

### Developing New Therapies To Slow Progressive Kidney Disease

May 2023





BÖRSE FRANKFURT : ANU



### **Forward Looking Statements**

Certain information included in this Presentation constitutes forward-looking information or forward-looking statements under applicable securities legislation ("**forward-looking statements**"). These statements relate to future events or future performance of the Company. Forward-looking statements are statements that are not historical facts and are often, but not always, identified using words or phrases such as "can", "continue", "develop", "expect", "forecast", "future", "may", "milestone", "plan", "potential", "proposed", "will" and other similar expressions. In particular, but without limiting the foregoing, this Presentation contains forward-looking statements pertaining to, among other things: the industry in which Company operates, including the value thereof; strategic plans, including the timing and results thereof; the effects of end-stage renal disease and onset delay of end-stage renal disease; timing and occurrence of certain milestones, including the success of preclinical studies and clinical trials; and the Company's products, services and assets, including the benefits thereof. In addition, this Presentation may contain forward-looking statements attributed to third party industry sources.

By their nature, forward-looking statements involve known and unknown risks, uncertainties, and other factors that may cause actual results or events to differ materially from those anticipated. Such forward-looking statements are provided for the purpose of providing information about management's current expectations and plans relating to the future. Readers are cautioned that reliance on such statements may not be appropriate for other purposes, such as making investment decisions. These factors and risks include, without limitation: incorrect assessments of the value of acquisitions, licenses and development programs; technical, manufacturing and processing problems; actions by governmental authorities, including increases in taxes; the availability of capital on acceptable terms; fluctuations in foreign exchange, currency, or interest rates and stock market volatility; failure to realize the anticipated benefits from licenses or acquisitions; and potential labor unrest. This list is not exhaustive of the factors that may affect any of the Company's forward-looking statements. Some of the important risks and uncertainties that could affect forward-looking statements are described further under the heading "Key Information - Risk Factors" in its annual report on Form 20-F filed with the Securities and Exchange Commission and under the heading "Risks Related to the Business" in its management's discussion and analysis filed as an Exhibit to its annual report on Form 20-F, which annual report is available on www.sec.gov.

With respect to forward-looking statements in this Presentation, the Company has made assumptions, regarding, among other things: the availability of capital to fund planned expenditures; prevailing regulatory, tax and environmental laws and regulations; the ability to secure necessary personnel, equipment, supplies and services; the Company's ability to manage the Company's growth effectively; the absence of material adverse changes in the Company's industry or the global economy; trends in the Company's industry and markets; the Company's ability to maintain good business relationships with the Company's strategic partners; the Company's ability to comply with current and future regulatory standards; the Company's ability to protect the Company's intellectual property rights; the Company's ability to manage and integrate acquisitions; the Company's ability to raise sufficient debt or equity financing to support the Company's continued growth.

Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, such statements are not guarantees of future performance and actual results may differ materially from those in forward-looking statements. Undue reliance should not be placed on forward-looking statements because the Company can give no assurance that such expectations will prove to be correct and such statements are based on the beliefs, estimates and opinions of the Company's management on the date such statements are made. Many factors could cause the Company's actual results, performance or achievements to vary from those described herein. Should one or more of these risks or uncertainties materialize, or should assumptions underlying forward-looking statements prove incorrect, actual results may differ materially from those described in this Presentation as intended, planned, anticipated, believed, estimated or expected.

The forward-looking statements included in this Presentation are expressly qualified in their entirety by this cautionary statement. The Company cautions that the foregoing lists of assumptions, risks and uncertainties are not exhaustive. The forward-looking statements contained in this Presentation are made as of the date hereof and the Company undertakes no obligation to update publicly or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by applicable securities laws.

### **Investment Summary**

- The global end stage renal disease market was valued at USD 74.5 billion in 2020 and is expected to expand at a compound annual growth rate (CAGR) of 12.7% from 2021 to 2028 <sup>(1)</sup>.
- Developing drug-based therapies for serious progressive kidney diseases with a high unmet medical need, including ADPKD, T2DN and AKI due to COVID-19.
- A growing patent portfolio based upon key discoveries, using proprietary small molecule technology accompanied by broad therapeutic claims.
- Near term potential for significant licensing deal;



