May 28, 2024

Unicycive Therapeutics Delivers Multiple Presentations on Oxylanthanum Carbonate (OLC) and UNI-494 at the European Renal Association Congress

– Results from Preclinical Model of Hyperphosphatemia Demonstrate the Relative Potency of OLC Compared to Tenapanor –

– Oral UNI-494 Shows Promise in a Preclinical Model as a Potential Candidate for Prevention of Delayed Graft Function Related to Acute Kidney Injury –

LOS ALTOS, Calif., May 28, 2024 (GLOBE NEWSWIRE) -- Unicycive Therapeutics, Inc. (Nasdaq: UNCY), a clinical-stage biotechnology company developing therapies for patients with kidney disease (the "Company" or "Unicycive"), today announced that several presentations were delivered on the Company's two product candidates, oxylanthanum carbonate (OLC) and UNI-494, at the 61st European Renal Association (ERA) Congress. OLC is a next-generation lanthanum-based phosphate binding agent utilizing proprietary nanoparticle technology being developed for the treatment of hyperphosphatemia in patients with chronic kidney disease (CKD). UNI-494 is a novel nicotinamide ester derivative and a selective ATP-sensitive mitochondrial potassium channel activator initially targeting acute kidney injury (AKI).

"We were pleased to have such a meaningful presence at the ERA Congress with multiple oral and poster presentations on both OLC and UNI-494 demonstrating promising data in two forms of kidney disease," said Shalabh Gupta, MD, Chief Executive Officer of Unicycive. "For OLC, we presented data showcasing the potent phosphate lowering capacity of OLC, which was three-fold greater than that of tenapanor in an established preclinical model of CKD. A second phase of this study, which we hope to present at a future scientific forum, will explore the potential complementary mechanisms of action of these two new phosphate lowering agents when administered in combination."

"We also presented valuable preclinical data of oral UNI-494 in a model of AKI that showed that a single oral dose of UNI-494 significantly reduced important markers related to kidney disease and that kidney functional data were well supported at both low and high doses. This data compliments our previously reported data in the intravenous (IV) form of UNI-494. The study concluded that UNI-494 is a potential candidate for prevention of delayed graft function (DGF) and other clinical conditions resulting from AKI. For both OLC and UNI-494, we also outlined our current clinical trials in progress and look forward to presenting those results this year," added Dr. Gupta.

Oxylanthanum Carbonate (OLC) Presentation Details:

Title: Enhanced Urinary Phosphorous Reduction: Comparative Study of Oxylanthanum Carbonate and Tenapanor in Rats
Lead Author: Satya Medicherla, Ph.D., Vice President, Preclinical Pharmacology, Unicycive
Results: This oral presentation evaluated the effects of tenapanor and OLC on phosphate excretion in rats. Tenapanor is a sodium hydrogen exchanger inhibitor used to reduce serum phosphate in adults with CKD on dialysis as an add-on therapy with phosphate binders. In this study, modeled after an earlier study with tenapanor and sevelamer, OLC demonstrated a significant reduction in urinary phosphate excretion compared to vehicle treated animals which was 3X greater than the reduction in urinary phosphate excretion observed with tenapanor which was not statistically different from vehicle. OLC and tenapanor utilize two different mechanisms of action to manage phosphate levels. Subsequent analyses will focus on examining the combination of tenapanor and OLC as the combination may lead to synergistic effects on lowering phosphate levels while providing patients with the benefit of reduced pill burden with OLC.

