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XORTX Partners with Mount Sinai's Icahn School of Medicine on US-based Clinical Trial in COVID-19

Exploring Elevated Uric Acid in Acute Kidney Injury from COVID-19

CALGARY, Alberta, Aug. 04, 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 a partnership with the Icahn School of Medicine at Mount Sinai, New York to study the incidence of Acute Kidney Injury and Hyperuricemia in patients hospitalized with COVID-19.

This clinical study in nearly 4,000 patients with COVID-19 builds upon unpublished observations from over 1,100 individuals, where greater than 60% of individuals with acute kidney injury had elevated uric acid levels above the normal range. This partnership with Dr. Coca and the Icahn School of Medicine at Mount Sinai in New York is an investigator-led study focused on evaluation of more than 5,600 individuals with COVID-19 infection.

Dr. Steven Coca, lead investigator and Associate Professor of Medicine at the Icahn School of Medicine at Mount Sinai stated: "We have witnessed a hypercatabolic phenotype in a significant proportion of patients with AKI, manifested by extremely high serum uric acid levels, along with hyperkalemia and hyperphosphatemia, without overt evidence of rhabdomyolysis. 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. We are pleased to partner with XORTX and perform these analyses to inform future clinical trials for this syndrome."

Dr. Allen Davidoff, CEO commented: "We are pleased to be advancing this investigator-led clinical study with Drs. Steven Coca and Jaime Uribarri and several other clinicians and investigators at the Icahn School of Medicine at Mount Sinai. This group is arguably the leading medical network in the world and the ability to expand on observations that hospitalized individuals with COVID-19 have very high uric acid level will provide clarity on the association of xanthine oxidase and uric acid acute kidney injury and multi-organ injury with infection. The data collected will be critical for further therapeutic development."

This news release contains forward-looking information relating to, among other things, statements with respect to the potential for XRx-101 as a treatment to suppress the severity of the coronavirus / COVID-19 infection. Although the Company believes that any such intentions, plans, estimates, beliefs and expectations in this news release are reasonable, there can be no assurance that any such intentions, plans, beliefs and expectations will prove to be accurate.

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 ischaemia, 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 with allopurinol 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]

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

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. Additional information on XORTX Therapeutics is available at www.xortx.com.

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