. These biomarkers were: MMP-3, MMP-10, MMP-12, MMP-13, IL-6, IL-10, CCL20 (MIP-3alpha), A2M, ICAM-1 and VEGF-C.

"Osteoarthritis of the knee impacts a significant portion of the population as we age," said Jamie Dananberg, chief medical officer of UNITY. “The observed changes in this early setting were greater than what are generally considered to be clinically meaningful. We look forward to continuing to explore the utility of UBX0101 in this important disease setting.”

UNITY plans to present additional data at an upcoming scientific meeting.

Additional information about the study design can be found on www.clinicaltrials.gov (NCT03513016).

Conference Call Information

UNITY will host a conference call and webcast for investors on Tuesday, June 18, 2019 at 8:00 a.m. EDT to discuss the UBX0101 clinical data. 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. You may also listen to the call by dialing 1-877-235-8637 within the U.S. or 1-704-815-6400 outside the U.S. and providing conference ID 2690589. 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, www.unitybiotechnology.com, under “Events and Presentations.”

About Cellular Senescence and Senolytic Medicines
Cellular senescence is a natural biological state in which a cell permanently halts division. Senescent cells accumulate with age and secrete as many as 100 different biologically active proteins, including pro-inflammatory factors, proteases, pro-fibrotic factors and growth factors that disturb the tissue microenvironment. This collection of secreted proteins is referred to as the SASP. In addition to its effects on tissue function, the SASP contains factors

that induce senescence in neighboring cells, setting off a cascade of events that culminates in the formation of the functionally aged and/or diseased tissue that appears to underlie a variety of age-related diseases. UNITY believes that the elimination of senescent cells will modulate SASP factors —addressing a root cause of diseases of aging. Senolytic medicines, or treatments designed to selectively remove senescent cells, target the SASP at its source, and may have a more durable impact on certain diseases of aging than current therapies.

About UNITY
UNITY is developing therapeutics to extend healthspan by slowing, halting or reversing diseases of aging. UNITY's initial focus is on creating senolytic medicines to selectively eliminate senescent cells and thereby treat age-related diseases, such as osteoarthritis, eye diseases and pulmonary diseases. More information is available at www.unitybiotechnology.com or follow us on Twitter.

Forward-Looking Statements
This press release contains forward-looking statements, including: statements related to our understanding of cellular senescence and the role cellular senescence plays in diseases of aging; our expectations regarding the potential benefits, activity, effectiveness and safety of UBX101, and our expectations with regard to the results of our clinical studies. 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. 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 recently filed Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed with the Securities and Exchange Commission on May 8, 2019, as well as other documents that may be filed by UNITY from time to time with the Securities and Exchange Commission. This press release concerns a drug candidate that is under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it are being investigated.

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