Title: Oxylanthanum Carbonate for Hyperphosphatemia in End Stage Kidney Disease (ESKD): Tolerability Trial in Progress
Lead Author: Pablo E. Pergola, M.D., Ph.D., Renal Associates, P.A.
Results: This poster describes a pivotal trial in progress to evaluate the tolerability of clinically effective (serum phosphate ≤5.5 mg/dL) doses of OLC in patients on hemodialysis. OLC is a new lanthanum-based nanotechnology product in development with a high in vitro binding capacity as compared to other phosphate binders. OLC is formulated as a small pill that is swallowed whole instead of being chewed. This open-label, single-arm, multicenter, multidose study will enroll up to 90 patients on hemodialysis who require phosphate binder therapy and have mean historical serum phosphate levels between ≥4.0 and ≤7.0 mg/dL for ≥8 weeks. Participants will undergo up to 3 weeks of phosphate binder washout until their serum phosphate levels reach >5.5 and ≤10.0 mg/dL. During the 6-week Titration Period, all patients will receive 1500 mg/day OLC (500 mg TID with meals/snacks) for the initial two weeks, with subsequent titration every two weeks until achieving a target serum phosphate level (≤5.5 mg/dL) or to a maximum OLC dose of 3000 mg/day. After titration, patients will enter a 4-week Maintenance Period at the effective OLC dose. The primary endpoint of the study is tolerability as assessed by the incidence of discontinuations due to treatment-related AEs; the pharmacokinetics of OLC will also be evaluated.

UNI-494 Presentation Details:

Title: Oral Administration of UNI-494 Ameliorates Acute Kidney Injury in a Rat Model of Delayed Graft Function
Lead Author: Satya Medicherla, Ph.D., Vice President, Preclinical Pharmacology, Unicycive
Results: This oral presentation evaluated the *in vivo* efficacy of oral (PO) UNI-494 to prevent damage in the unilateral renal ischemia-reperfusion (I/R) rat model of AKI, which is a well-established model of DGF. In the study, a single oral dose of UNI-494 at 50 mg/kg/PO or 100 mg/kg/PO significantly reduced important kidney functional markers including tubular injury, and proximal tubular injury scores. Additionally, kidney functional biomarker serum creatinine and tubular injury biomarker urinary neutrophil gelatinase-associated lipocalin (NGAL). Additionally, these two biomarkers were very well supported by kidney histology data on proximal tubular injury scores at both low and high doses reflecting a non-dose related trend with biomarkers and dose-dependency for proximal tubule injury scores. The study concluded that UNI-494 is a potential candidate for prevention of DGF and other

clinical conditions dealt with AKI.

Title: UNI-494 Phase I Tolerability and Pharmacokinetics: Trial in Progress
Lead Author: Guru Reddy, Ph.D., Vice President of Preclinical R&D, Unicycive
Results: This oral presentation described the ongoing Phase 1 dose-escalating single-center, double-blind, placebo-controlled, randomized clinical trial in healthy volunteers. The trial consists of two parts: Part 1 is a single ascending dose (SAD) study to determine the maximum tolerated dose (n=40); Part 2 is a multiple ascending dose (MAD) study to understand the effect of multiple doses administered of UNI-494 (n=20). The trial is designed to evaluate the safety, tolerability, and pharmacokinetics of UNI-494 in healthy subjects. The SAD study was successfully completed, and a dose of 80 mg twice a day (BID) was carried over to the MAD study, which is currently ongoing. Results of this study are expected in the second half of 2024.

About Oxylanthanum Carbonate (OLC)

Oxylanthanum carbonate is a next-generation lanthanum-based phosphate binding agent utilizing proprietary nanoparticle technology being developed for the treatment of hyperphosphatemia in patients with chronic kidney disease (CKD). OLC has over forty issued and granted patents globally. Its potential best-in-class profile may have meaningful patient adherence benefits over currently available treatment options as it requires a lower pill burden for patients in terms of number and size of pills per dose that are swallowed instead of chewed. Based on a survey conducted in 2022, Nephrologists stated that the greatest unmet need in the treatment of hyperphosphatemia with phosphate binders is a lower pill burden and better patient compliance.[1] The global market opportunity for treating hyperphosphatemia is projected to be in excess of $2.5 billion in 2023, with the United States accounting for more than $1 billion of that total. Despite the availability of several FDA-cleared medications, 75 percent of U.S. dialysis patients fail to achieve the target phosphorus levels recommended by published medical guidelines.

Unicycive is seeking FDA approval of OLC via the 505(b)(2) regulatory pathway. As part of the clinical development program, two clinical studies were conducted in over 100 healthy volunteers. The first study was a dose-ranging Phase I study to determine safety and tolerability. The second study was a randomized, open-label, two-way crossover bioequivalence study to establish pharmacodynamic bioequivalence between OLC and Fosrenol. Based on the topline results of the bioequivalence study, pharmacodynamic (PD) bioequivalence of OLC to Fosrenol was established.

