

XORTX Highlights New Studies of Acute Kidney Disease Due to COVID-19 Infection

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CALGARY, Alberta, Sept. 15, 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, highlights newly published information related to COVID-19 infection. Early in the COVID-19 pandemic lung infection and acute kidney injury (AKI) were closely associated with worse outcomes and death. More recently the mechanism of injury connecting acute respiratory distress syndrome (ARDS), a hypercatabolic phenotype, inflammatory cytokine expression and AKI in patients with COVID-19 infection has become clearer as has the contribution of each of these symptoms to disease severity and mortality. A study by Chan et al, published September 9, 2020 highlights the seriousness of AKI in individuals hospitalized with COVID-19 coronavirus, and shows a large proportion of individuals have slow recovery of their kidney injury even months after COVID-19 if they are fortunate enough to survive and avoid fulltime dialysis.

The COVID-19 pandemic has seen a surge of patients with AKI and ARDS in intensive care units across the globe⁽¹⁾. Historically, patients with ARDS have many fold increased xanthine oxidase activity⁽²⁾, the enzyme responsible for over production of uric acid and intravascular oxygen metabolite production and its health consequences. Epidemiological and animal data suggesting a cross-talk between lung and kidney in ARDS with injury in one organ initiating and aggravating injury to the other and both AKI and ARDS synergistically worsening mortality in ICU patients⁽³⁾. AKI of greater than 65% has been associated with ARDS⁽⁴⁾. Importantly, increased serum uric acid level predicts mortality in ARDS patients with 89% sensitivity and 80% specificity⁽⁵⁾.

AKI has been identified as a serious consequence of COVID-19 infection and has not been well characterized thus far in the United States. A new study this week, by Chan et al, characterizes US patient data and results, shows important new findings that describe the scope and severity of the developing kidney disease crisis. This study concludes:

- 1. In 3,993 hospitalized patients with COVID-19 AKI occurred in 46%, 19% of patients required dialysis.
- 2. In-patient mortality was 50% amongst those patients with AKI.
- 3. Of all patients with AKI, only 30% survived with recovery of kidney function by the time of hospital discharge.

Other studies are also shifting early focus on "cytokine storm" – cytokine inflammatory injury $^{(12,13)}$, toward a focus on endothelial/ blood vessel injury $^{(14)}$ and susceptibly of those

with pre-existing conditions characterized by endothelial dysfunction, such as obesity, hypertension, metabolic syndrome or diabetes. In the US, obesity, hypertension, metabolic syndrome or diabetes represent, ~42%, ~45%, ~30% and ~10% of the population, respectively⁽¹⁵⁾.

Dr. Allen Davidoff, CEO of XORTX stated, "For the 1 in 5 individuals who are hospitalized due to COVID-19 infection, the pattern of AKI is concerning. This includes a substantial number of patients who have long-term kidney injury and those who will remain on dialysis for the remainder of their lives. We strongly believe that xanthine oxidase inhibition with our XRx-101 program can attenuate the progression and severity of injury for many hospitalized COVID-19 patients."

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.

About ARDS

ARDS is a life threatening respiratory condition characterized by hypoxemia(7). Serum uric acid levels increases significantly during hypoxia(8-10). Elevated uric acid levels have been associated with the presence of systemic inflammation (11).

About AKI

Acute Kidney Injury (AKI) or Acute Renal Failure (ARF) refer to a stark decrease in kidney function, increased blood nitrogenous waste products and urea, as well as a dysfunction of blood volume and electrolyte balance. The acronyms AKI and ARF increasing recognize that small decreases in kidney function that do not result in overt organ failure are of substantial clinical relevance and are associated with increased occurrence of symptoms and rate of death⁽¹⁶⁾.

About XRx-101

XORTX Therapeutics has developed XRx-101 a novel proprietary formulation of xanthine oxidase inhibitor for the treatment of COVID-19 induced AKI. 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. In concept, XRx-101 may ameliorate the severity of COVID-19 infection comorbidity, mortality, and damage to kidneys.

In other news, the Company announces that it has retained Lakeshore Securities Inc. ("Lakeshore Securities") to provide market making services to the Company in compliance with the policies and guidelines of the CSE and other applicable legislation. Lakeshore Securities will trade shares of XORTX on the CSE with the objective of maintaining a reasonable market and improving the liquidity of XORTX common shares. There are no performance factors contained in the agreement and Lakeshore Securities will not receive shares or options as compensation. Lakeshore Securities and the Company are unrelated and unaffiliated entities, but Lakeshore Securities and/or its clients may have an interest, directly or indirectly, in the securities of the Company.

References:

- 1. Fan E, Beitler, JR, Brochard L, Calfee CS, Feruguson ND, Slutsky AS, Brodie D, COVID-19-associated acute respiratory distress syndrome is a different approach to management warranted?
- 2. Grum CM_Plasma xanthine oxidase activity in patients with adult respiratory distress syndrome_Journal of Critical Care_Vol 2_No 1_22-26_1987
- 3. Doi K, Ishizu T, Fujita T, et al. Lung injury following acute kidney injury: kidney-lung crosstalk. Clin Exp Nephrol. 2011;15(4):464–470.
- 4. Panitchote2019_Article_FactorsAssociatedWithAcuteKidn_Annals of Intensive Care 9 74 2019
- 5. Elshafey M et al, Prognositc role of serum uric acid in ARDS patients, EJCDT, 64, 197 2015
- 6. Chan L., et al, AKI in Hospitalized Patients with COVID-19, Mount Sinai COVID Informatics Center (MSCIC), Journal of American Society of Nephrology, Sept 9, 2020 https://jasn.asnjournals.org/content/early/2020/09/02/ASN.2020050615.abstract
- 7. L.B. Ware, M.A. MatthayThe acute respiratory distress syndrome, N. Engl. J. Med., 342 (2000), pp. 1334-1349
- 8. K. Bartziokas, A.I. Papaioannou, S. Loukides, A. Papadopoulos, A. Haniotou, S. Papiris, uric acid as a predictor of mortality and future exacerbations of COPD, Eur. Respir. J., 43 (2014), pp. 43-53
- 9. Y. Aida, Y. Shibata, D. Osaka, S. Abe, S. Inoue, K. Fukuzaki, Y. Tokairin, A. Igarashi, K. relationship between serum uric acid and spirometric values in participants in a health check: the Takahata study, Int. J. Med. Sci., 8 (2011), pp. 470-478
- 10. L.M. Fabbri, K.F. RabeFrom COPD to chronic systemic inflammatory syndrome? Lancet, 370 (2007), pp. 797-799
- 11. C. Ruggiero, A. Cherubini, E. Miller 3rd, M. Maggio, S.S. Najjar, F. Lauretani, S. Bandine Usefulness of uric acid to predict changes in C-reactive protein and interleukin-6 in 3-year period in Italians aged 21–98 years, Am. J. Cardiol., 100 (2007), pp. 115-121
- 12. Del Valle DM., et al, An Inflammatory cytokine signature predicts COVID-19 severity and survival, Nature Medicine, August 2020
- 13. Sinha P, Matthay M, Calfee C, Is a "Cytokine storm" Relevant to COVID-19, JAMA Intern Med, 180(9):1152-1154, 2020
- 14. Luscher TF., Understanding COVID-19: in the end it is the endothelium-what else?, European Heart Journal, 41, 0323-3027_2020
- 15. Source: <u>www.cdc.gov</u>
- 16. Source: https://www.uptodate.com/contents/definition-and-staging-criteria-of-acute-kidney-injury-in-adults

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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