



XORTX Announces Pioneering Research on Genome-Wide Pathogenic Pathways in Gout and Provides a Corporate Update

• Clinical Data doubles known genetic factors associated with urate and Gout •

CALGARY, AB – December 31, 2025 – 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 gout and progressive kidney disease, highlights recent peer-reviewed, independent, published research reports that expand current knowledge that genetic factors are linked to the over-expression of xanthine oxidase ("XO"), high chronic uric acid concentrations in the blood and gout. These ground breaking findings further support the Company's approach to treating gout, kidney and other diseases by inhibiting XO.

Historically, high uric acid concentration in the blood has been associated with increased incidence of gout, inflammation and health consequences, attributed to diet and lifestyle choices. Xanthine oxidase is an essential enzyme within the uric acid metabolic pathway and is required for the breakdown of purine nucleotides. The breakdown products of XO, uric acid and reactive oxygen species, are released during the enzymatic reaction and may play a detrimental role in the circulatory system and within tissue during disease. XORTX-sponsored discoveries in rodent models of gout and polycystic kidney disease ("PKD") implicate over-expression or over-activity of XO as a potentially important target in treating this disease. Gout is a chronic disease that is caused by an innate immune response to deposits of uric acid crystals when uric acid is high.

Recent work by TJ Major and colleagues presented evidence that in a large clinical study of 2.6 million individuals that as many as 410 genetic factors (including 149 new factors) are associated with molecular mechanisms of the inflammatory component of gout¹. This clinical study aligns closely with evidence for over-expression of XO in human² and with work by Wang *et al.* suggests linkage of genetic factors to PKD². Recently, new emerging discoveries link genetic factors to specific populations and show that higher XO expression is associated with a variety of conditions including hyperuricemia³, sepsis, organ failure and sepsis associated acute respiratory distress syndrome (ARDS)^{4,5}, kidney dysfunction^{3,4}, diabetes⁵, polycystic kidney disease^{2,6} and kidney failure^{7,8}. From a mechanistic standpoint, these studies advocate for a precision medicine approach in which genetic risk variants would guide treatment decisions².

Commenting on the research, Allen Davidoff, Ph.D., Chief Executive Officer of XORTX, stated, "This pioneering into the health consequences of hyperuricemia and linkage to genetic factor in gout and autosomal dominant polycystic kidney disease (ADPKD) sponsored by XORTX and these peer-reviewed, published research papers support our belief that pharmacologic targeting of XO holds enormous therapeutic potential, specifically where increased XO activity is associated with non-diabetic or diabetic kidney diseases. These discoveries highlight an opportunity to develop a personalized therapeutic approach for individuals whose unique genetic factors predispose them to disease, and the need for xanthine oxidase inhibition to treat those individuals at risk. We believe that XORTX's expertise in developing XO inhibitors, protected by a patent portfolio that anticipated this opportunity, combined with our therapeutic platform is ideally positioned to deliver targeted therapeutics to individuals. Our planned clinical



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trial using our commercial formulation of oxypurinol will bring us ever closer preparing a NDA (new drug application) for this important gout therapy.”

Corporate Updates – Board Changes, Financing and Vectus

XORTX announces the appointment of Krysta Davies Foss as a director and the resignation of Bill Farley, Abigail Jenkins and Patrick Treanor reducing the board to five members. Ms. Davies Foss is a seasoned biotechnology executive with more than 25 years of experience advising pharmaceutical and biotechnology companies on development strategy, commercialization, and market preparedness across a broad range of therapeutic areas. She currently serves as Chief Executive Officer of Triad Strategic Services, a leading pharma and biotech strategy consulting firm. In addition to her executive role, Ms. Davies Foss serves on multiple boards, including the Canadian Organization for Rare Disorders (CORD), and has provided strategic intelligence and advisory services to organizations ranging from incubators and early-stage startups to large multinational pharmaceutical companies. Her experience spans the full product development lifecycle, from early innovation through global commercialization.

