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XORTX Files IND with US FDA

• Autosomal Dominant Polycystic Kidney Disease – XRx-008 Program IND Filed •

CALGARY, Alberta, March 31, 2022 (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 announce the filing of an investigational new drug ("IND") application with the United States Food and Drug Administration ("FDA"). This IND filing is in support of the Company's XRx-008 program for treatment of progressing kidney disease due to autosomal dominant polycystic kidney disease ("ADPKD") and contains the protocol for the bridging pharmacokinetics study – XRx-OXY-101.

XORTX's XRx-008, for ADPKD, is a proprietary combination of uric acid lowering agents and other excipients. At present, there are few therapeutic options available to treat progressing kidney disease due to ADPKD. XORTX's IND application documents provide a robust overview of program status with respect to chemistry, manufacturing, pharmacology, toxicology, and clinical work to date and facilitate formal communications with the FDA regarding development of XRx-008 for the treatment of progressing kidney disease due to ADPKD. Further announcements regarding this filing, and future meeting with the FDA will be forthcoming.

XORTX is focused on advancing XRx-008 through bridging pharmacokinetic, as well as registration clinical trials for the treatment of ADPKD. At the present time, very few approved therapeutic options exist to treat progressive kidney disease in individuals due to this disease. There is reason for hope, however, as recent clinical study evidence confirms that uric acid is an independent risk factor for progression of PKD and that managing purine metabolism and serum uric acid concentrations can positively affect the kidney health thereby improving the lives of patients with PKD.

Dr. Allen Davidoff, CEO of XORTX stated, "The filing of this IND package facilitates ongoing communications with the FDA regarding XORTX's XRx-008 program and development plans. The Company looks forward to advancing this program through our planned clinical trials this year in patients with ADPKD. Feedback from the FDA will support and guide XORTX efforts to optimize the critical path steps needed to gain marketing approval of this therapy for PKD patients."

About Polycystic Kidney Disease and XRx-008

PKD is considered a rare disease with two main types - ADPKD and autosomal recessive PKD (ARPKD), with prevalence of 1:800 and 1:20,000, respectively. PKD is a disorder that originates due to genetic changes and results in numerous fluid-filled cysts that can form in the kidneys. This genetic disorder tends to worsen with progressing age and is characterized by increasing cyst numbers and size that change the shape of kidneys making them much

larger. Progression of this disease reduces kidney function and may lead to kidney failure and the need for transplant or dialysis. Statistically, greater than 50% of individuals reach end stage kidney failure by the age of 60 years. Typically, diagnosis of ADPKD occurs between the ages of 30 and 50, when signs and symptoms begin to appear. Progression of PKD is frequently accompanied by high blood pressure, hyperuricemia, gout, kidney stones, proteinuria, abdominal pain, hematuria and declining kidney filtering capability. Like many progressing kidney diseases, the rate of filtering capacity accelerates with time leading to end stage kidney failure and the need for kidney transplant or dialysis.

Recently, non-clinical and clinical evidence has accumulated showing that high serum uric acid concentration may mediate disease progression in ADPKD including:

1. Individuals with ADPKD have high reported incidences of hyperuricemia (>60%) and clinical gout (24%) and, conditions that are associated with uric acid crystal formation in the kidneys such as low serum and urine pH^{1,2,3}.
2. A high prevalence of kidney stones of approximately equal uric acid composition or oxalate composition⁴.
3. High serum uric acid is an independent risk factor for cyst genesis, cyst growth and declining filtering capacity of kidneys¹.
4. Xanthine oxidase inhibition in ADPKD patients may reverse progression of glomerular filtration rate decline⁵.

At the present time, few therapeutic options to treat, stabilize or slow this progressing kidney disease are available. At the present time, only a single drug is approved to date - Tolvaptan. Although helpful for slowing cyst growth, the need to develop therapeutic options that slow progressive decline of filtering capacity remains, and is critical to improving the quality of life and kidney health for individuals facing this disease. XRx-008 represents a first-in-class opportunity to help individuals with decreasing renal filtering capacity and slow or prevent end stage renal disease and the need for dialysis.

References:

1. Helal, I., et al., *Serum uric acid, kidney volume and progression in autosomal-dominant polycystic kidney disease*. Nephrol Dial Transplant, 2013. **28**(2): p. 380-5.
2. Torres, J.A., et al., *Crystal deposition triggers tubule dilation that accelerates cystogenesis in polycystic kidney disease*. J Clin Invest, 2019. **129**(10): p. 4506-4522.
3. Errasti, P., et al., *Autosomal-dominant polycystic kidney disease: high prevalence of graft loss for death-related malignancies and cardiovascular risk factors*. Transplant Proc, 2003. **35**(5): p. 1717-9.
4. Idrizi, A., et al., *Prevalence of nephrolithiasis in polycystic kidney disease* Cent. Eur. J. Med, 2011. **6**: p. 497.
5. Han, M., et al., *Hyperuricemia and deterioration of renal function in autosomal dominant polycystic kidney disease*. BMC Nephrol, 2014. **15**: p. 63.

About XORTX Therapeutics Inc.

XORTX Therapeutics Inc. is a pharmaceutical therapeutics company with three clinically advanced products in development – XRx-008 for 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 uric acid lowering as a method of treating progressive kidney disease. At XORTX, 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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Forward Looking Statements

This press release may contain 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 reasonable 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 such forward-looking statements. Except as otherwise required by law, XORTX undertakes no obligation to publicly release any revisions or updates 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 most recently filed Annual Information Form and the Management Discussion and Analysis for its most recent financial reporting period 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.



Source: XORTX Therapeutics Inc.