Fosrenol® is a registered trademark of Shire International Licensing BV.
[1]Reason Research, LLC 2022 survey. Results here.

About Hyperphosphatemia

Hyperphosphatemia is a serious medical condition that occurs in nearly all patients with End Stage Renal Disease (ESRD). If left untreated, hyperphosphatemia leads to secondary hyperparathyroidism (SHPT), which then results in renal osteodystrophy (a condition similar to osteoporosis and associated with significant bone disease, fractures and bone pain); cardiovascular disease with associated hardening of arteries and atherosclerosis (due to deposition of excess calcium-phosphorus complexes in soft tissue). Importantly,

hyperphosphatemia is independently associated with increased mortality for patients with chronic kidney disease on dialysis. Based on available clinical data to date, over 80% of patients show signs of cardiovascular calcification by the time they become dependent on dialysis.

Dialysis patients are already at an increased risk for cardiovascular disease (because of underlying diseases such as diabetes and hypertension), and hyperphosphatemia further exacerbates this. Treatment of hyperphosphatemia is aimed at lowering serum phosphate levels via two means: (1) restricting dietary phosphorus intake; and (2) using, on a daily basis, and with each meal, oral phosphate binding drugs that facilitate fecal elimination of dietary phosphate rather than its absorption from the gastrointestinal tract into the bloodstream.

About UNI-494

UNI-494 is a novel nicotinamide ester derivative and a selective ATP-sensitive mitochondrial potassium channel activator. Mitochondrial dysfunction plays a critical role in the progression of acute kidney injury and chronic kidney disease. UNI-494 has a novel mechanism of action that restores mitochondrial function and may be beneficial for the treatment of several diseases including kidney disease. Unicycive is currently conducting a Phase 1 dose-ranging safety study in healthy volunteers in the United Kingdom that is expected to complete in 2H of 2024. UNI-494 is protected by issued patent(s) in the U.S. and Europe and a wide range of patent applications worldwide. UNI-494 has been granted orphan drug designation (ODD) by the U.S. Food and Drug Administration (FDA) for the prevention of Delayed Graft Function (DGF) in kidney transplant patients.

About Delayed Graft Function

Delayed Graft Function (DGF) refers to the acute kidney injury (AKI) that occurs in the first week after kidney transplantation, which necessitates dialysis intervention. As the name indicates, DGF can result in sub-optimal or impaired graft function and is one of the most common and serious complications of kidney transplantation. Poor kidney function in the first week of graft life is detrimental to the longevity of the allograft. DGF is also associated with higher rates of tissue rejection and decreased patient survival. Currently, there are no FDA approved drugs for the treatment of DGF.

Ischemia/reperfusion injury (IRI) is known to be a major causative factor for the AKI that results in DGF during kidney transplantation. Ischemic preconditioning, that works by activating K_{ATP} channels in mitochondria, is a natural endogenous mechanism which protects cells from IRI in the heart, kidney, liver, and other organs. UNI-494 is a pharmacological approach that emulates and enhances this natural phenomenon of ischemic preconditioning.

About Unicycive Therapeutics

Unicycive Therapeutics is a biotechnology company developing novel treatments for kidney diseases. Unicycive's lead drug candidate, oxylanthanum carbonate (OLC), is a novel investigational phosphate binding agent being developed for the treatment of hyperphosphatemia in chronic kidney disease patients on dialysis. UNI-494 is a patent-protected new chemical entity in late preclinical development for the treatment of acute

kidney injury. For more information, please visit Unicycive.com and follow us on LinkedIn and YouTube.

Forward-looking statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified using words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern Unicycive's expectations, strategy, plans or intentions. These forward-looking statements are based on Unicycive's current expectations and actual results could differ materially. There are several factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidates; risks related to business interruptions, which could seriously harm our financial condition and increase our costs and expenses; dependence on key personnel; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the uncertainties related to market conditions and other factors described more fully in the section entitled ‘Risk Factors’ in Unicycive’s Annual Report on Form 10-K for the year ended December 31, 2023, and other periodic reports filed with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Unicycive specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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