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XORTX Therapeutics Announces Publication of Mt. Sinai Study of Hospitalized COVID-19 Patients

CALGARY, Alberta, Dec. 10, 2021 (GLOBE NEWSWIRE) -- XORTX Therapeutics Inc. (**"XORTX"** or the "**Company**") (NASDAQ: XRTX | TSXV: XRTX | Frankfurt: ANU), a pharmaceutical therapeutics company focused on developing innovative therapies to treat progressive kidney disease, is pleased to highlight and announce the online publication of the peer reviewed paper entitled "Prevalence and Outcomes Associated with Hyperuricemia in Hospitalized Patients with COVID-19" in the American Journal of Nephrology and available at the link below.

This paper highlights the results of the study that was conducted by the Icahn School of Medicine at Mount Sinai in partnership with XORTX and focused on the clinical outcomes of 834 patients with COVID-19 infection who were hospitalized at Mount Sinai Hospital in New York City. As is typical for COVID-19 infection, the patients were very sick with approximately 60% developing acute kidney injury (AKI) and with 31.7% dying in hospital.

The study investigated the potential predictive role of serum uric acid on clinical outcomes. Serum uric acid was elevated in nearly 38 percent of subjects when first measured. The striking finding was that an elevation in serum uric acid was found to be a major risk factor for AKI, major adverse kidney events and in-hospital mortality even after controlling for initial kidney function and other variables. In addition, hyperuricemia was associated with higher procalcitonin and troponin levels.

Dr. Steven Coca commented, "Early in the pandemic, we saw several patients that had elevated markers of cellular damage and markedly deranged serum chemistries. In this study, we sought to quantify the degree of hyperuricemia and its association with major adverse kidney outcomes. While we could not determine the degree to which hyperuricemia contributed to the poor outcomes, the results from the manuscript serve as a reminder that serum uric acid should be measured in patients hospitalized with COVID-19 as a marker of risk for acute kidney injury."

Dr. Richard Johnson, a Professor at the University of Colorado and an author on the study, stated, that, "An elevated serum uric acid has been found to be a risk factor for acute kidney injury in other studies, such as following cardiovascular surgery. This, however, is the first paper to my knowledge that has shown that a high uric acid is common in subjects with COVID and predicts both the development of kidney damage and mortality."

Dr. Allen Davidoff, CEO of XORTX added, "The results of this study support the Company's provisional patent filings in March 2020 and 2021 that contain claims to the use of any uric acid lowering agents to prevent and treat acute kidney, acute organ injury or sepsis

associated with COVID-19 infection. Resulting from this study is a more fulsome understanding that measurement of uric acid at the time of hospitalization, rapid uric acid lowering in patients who show evidence of acute kidney injury plus hyperuricemia may improve outcomes in hospitalized patients."

This study authored by the Mount Sinai team contains several key findings that will help in understanding the acute injury occurring in hospitalized patients with accompanying COVID-19 infection, including:

1/ A large proportion of individuals hospitalized with COVID-19 arrive at hospital, or soon after admission, develop acute kidney injury and concerningly high serum uric acid concentrations.

2/ High serum uric acid is associated with increased biomarker indicators of kidney and heart injury and increased propensity toward sepsis.

3/ Hyperuricemia has historically been associated with increased systemic and local inflammation and in the setting of COVID-19 may play a potential role for inflammation in kidney, heart and other organs.

4/ Patients with hyperuricemia and COVID-19 have worse outcomes.

The authors of this paper and XORTX interpret these findings as one explanation of why individuals with obesity, diabetes and hyperuricemia are more at risk to increased harm due to COVID-19. Building upon this data is a compelling rationale for physicians admitting COVID-19 patients to hospital to test and characterize serum uric acid concentrations. These findings also provide a strong impetus for clinical trial testing where the benefit of rapid and rigorous uric acid lowering in patients admitted to hospital could demonstrate beneficial outcomes with respect morbidity and mortality in COVID-19 patients.

https://www.karger.com/Article/FullText/520355

XORTX sponsored this study in partnership with the Ichan School of Medicine. 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 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]

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.

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About XORTX Therapeutics Inc.

XORTX Therapeutics Inc. is a pharmaceutical company with two clinically advanced products in development – XRx-008 for Autosomal Dominant Polycystic Kidney Disease (ADPKD), XRx-101 for acute kidney and other acute organ injury associated with Coronavirus / COVID-19 infection and XRx-225 is a pre-clinical stage program for Type 2 Diabetic Nephropathy (T2DN). XORTX is working to advance its clinical development stage products that target aberrant purine metabolism and xanthine oxidase to decrease or inhibit production of uric acid. At XORTX Therapeutics, we are dedicated to developing medications to improve the quality of life and future health of patients. Additional information on XORTX Therapeutics is available at www.xortx.com.

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Forward Looking Statements

This press release contains express or implied forward-looking statements pursuant to Canadian and U.S. Federal securities laws. These forward-looking statements and their implications are based on the current expectations of the management of XORTX only, and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Except as otherwise required by law, XORTX undertakes no obligation to publicly release any revisions to these forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. More detailed information about the risks and uncertainties affecting XORTX is contained in the Company's Management's Discussion and Analysis for the interim period ended June 30, 2020 filed on the Company's SEDAR profile (www.sedar.com) and under the heading "Risk Factors" in XORTX's Registration Statement on Form F-1 filed with the Securities and Exchange Commission ("SEC") available on the

SEC's website, www.sec.gov.

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