XRX-101 XORTX THERAPEUTICS INC

for Autosomal Dominant Polycystic Kidney Disease (ADPKD > 150 k patients in the US) where there are very limited treatment options and expected to initiate Ph3 pivotal registration clinical trial within 12 months AKI due to Coronavirus infection/ COVID-19 (WW Pandemic) XRX-225

for type 2 Diabetic Nephropathy (T2DN > 12 m patients in the US)

- Senior R&D team was responsible for Oxypurinol development in prior ventures.
- Management and Board of Directors with multiple high value Partnership Successes/ Exits



### First-in-class Product Candidate Ready for Ph3 Clinical Trials of Xanthine Oxidase Inhibitor for ADPKD

### **XORTX Therapeutics, Inc.**

XORTX Therapeutics is a publicly traded company (NASDAQ: XRTX) with a proprietary Xanthine Oxidase (XO) inhibitor pipeline targeting serious progressive kidney diseases via reduction of uric acid levels

**XORTX's pipeline targets areas of high unmet medical need**, including Autosomal Dominant Polycystic Kidney Disease (ADPKD), Acute Kidney Injury (AKI) due to COVID-19, and Type 2 Diabetic Nephropathy (T2DN).



End-stage Renal Disease (ESRD) market valued at \$75B globally in 2020 with a CAGR of 13% from 2021-20281

Management team was responsible for Oxypurinol development in prior ventures and company has engaged leading renal key opinion leaders on Clinical Advisory Board (see Appendix)



### **Consistent Clinical & Regulatory Progress**

#### Milestones & Value Creation → XRx-008

2023/2024 - continued progress coming over the next 4 quarters

- A. POSITIVE TOPLINE RESULTS RELEASED PK Bridging Clinical Trial (Jan, 2023)
- B. FDA GRANTED Orphan Drug Designation (ODD) for Oxypurinol in ADPKD (April, 2023)
- C. POSITIVE Type D meeting with FDA CONFIRMS Eligibility for ACCELERATED APPROVAL (May, 2023)
- D. Invited presentation at PKD Foundation meeting June Denver
- E. Initiation of Phase Registration Trial for XRx-008 in individuals with ADPKD (accelerated approval);
- F. Potential significant licensing deal;
- G. Special Protocol Assessment ("SPA") TBD and,
- H. Novel Patent Filings in preparation ADPKD discoveries; Dose ranging; New NCE Drug Candidates



### Designed to Slow the Decline in Renal Function

#### **Product Candidate Summary**

- XORLO<sup>TM</sup> Novel, proprietary, well tolerated oral formulation of oxypurinol.
- Oxypurinol is a Past recipient of NDA Approvable Letter.

#### Differentiation

- Oxypurinol is minimally metabolized and excreted unchanged. Few Liver Toxicity signals observed in over 700 patients.
- Combined extracellular and intracellular action of XRx-008 is fundamental.
- Potential to modify underlying disease pathology supported by third-party clinical trials in over 700 patients with no reported adverse events unique to oxypurinol.



### XORTX Technology: Xanthine Oxidase Inhibitor for Aberrant Purine Metabolism and Increased Uric Acid



**Xanthine Oxidase** 



### **Common ADPKD Progression & Symptoms**



- Pain and Discomfort
  - Cysts put pressure on abdomen and impinge on organs
- Liver cysts (40%);
- 10X increase in Neurologic Aneurisms;
- Increased Cardiovascular disease
- Hypertension
- Kidney Stones
- Bleeding into Cysts
- Increased Cyst Infections
- Declining Renal Function  $\rightarrow$  End Stage Kidney Disease
- Proteinuria increased urine protein loss

### Aberrant Purine Metabolism and Chronically Increased Uric Acid is Associated with Kidney Injury and Failure

#### Uric Acid Crystals – Mechanism of Injury 1 of 2

NORMAL





Aberrant Purine Metabolism and Dietary Sources of Uric Acid Such As Fructose, Foods Containing Yeast, Oily Fish, Shellfish and Organ meats.



IMPAIRMENT

2. Uric Acid Crystals Form in Kidneys. Uric Acid Crystals 2' "seed" Oxalate crystal formation.







3. Acute Kidney Failure is caused by elevated uric acid in plasma and crystal formation in multiple organs including heart, lungs, skin and eyes.



# ADPKD's Disease Progression Driven by Growth of Renal Cysts, Tissue Uric Acid and Loss of Glomeruli

#### Insoluble XO and UA effects - Mechanism of Injury 2 of 2



C XORTX THERAPEUTICS INC.

