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XORTX Highlights New Research on Polycystic Kidney Disease Awareness Day

● New Study Shows a Novel Form of Injury Linking Uric Acid Crystals in Urine and ADPKD Progression ●

CALGARY, Alberta, Sept. 04, 2019 (GLOBE NEWSWIRE) -- XORTX Therapeutics Inc. ("**XORTX**" or the "**Company**") (CSE: XRX; OTCQB: XRTXF; ANU1: FWB), a biopharmaceutical company focused on developing innovative therapies to treat progressive kidney disease, is pleased to highlight in conjunction with Polycystic Kidney Disease Awareness Day, a new, eloquent research paper that describes a previously unrecognized form of injury that can occur when uric acid or calcium oxalate crystals form in the kidneys of individuals with polycystic kidney disease. For the first time this research identifies a new pathway for accelerated cyst growth and decline of kidney function.

Dr. Allen Davidoff stated, "This new research aligns closely with the therapies that XORTX is developing to slow or reverse progression of autosomal dominant polycystic kidney disease (ADPKD) in individuals with progressing kidney disease. Accumulating evidence over the past decade has identified uric acid as an independent risk factor for accelerated progression of kidney injury and cyst growth. The mechanism of disease action for uric acid is considered to be due to a combination of blood vessel injury, and inflammatory injury to the kidney. This study identifies a new type of injury to the tubules of the nephron that occurs after blood filtration of urine and during the time that nutrients are being reabsorbed from urine, before excretion. This study contributes additional strong evidence and hope that decreasing the overall production of uric acid in individuals with high uric acid and ADPKD will be therapeutically important and minimizing kidney injury due to this risk."

This study by Jacob A. Torres et al, entitled "Crystal Deposition Triggers Tubule Dilation That Accelerates Cytogenesis in Polycystic Kidney Disease" in the Journal of Clinical Investigation, 2019, for the first time shows that PKD progression may be accelerated by commonly occurring renal crystal deposition.[4]

ADPKD is a serious, life-threatening genetic kidney disease for individuals with progressing renal disease. Progressive renal cyst growth leads to deterioration of kidney structure, such that ~50% of patients require dialysis or kidney transplantation in adulthood. The disease is associated with symptoms that range from high blood pressure to debilitating chronic abdominal or flank pain, to kidney stones and gout. ADPKD patients also have high incidences of clinical gout (24%) and hyperuricemia (>60%) [5,6], conditions that are associated with uric acid crystal formation in the kidneys. Hyperuricemia correlates with faster disease progression in ADPKD[7].

ADPKD often leads to progressive renal failure due in part to continued enlargement of the cysts. Kidney size typically increases to more than five times normal in the years prior to the

loss of kidney function, and measured total kidney volume is the strongest predictor for the development of renal insufficiency[1]. Other renal manifestations that can occur include hypertension, urinary tract infection, concentrating defect, hematuria, nephrolithiasis, and acute or chronic flank and abdominal pain; protein excretion is generally not a prominent feature [2,3]. All complications relate directly to the extent of renal cyst involvement, which can be assessed by total kidney volume measurements.

These researchers have successfully shown that urinary crystals are increased in PKD patients and accumulate in the kidney. Microcrystal accumulation and kidney stone formation can profoundly harm the kidney leading to local inflammation and injury in both animals and man. This “third” mechanism of injury/disease action, in the tubules of kidneys, was previously undescribed, and is apparently fundamental to generation of new cysts, cyst growth and kidney dysfunction. The discovery of this new mechanism of disease action is prevalent, and clinically relevant, and suggests tubule occlusion or injury by sporadically lodged microcrystals is a fundamental culprit in kidney disease progression.

XORTX is developing a uric acid lowering drug that focuses on lowering uric acid production in individuals with ADPKD and is preparing for a phase 3 registration trial to test this promising first-in-class approach to slowing or reversing decline of filtration rate.

References:

1. Chapman AB, Bost JE, Torres VE, et al. Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. Clin J Am Soc Nephrol 2012; 7:479.
2. Gabow PA. Autosomal dominant polycystic kidney disease. N Engl J Med 1993; 329:332.
3. Rizk D, Chapman AB. Cystic and inherited kidney diseases. Am J Kidney Dis 2003; 42: 1305.
4. Torres JA et al, Crystal Deposition Triggers Tubule Dilation That Accelerates Cystogenesis in Polycystic Kidney Disease, J Clin Invest 2019
5. Nishiura JL, Neves RFCA, Eloi SRM, Cintra SMLF, Ajzen SA, Heilberg IP. Evaluation of nephrolithiasis in autosomal dominant polycystic kidney disease patients. Clin J Am Soc Nephrol CJASN. 2009; 4(4):838-844.
6. Mejías E, Navas J, Lluberes R, Martínez-Maldonado M. Hyperuricemia, gout, and autosomal dominant polycystic kidney disease. Am J Med Sci. 1989; 297(3):145-148. 13
7. Panizo N, Goicoechea M, García de Vinuesa S, et al. Chronic kidney disease progression in patients with autosomal dominant polycystic kidney disease. Nefrol Publ Of Soc Esp Nefrol. 2012; 32(2):197-205.

About XORTX Therapeutics Inc.

XORTX Therapeutics Inc. is a biopharmaceutical company focused on developing innovative therapies to treat progressive kidney disease. XORTX has two lead programs to develop treatments for progressive kidney disease due to diabetes, diabetic nephropathy and polycystic kidney disease. XORTX’s XRx-008 (a proprietary reformulation of Oxypurinol) is a late stage drug development program to treat autosomal dominant polycystic kidney disease (ADPKD) and TMX-049, is a late phase 2b stage program to treat type 2 diabetic nephropathy (T2DN), under a co-development agreement with Japan’s Teijin Pharma

Limited, pursuant to a non-binding Letter of Intent. Secondary programs focus on developing therapies for health consequences that accompany pre-diabetes, diabetes and cardiovascular disease. Additional information on XORTX Therapeutics is available at www.xortx.com.

For further information, please contact:

Allen Davidoff, CEO
adavidoff@xortx.com or +1 403 455 7727

or Erik Matthews, Corporate Communications
erik@xortx.com or +1 747 203 5240

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