

XORTX Announces Grant of European Patent

• Patent Supporting Gout and Autosomal Dominant Polycystic Kidney Disease Programs •

CALGARY, AB – April 28, 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, is pleased to announce receipt of notification that the patent "Xanthine Oxidase Inhibitor Formulations" will be granted by the European Patent Office. The patent covers compositions and methods of formulating using XORTX's proprietary formulations of xanthine oxidase inhibitors ("XOI") for the treatment of health consequences of chronically high uric acid, gout, renal, cardiovascular and other diseases where aberrant purine metabolism has been implicated in disease progression.

Dr. Allen Davidoff, CEO of XORTX stated, "This patent covers compositions of formulations key to XORTX's platform technology and this issuance strengthens our intellectual property portfolio in the European Union ("EU"). Importantly, this European patent broadens protection of our first-in-class program for gout as well as supporting our autosomal dominant polycystic kidney disease ("ADPKD") program. This patent focuses on the health consequences that arise from uric acid crystal formation due to hyperuricemia in conditions including gout, kidney stone formation, cardiovascular disease and covers novel therapeutic solutions developed specifically to address these problems. The granting of this patent provides additional breadth of patent to XORTX for commercialization and partnering opportunities throughout Europe. Including this newly granted patent, XORTX now has five granted patents in the United States ("US") and/or EU covering compositions and uses of uric acid lowering agents to treat gout, the health consequences of hyperuricemia, and progressive kidney disease."

About Hyperuricemia, Gout and Health Consequences

It is estimated that 14% of the adult population has hyperuricemia – i.e. serum uric acid levels greater than the normal range. Approximately 3% of the US population suffer from gout as a result of their hyperuricemia, though not all individuals who have hyperuricemia develop gout. The factors that contribute to hyperuricemia include genetic factors⁽¹⁾, dietary factors and lifestyle choices. Nucleotides are normally broken down in the blood by the xanthine oxidase ("XO") enzyme through the purine metabolic pathway. This results in the formation of uric acid. However, if an individual experiences chronically high blood uric acid concentrations (hyperuricemia), they often experience health consequences including gout, kidney stones, diabetes, cardiovascular disease, and renal failure. Evidence that unique health consequences may arise from hyperuricemia, independent of the health consequences of gout, suggest that aberrant purine metabolism, hyperuricemia, merits an increased therapeutic focus. Lowering blood levels of uric acid in gout patients is strongly correlated with improved health outcomes.

Recent groundbreaking studies by Wang et al. suggests linkage of genetic factors to the overexpression of XO⁽¹⁾. Recently, emerging discoveries link genetic factors to specific populations and show that higher XO expression is associated with a variety of conditions including hyperuricemia⁽²⁾, general sepsis, organ failure and sepsis associated with acute respiratory distress syndrome (ARDS)^(3,4), kidney dysfunction^(3,4), diabetes⁽⁵⁾, polycystic kidney disease^(1,5) and kidney failure^(6,7). From a mechanistic standpoint, these studies advocate for a precision medicine approach in which genetic risk variants would guide treatment decisions⁽¹⁾.



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Addressable Gout Market Opportunity

In North America, approximately 3.5 million people suffer from gout due to elevated uric acid levels in blood. The therapeutic options to lower uric acid levels include three major classes of drugs: 1) oral uricosurics that are used to decrease the reabsorption of uric acid by the kidney; 2) intravenous uricase enzymes that are used to metabolize uric acid in the blood for excretion; and 3) oral XOIs that are used to inhibit the production of uric acid by the purine metabolic pathway. XOIs are the preferred first-line treatment for gout. Allopurinol is the most commonly prescribed XOI, with approximately 3 million prescriptions written per year in North America, however 3 to 5% of patients cannot tolerate allopurinol. An alternative XOI, Febuxostat, was launched in the US in 2009 with the hope of treating allopurinol intolerant patients. While Febuxostat achieved peak sales of approximately US\$450 million¹, it now carries a Black Box warning due to its associated risk of sudden cardiovascular death and its use has declined significantly. This decline in Febuxostat use has created an opportunity for a novel XOI to address the underlying unmet medical need which the XRx-026 program aims to fill.

References:

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2. Major TJ, et al., Evaluation of the diet wide contribution to serum urate levels: Met-analysis of population based cohorts, *BMJ*, 363, k3952, 2018
3. Gao, Li et al., Xanthine oxidoreductase gene polymorphism are associated with high risk of sepsis and organ failure, *Respir. Res.*, 24, 177, 2023
4. Liu H, et al., Genetic variants in XDH are associated with prognosis off gastric cancer in a Chines population, 663, 196, 2013
5. 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.
6. 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
7. 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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¹ Source: Takeda Pharmaceutical Company 2018 Annual Report.

Forward Looking Statements

This press release contains express or implied forward-looking statements pursuant to applicable securities laws. These forward-looking statements include, but are not limited to, the Company's beliefs, plans, goals, objectives, expectations, assumptions, estimates, intentions, future performance, other statements that are not historical facts and statements identified by words such as "expects", "anticipates", "intends", "plans", "believes", "seeks", "estimates" or words of similar meaning. 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. Such risks, uncertainties, and other factors include, but are not limited to, our ability to obtain additional financing; the accuracy of our estimates regarding expenses, future revenues and capital requirements; the success and timing of our preclinical studies and clinical trials; the performance of third-party manufacturers and contract research organizations; our plans to develop and commercialize our product candidates; our plans to advance research in other kidney disease applications; and, our ability to obtain and maintain intellectual property protection for our product candidates. 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.