#### <u>Translational Evidence in Man, Mouse & Rat aligns</u> Xanthine Oxidase & Serum Uric Acid →ADPKD Mechanism of Injury

Health: Xanthine Oxidase (XO) Enzyme Breaks Down Purines into Uric Acid for excretion

Kidney Disease: Xanthine Oxidase (XO) increased in Serum (ADPKD & Diabetic Nephropathy)



Evidence suggests that XORLO<sup>™</sup> may slow progression of kidney disease Stage 2,3,4 ADPKD: (mild to severe)

## **Designed to Slow the Decline in Renal Function**



- Serum uric acid concentrations are higher in ADPKD patients than in non-ADPKD patients with CKD. (Mejias et. Al. Hyperuricemia, Gout, and Autosomal dominant polycystic kidney disease Am. J. Med Sci 1989: 297 145-148)
- Higher SUA is associated with increased kidney volumes, increased End-Stage Renal Disease (ERSD) and ADPKD disease progressions. (Helal, 2013, Han, 2014)
- Increased SUA is strongly associated with endothelial dysfunction via decreased nitric oxide bioavailability. (Khosla, 2005. Zoccali 2006, Kurowska 2002, Portaluppi 2004)
- In early stage ADPKD patients, uric acid levels and eGFR are independent predictors of endothelial dysfunction. (Kocygit et al. Clinical Practice. Nephron Clin Pract 123: 157-164, 2013)

Xanthine Oxidase Inhibition in ADPKD Patients is Associated with a Reversal of Glomerular Filtration Rate Decline – an FDA approvable endpoint -





### The Effect of Xanthine Oxidase Inhibition On Chronic KD Progression

Effect of 2 years XOI treatment, 100 mg daily (n=113:56;57)





## **US FDA Orphan Drug Status & Validation**

#### **Orphan Drug Grant: Key Scientific Criteria for Approval**

- I. **Mechanism of Injury (MOI)** exists in models of Autosomal Dominant Polycystic kidney disease.
- a) Xanthine Oxidase (XO) enzyme expression in Kidney
- b) Hyperuricemia accelerates disease progression

II. The **<u>identical</u>** drug formulation inhibits the MOI in a substantial and statistically significant manner.

#### Demonstrated

#### Over-Expression of XO in PKD kidney

Hyperuricemia Accelerates TKV & GFR decline

Oxypurinol attenuates both TKV and GFR progression.

#### Key Benefits of Orphan Drug Status:

- 7 years Market Exclusivity
- Premium Pricing of Product
- 25% Tax Credit on Revenues
- Reduced FDA application fees ( ~\$2M)
- Funding Support through Grants

### US FDA Type D meeting: <u>Confirmed</u> that the XRx-008 program for ADPKD is eligible for <u>Accelerated Approval</u>

 Is Total Kidney Volume(TKV) or Glomerular Filtration Rate (GFR) eligible for Accelerated Approval if demonstrated after 1 year of treatment → "YES"

### Milestone Timeline (Milestones in Black Text are Anticipated / Planned)



-	2022	2023 Q1	2023 Q2			Q3			Q4		
CMC — Mfg Drug Substance & Drug Product			Clinical Trial Drug Supply mfg						Commercial Drug Supply & Mfg		→ →
Clinical Development	Trial Completed	+ve Topline				XO Overexpression Studies in		T2DN			
		reported						ADPKD			
						ADPKD & 12DN					
FDA Reg	ADPKD – IND granted			US FDA – ODD granted	Accelerated Approval Confirmed	Assessment ("SPA")					
	EU – EMA					Orphan Drug Designation					
EIVIA Keg											
ADPKD							Phase 3 - protocol		FDA & EMA Protocol review	Ph 3 - 1	<sup>t</sup> Patient
PII 5 -Neg							Finalization		Ph3 Site Initiation	recruite	d/dosed
Licensing											
Conferences: IR/PR				AGP - Conf Singular - Conf	NPR - Interview		BIO – Boston PKD Fndtn – Denver				



### **Clinical Development Plan**

2023		2024			2025			2026			2027			•••		2029			2030									
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4

Two registrational trials approach enables staging of investment and earlier accelerated approval<sup>1</sup>