Dr Allen Davidoff stated, “The addition of Ms. Foss adds a strong board member to the Company. Her depth of strategic insight and industry leadership will be a valuable asset as the Company advances its clinical programs and long-term growth strategy. The Company wishes to thank Bill Farley, Abigail Jenkins and Pat Treanor for their efforts on behalf of XORTX over the past several years.”

The Company also wishes to clarify its disclosure included in its news release of October 29, 2025 announcing the closing of the US\$1.1 million Registered Direct Offering (the “Offering”). In that news release, the number of pre-funded warrants of 1,117,530 was incorrect. On closing, the Company issued 572,470 common shares and 1,177,530, a difference of 60,000 pre-funded warrants, for total aggregate common shares and pre-funded warrants of 1,750,000. Further, the Company confirms that in addition to the 87,500 agent warrants granted to D. Boral Capital LLC exercisable at USD\$0.69 per common share commencing 181 days following issuance for a period of 18 months, D. Boral Capital LLC was also paid a cash commission of USD\$77,175, equal to 7% of the gross proceeds of the Offering.

Finally, the Company wishes to provide an update on timing for closing its acquisition of the Renal Anti-Fibrotic Therapeutic Program from Vectus Biosystems Limited’s (“Vectus”), an Australian Securities Exchange (“ASX”) listed company that was announced on October 17, 2025. Vectus is awaiting approval from the ASX on whether shareholder approval is required for the sale of the VB4-P5 intellectual property. Pursuant to the binding term sheet that was entered into between XORTX and Vectus, closing is to occur no later than 90 days post signing, being January 13, 2026. XORTX and Vectus remain committed to finalizing the acquisition. The Company will provide additional updates on timing for closing when clarity on ASX approval is received by Vectus.

References:

1. Major TJ, et al, A genome-wide association analysis reveals new pathogenic pathways in gout, *Nature Genetics*, 56, 2392-2406, 2024
2. Korsmo HW, Emerging roles of xanthine oxidoreductase in chronic kidney disease, *Antioxidants*, June 2024
3. Major TJ, et al Evaluation of the diet wide contribution to serum urate levels: Met-analysis of population based cohorts, *BMJ*, 363, k3952, 2018
4. Gao, Li et al., Xanthine oxidoreductase gene polymorphism are associated with high risk of sepsis and organ failure, *Respir. Res*, 24, 177_2023
5. Liu H, et al., Genetic variants in XDH are associated with prognosis off gastric cancer in a Chines population, 663, 196, 2013
6. Wang et al., Genetic susceptibility to diabetic kidney disease is linked to promoter variants of XOR.” The authors identified an expression quantitative trait loci (QTL) in the *cis*-acting regulatory region of the xanthine dehydrogenase, or xanthine oxidoreductase (XO), a binding site for C/EBP β , to be associated with diabetes-induced podocyte loss in diabetic kidney disease in male mice. They concluded that certain types of alleles of a gene that controls the expression of xanthine oxidase can be over expressed in CKD, diabetic kidney disease and polycystic kidney disease.
7. Kudo M et al., Functional Characterization of Genetic Polymorphisms Identified in the Promotor Region of the Xanthine Oxidase Gene, *Drug Metab. Pharmacokinet.*, 25, 599, 2010
8. Boban M, et al., Circulating purine compound, uric acid, and xanthine oxidase/dehydrogenate relationship in essential hypertension and end stage renal disease., *Ren. Fail.*, 36, 613, 2014



About XORTX Therapeutics Inc.

XORTX is a pharmaceutical company with three clinically advanced products in development: 1) our lead program XRx-026 program for the treatment of gout; 2) XRx-008 program for ADPKD; and 3) XRx-101 for acute kidney and other acute organ injury associated with respiratory virus infections. In addition, the Company is developing XRx-225, a pre-clinical stage program for Type 2 diabetic nephropathy. XORTX is working to advance 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 that improve the quality of life and health of individuals with gout and other important diseases. Additional information on XORTX 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 applicable 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 applicable law and stock exchange rules, 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 Annual Report on Form 20-F 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.sedarplus.ca.