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XORTX Sponsored American Society of Nephrology Study Abstract Available Online

• Chronically Increased Uric Acid Accelerates Structural and Functional Changes in Polycystic Kidney Disease •

CALGARY, Alberta, Oct. 25, 2022 (GLOBE NEWSWIRE) -- XORTX Therapeutics Inc. ("XORTX" or the "Company") (NASDAQ: XRTX | TSXV: XRTX | Frankfurt: ANU), a late stage clinical pharmaceutical company focused on developing innovative therapies to treat progressive kidney disease, is pleased to announce online availability of the peer-reviewed abstract to be presented November 4, 2022 at the American Society of Nephrology ("ASN") Annual Conference – Kidney Week. The abstract presents new discoveries in two species – mouse and rat models of polycystic kidney disease ("PKD") and reports original work showing the harmful consequence of chronically increased uric acid on both structure and function of kidneys. The Abstract "**Raising Serum Uric Acid with a Uricase Inhibitor Worsens PKD in Rat and Mouse models**" will be presented during the Session Title: Genetic Diseases of the Kidneys, by Dr. Charles Edelstein of the University of Colorado and Dr. Allen Davidoff of XORTX.

The abstract presents the findings of studies conducted at the University of Colorado, by Dr. Charles Edelstein and the PKD research team. Results of this study, in two models of PKD, show similar results and reach similar conclusions, confirming that increasing uric acid by inhibiting uricase enzyme metabolism of uric acid to allantoin, results in substantially and statistically significant increases in:

- i. Total kidney / body weight ratio – indicating the possibility of accelerated formation or growth of cysts and represents a measure analogous to total kidney volume measures in humans with PKD;
- ii. Creatinine, supporting the concept of a decrease in filtering capacity of kidneys; and
- iii. Cyst index is increased, suggesting uric acid may act to specifically accelerate disease progression in PKD.

In summary, increasing serum uric acid by inhibiting uricase with oxonic acid ("OXO") results in an increase in kidney weight, cyst index, creatinine in PCK rat and RC mouse models of PKD. Further characterization of potential mechanisms of injury, including increased cyst growth that will be investigated include crystal deposition causing tubular dilatation, increased reactive oxygen radicals and pro-inflammatory cytokines/chemokines causing tubular cell proliferation and endothelial injury are ongoing.

About this study

Unlike most forms of life, humans lack an active uricase enzyme that converts uric acid to allantoin. In rodents, uricase converts uric acid to allantoin and uricase inhibition raises serum uric acid. The aim of this study was to determine whether raising serum uric acid with OXO was associated with worse PKD.

Dr. Allen Davidoff, CEO of XORTX, stated, “We are pleased to participate in the ASN annual meeting during Kidney Week 2022 with this poster presentation. The results of this study show that increased serum uric acid can accelerate injury in two separate models of PKD and importantly reports fundamental findings in support of the Company’s XRx-008 program. These results and additional novel key discoveries associated with this study will provide the opportunity to further enhance our patent portfolio, through a recent continuation of our formulation patent and a new provisional patent application. We anticipate a further updated information near the time that the abstract for the ASN becomes public.”

About the American Society of Nephrology – Kidney Week

ASN represents more than 21,000 kidney health professionals working to help people with kidney diseases and their families. Source: <https://www.asn-online.org/>.

The Kidney Week Conference is attended by approximately 10,000 kidney professionals from across the globe at Kidney Week 2022 in Orlando, Florida. The world's premier nephrology meeting, Kidney Week provides participants exciting and challenging opportunities to exchange knowledge, learn the latest scientific and medical advances, and listen to engaging and provocative discussions with leading experts in the field. Source: <https://www.asn-online.org/education/kidneyweek/>.

American Society of Nephrology – Program and Abstracts

The Kidney Week program and abstracts are available on the [ASN website](#).

About ADPKD

ADPKD is a rare disease that affects more than 10 million individuals worldwide.^{1,2} ADPKD is typically diagnosed based upon expansion of fluid-filled cysts in the kidneys. Over time, the increasing number and size of cysts can contribute to structural and functional changes to kidneys and is frequently accompanied by chronic pain which is a common problem for patients with ADPKD.³ Expansion of cysts is thought to compress healthy functioning tissue surrounding the cysts and contribute to further loss of kidney function, fibrosis, impaired nutrient exchange and impaired kidney function, accompanied later by end-stage renal disease.¹ Health consequences of high uric acid have been reported to be increased in ADPKD individuals, including increased incidence of kidney stones⁵ and gout.^{6,7} For individuals with progressing ADPKD, treatment recommendations include anti-hypertensive treatment, dietary restrictions, and, for a limited percentage of suitable patients, pharmacotherapy.⁴ New, more broadly applicable therapies to effectively slow decline of kidney function in ADPKD are needed.

About XORTX Therapeutics Inc.

XORTX is a pharmaceutical company with two clinically advanced products in development:

1) our lead, XRx-008 program for ADPKD; and 2) our secondary program in XRx-101 for acute kidney and other acute organ injury associated with Coronavirus / COVID-19 infection. In addition, XRx-225 is a pre-clinical stage program for Type 2 Diabetic Nephropathy. 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, we are dedicated to developing medications to improve the quality of life and future health of patients. Additional information on XORTX is available at www.xortx.com.

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Neither the TSX Venture Exchange nor Nasdaq has approved or disapproved the contents of this news release. No stock exchange, securities commission or other regulatory authority has approved or disapproved the information contained herein.

References:

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3. <https://pkdcure.org/living-with-pkd/chronic-pain-management>
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7. Rivera JV Martinez, et al, Association of hyperuricemia and polycystic kidney disease, *Bol Asoc Med P R*, 1965 vol 7 251-263

Forward Looking Statements

This press release contains express or implied forward-looking statements pursuant to 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 under the heading "Risk Factors" in XORTX's Registration Statement on Form F-1 filed with the SEC, which is available on the SEC's website, www.sec.gov (including any documents forming a part thereof or incorporated by reference therein), as well as in our reports, public disclosure documents and other filings

with the securities commissions and other regulatory bodies in Canada, which are available on www.sedar.com.



Source: XORTX Therapeutics Inc.