1. As compared with single registrational trial (see Appendix)

2. Randomized sample size (dose titration sample sizes larger)

3. Represents 6-month review timeline (e.g., Priority Review)



### $\mathsf{ADPKD} \to \mathsf{ESTIMATED} \ \mathsf{ADDRESSABLE} \ \mathsf{MARKET} \ \textbf{-} \ \mathsf{US}$



### ADPKD – Only One Therapy is Approved, Consequently, Suboptimal Treatment Options Remain

- 150,000 patients diagnosed with ADPKD in the US <sup>(1)</sup>
- ADPKD is the largest kidney disease market with a genetic origin
- A majority of ADPKD patients require dialysis or kidney transplantation
- Otsuka's JYNARQUE® (tolvaptan) was approved in 2018 for the treatment of ADPKD with black box warning "for risk of serious liver injury".
- Annual Treatment Cost of JYNARQUE® (tolvaptan) ~\$156,000. Otsuka reported 2022 sales of tolvaptan of \$962 m, ~8,000 ADPKD patients (~5%) are treated with tolvaptan each year. <sup>(2)</sup>
- 85% of ADPKD patients can't take or tolerate JYNARQUE® (tolvaptan) <sup>(3)</sup>

### **Competitive Landscape**

### DRUG

Tolvaptan (oral vasopressin V2 antagonist) Otsuka Pharma

Lixivaptan (oral vasopressinV2 antagonist) Centessa Pharma

#### **Bardoxolone**

(oral Nrf2 activator) Reata Pharmaceuticals Inc.

#### **GLPG2737**

(a Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) inhibitor)

#### Galapagos



Black Box Warning - Liver toxicity Extremely low usage du to tolerability

#### ABANDONED (May2023) Phase III

Phase II

#### IN DEVELOPMENT

Preparing to Enter Phase III

#### **ABANDONED** (Apr2022)

**STATUS** 

#### **FDA-APPROVED**

Phase III

### **Capitalization Table**

#### Capitalization as of March 31, 2023

Fully Diluted Shares TOTAL:	29,608,818			100.00%
Options Outstanding:	1,039,335	C\$2.03	C\$2,109,850	3.51%
Warrants Outstanding:	10,579,796	USD\$2.97	\$31,421,994	35.73%
Common Shares Outstanding (Other):	17,989,687			55.55%
Common Shares Outstanding (Insiders):	1,541,987			5.21%
	# of Shares	WAEP	C\$ Value	% of Fully Diluted

#### CURRENT CASH: ~\$8.0 M USD



### Investment Summary Uric Acid Lowering Agents Use in Kidney Disease

- XORTX is poised to advance therapies into the global markets at a time when the global end stage renal disease market is expanding rapidly and yet, few therapeutic options exist.
- XORTX is developing a potential first-in-class therapeutic solution for ADPKD, with a unique mechanism of action, focused on slowing the progression of kidney disease.
   XORTX THERAPEUTICS INC.
- We believe Key Regulatory and Clinical milestones ahead and Pharma Partnership opportunities will support the evolution of XORTX into a high value company.
- We believe the successful completion of a Ph3 trial in ADPKD, requiring only 1 year of treatment will
  permit submission of a registration application to the FDA for accelerated marketing approval in the US.

XORTX's technologies are supported by management's disciplined strategy to generate IP, clinical data, reimbursement, manufacturing and commercial infrastructure



### **Contact Us**

### **XORTX** Therapeutics Inc.

### **Redefining Kidney Disease**









#### **XORTX** Therapeutics Inc.

3710, 33st NW Calgary, Alberta T2L 2M1 Ph: +1 (403) 455-7727 info@xortx.com www.xortx.com









### **Management Team**



#### Dr. Allen W. Davidoff, Ph.D., Chief Executive Officer

Dr. Davidoff has 20 years of drug development experience and is the founder and CEO of XORTX. Allen has a broad range of clinical and regulatory experience and senior management experience in pharmaceutical R&D. Previously, Allen was co-founder, CSO at Stem Cell Therapeutics Corp. which merged with Trillium and thereafter was acquired by Pfizer. Prior to his role at Stem Cell, Allen was Senior Scientist/Head of Pharmacology at Cardiome Pharma Corp. Allen earned his PhD in Cardiovascular Physiology and Biophysics at University of Calgary.



