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XORTX Announces Topline Results from Mount Sinai's COVID-19 Clinical Study

● Early & High Uric Acid dose dependent association in Acute Kidney Injury from COVID-19 ●

CALGARY, Alberta, Nov. 16, 2020 (GLOBE NEWSWIRE) -- XORTX Therapeutics Inc. ("XORTX" or the "Company") (CSE: XRX) (OTCQB: XRTXF), a biopharmaceutical company focused on developing innovative therapies to treat progressive kidney disease, is pleased to announce topline results from the Company's partnership with the Icahn School of Medicine at Mount Sinai, New York ("Icahn School of Medicine"). The aim of this study was to characterize the incidence of Acute Kidney Injury ("AKI") and Hyperuricemia (high serum uric acid levels) in patients hospitalized with COVID-19 as announced on August 4, 2020 ("Icahn Clinical Study"). Results of the data analysis show that in some individuals with COVID-19 infection, hyperuricemia increases early in and is associated with AKI. The data also strongly suggests that for those individuals with very high serum uric acid levels, this can contribute to worsening kidney outcomes. These topline results indicate that further clinical studies to lower uric acid in these individuals is warranted, and may improve AKI, dialysis, recovery and mortality outcomes.

The Icahn Clinical Study assessed data from nearly 7,000 patients with COVID-19. From this pool of hospitalized individuals approximately 800 patients had measurements of uric acid at the time of or during hospitalization and provided information for analysis. This analysis builds upon XORTX's previous announcement that greater than 60% of individuals with acute kidney injury had elevated uric acid levels above the normal range. This investigation led by Dr. Coca and team, at the Icahn School of Medicine at Mount Sinai in New York was broadened to study all hospitalized patients and to understand when hyperuricemia and AKI are occurring during COVID-19 illness and the association between them. The topline results, in patients hospitalized for COVID-19, demonstrated that:

1. AKI occurred early in COVID-19 infection - 36% of individuals had evidence of AKI at admission and an additional 23% developed AKI during hospitalization;
2. More than 50% of individuals admitted to hospital with AKI demonstrated very high serum uric acid levels (Mean: >8 mg/dL);
3. Overall, MAKE-D* (Major Adverse Kidney Events) occurred in nearly 90% of patients with severe hyperuricemia (serum concentrations > 9 mg/dL); and
4. A strong dose-dependent relationship between serum uric acid levels and severity of AKI in COVID-19 existed, with adjusted odds for MAKE-D > 4-fold for patients in the highest vs. lowest quartile of uric acid, even after adjusting for confounders including admission serum creatinine.

***MAKE-D:** Serum Creatinine ≥ 100% increase from baseline or, dialysis or, death.

Dr. Steven Coca, lead investigator and Associate Professor of Medicine at the Icahn School of Medicine at Mount Sinai stated, “This clinical study has confirmed that in a significant proportion of patients with COVID-19, AKI, manifested by extremely high serum uric acid levels, along with hyperkalemia (High Potassium) and hyperphosphatemia (High Phosphates), without overt evidence of rhabdomyolysis (Muscular Breakdown products and Cellular Debris) in the majority of patients. A better understanding of the pathophysiologic causes of COVID-associated AKI is needed, including the potential effect of hyperuricemia on the severity of kidney injury and contribution to poor outcomes.” Dr. Coca added, “We are pleased to partner with XORTX to expand these analyses in terms of depth and breadth of the relationships with uric acid and complications of COVID-19, and to inform future clinical trials for this syndrome.”

Dr. Allen Davidoff, CEO commented: “We are grateful for this groundbreaking and diligent work by Drs. Steven Coca and Jaime Uribarri and other investigators at the Icahn School of Medicine. These results from the Icahn Clinical Study establish that serum uric acid rises early in a majority of individuals hospitalized due to COVID-19 and is associated with AKI and worse kidney outcomes.”

“With these clinical study results and the uric acid lowering potential of XRx-101 - our proprietary formulation of Oxypurinol XORTX will continue to focus on the clinical development of this potential first-in-class, front-line treatment for patients hospitalized with COVID-19 infection. Additional results from this study and clinical planning for a proof of concept trial will be forthcoming.”

The Company is not making any express or implied claims that it has the ability to eliminate, cure or contain the COVID-19 coronavirus at this time.

Risk Factors for COVID-19

The US Center for Disease Control (CDC) has stated that “people of any age with certain underlying medical conditions are at increased risk for severe illness from COVID-19”. The most susceptible on this list are individuals with chronic kidney disease, chronic obstructive pulmonary disease (COPD), obesity, serious heart conditions, sickle cell disease and diabetes mellitus.[1] Common amongst these groups is a high incidence of endothelial dysfunction, suggesting limited capacity of the endothelium to face physiologic challenges such as viral infection. Evolving evidence suggests that COVID-19 involves direct infection of the endothelial lining of the cardiovascular system.[2] In support of this evidence, recent reports suggest that COVID-19 coronavirus attaches to the ACE2 receptor on the endothelial cell layer on blood vessels and that endothelial infection and inflammation – endotheliitis ensues thereafter. Although it is well documented that COVID-19 is primarily manifested as a respiratory tract infection, emerging data indicates that it should be regarded as a systemic disease involving multiple systems including cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic and immune system.

Endothelial dysfunction is a principal determinant of microvascular dysfunction by shifting the vascular equilibrium towards more vasoconstriction with subsequent organ ischemia, inflammation with associated tissue oedema, and a procoagulant state.[3]

Hyperuricemia (high uric acid levels) has been linked to cardiovascular and renal diseases,

possibly through the generation of reactive oxygen species (ROS) and subsequent endothelial dysfunction. Hyperuricemia is also closely associated with depletion of endothelial cell nitric oxide availability. The enzymatic effect of xanthine oxidase is the production of ROS and uric acid. Studies have shown that inhibiting xanthine oxidase can reverse endothelial dysfunction. Furthermore, rat studies have shown that hyperuricemia-induced hypertension and vascular disease is at least partially reversed by the supplementation of the nitric oxide synthase (NOS) substrate, L-arginine.[4] Studies of the harmful effects of increased uric acid conclude that serum uric acid concentration greater than 8 mg/dL can contribute to kidney injury. [12]

XORTX Therapeutics XRx-101 is a proprietary combination of xanthine oxidase inhibitor oxypurinol and other excipients.

About COVID-19 and Acute Kidney Injury

Acute kidney injury (AKI) has been identified as an independent risk factor for patients' in-hospital mortality due to COVID-19[1]. Though early reports suggested a low incidence (between 3% to 9%) of AKI in those with COVID-19[5,6,7], data from the United States indicate that 25-35% of patients hospitalized with COVID-19 develop AKI.[9-11] Up to 20% of those need renal replacement therapy (RRT), and the mortality rate in patients that experience AKI in the setting of COVID-19 is several-fold higher than patients without AKI. [10] Moreover, proteinuria (69-85%) and hematuria (50-65%) are common in COVID-19.[9-11] In previous peer reviewed studies, viral infections such as influenza, when severe, can produce a tumor lysis "like" syndrome, resulting in increased pulmonary, endothelial cell debris and serum uric acid (SUA) levels in the circulation as well as increased cytokine expression. Coronavirus infection appears to follow this pattern.

XORTX Therapeutics has developed XRx-101 (active ingredient Oxypurinol) a xanthine oxidase inhibitor for the treatment of COVID-19 induced AKI. Two key studies (one in a mouse model of influenza and another in herpes infection) have shown that XRx-101's active ingredient, Oxypurinol, can act as (1) an anti-viral, (2) uric acid lowering treatment, and (3) organ-protective therapy. Specifically, in the setting of serious viral infection and tissue damage, XRx-101 can act to inhibit xanthine oxidase expression due to hypoxia, or tissue destruction, thereby preventing increased serum uric acid (SUA) concentration from reaching saturation levels at which uric acid crystals could trigger acute organ injury. Additionally, excipients in the formulation such as L-arginine, a basic amino acid and nitric oxide source, can increase the aqueous solubility of uric acid, thereby also decreasing uric acid crystal formation associated with tumor lysis-like syndrome due to COVID-19 infection. L-arginine is also reported to protect against kidney injury, in the setting of ischemia reperfusion injury. In concept, XRx-101 may ameliorate the severity of COVID-19 infection comorbidity, mortality, and damage to kidneys. This, in turn, could increase COVID-19 survival rates, especially in vulnerable populations such as the elderly and those with underlying medical conditions, while also lessening dependence on medical infrastructure and medical services.

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About XORTX Therapeutics Inc.

XORTX Therapeutics Inc. is a biopharmaceutical company with three clinically advanced products in development – XRx-008 for Autosomal Dominant Polycystic Kidney Disease (ADPKD), XRx-101 for Coronavirus / COVID-19 infection and XRx-221 is a clinical stage program for Type 2 Diabetic Nephropathy (T2DN). The Company has strong intellectual property rights and established proof of concept through independent clinical studies. XORTX is working to advance its clinical development stage products that target xanthine oxidase to inhibit production of uric acid. At XORTX Therapeutics, we are dedicated to developing medications to improve the quality of life and future of patients with kidney disease. Additional information on XORTX Therapeutics is available at www.xortx.com.

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