#### Dr. Stephen Haworth, MD, Chief Medical Officer

Dr. Haworth has >25 years of successful global drug development and senior leadership in both "start-up" and Fortune 500 pharmaceutical firms in both the US and Europe. Stephen has a broad clinical and regulatory experience that ranges from nephrology, cardiovascular, and infectious disease. He has extensive regulatory experience with FDA and EMA submissions, as well as licensing and M&A transactions. Stephen holds a MD from University College Hospital Medical School, University of London, having graduated with Honors.

#### Dr. Taryn Boivin, Ph.D., Head Chemistry, Manufacturing and Controls (CMC)

Dr. Boivin is a pharmaceutical veteran with >30 years of experience leading all aspects of CMC and related disciplines. Her experience includes multiple worldwide drug submissions, post approval support activities, and commercial supply chain operations. Early in her career, Taryn was among a key group of leaders who established the Glaxo Canada (later GSK) pharmaceutical development organization, and was a pivotal contributor to this world-class research, development, and manufacturing facility. Dr. Boivin has held numerous Senior VP positions in large and small biopharma.



Amar Keshri has >15 years of accounting and finance experience in a number of sectors including the life science and oil and gas industries. His public practice audit, finance and accounting consulting roles include experience with Suncor, PWC, LLP and Ernst & Young. Mr. Keshri is a Member of the Institute of Chartered Accountants of Alberta.

#### Dr. Stacy Evans, M.D., MBA Chief Business Officer (Consultant)

Dr. Evans has >20 years of commercial development and business development experience, including 12 years at Pfizer where he was last responsible for leading transactions across all TAs. Stacy has been consulting at an executive level for small to mid-size private and public biopharma companies for the past 7 years including as part-time Chief Business Officer for Avillion, LLP, a Blackstone-backed late-stage financing and co-development company. Stacy holds a MD from McGill University and an Executive MBA from Columbia University.





### **Board of Directors**

#### Anthony Giovinazzo – Chair

43 years of total work experience, is an internationally recognized expert in intellectual property, drug development and commercialization, including numerous licensing agreements, with more than 25 years' experience in Central Nervous System diseases. Co-inventor, Chief Executive Officer and Director of Cynapsus Therapeutics, led a NASDAQ listed specialty pharmaceutical company that developed the first successful sublingual apomorphine thin film strip for Parkinson's disease and led a highly successful exit of Cynapsus by way of a 120% premium to market of an \$841 MM all cash M&A deal. Mr. Giovinazzo is currently Executive Chairman of Kalgene, and director of Titan Medical Inc.

#### Dr. Allen W. Davidoff Ph.D. – President and CEO

Over 19 years drug development experience) is the founder and CEO of XORTX. Allen has a broad range of clinical and regulatory experience and senior management experience in pharmaceutical R&D including four investigational new drug ("IND") applications or supplemental IND's, two phase I studies (four of which were multi-country), eight phase II studies, and one NDA. Prior to co-founding XORTX, Allen was the Chief Scientific Officer, VP Product Development and co-founder of Stem Cell Therapeutics Corp. (seven years) Trillium TRIL:NASDAQ acquired by Pfizer and Senior Scientist and Head of Pharmacology at Cardiome Pharma Corp.

#### **Dr. Raymond Pratt**

Raymond Pratt is an accomplished Physician Executive in clinical medicine, Nephrology, drug development, and the pharmaceutical industry. He has extensive experience troubleshooting issues concerning regulatory approval of drugs and devices and providing development strategies for global pharmaceutical companies.

#### Paul Van Damme

Held senior positions with a number of Canadian and US public companies. His experience focused on the biotech industry in Toronto when he joined GlycoDesign, a private biotech company. While at Allelix Pharmaceuticals Inc., he participated in the sale of that company to NPS Pharmaceuticals, Inc.

#### **William Farley**

Over 35 years experience in the Business Development, Sales and leading efforts in drug discovery, development and partnering. Prior to joining the board of directors of XORTX, Mr. Farley held a senior leadership position at Sorrento Therapeutics. Bill, began his career at Johnson and Johnson and has held sr. mgmt. positions at Pfizer and HitGen Ltd., V. P., WuXi Apptec, Inc., V.P., Business Development at ChemDiv.

#### lan Klassen

Brings almost 30 years of business management, public relations and government affairs experience. He previously served as Chief of Staff to the Canadian Speaker of the House of Commons. Ian is the recipient of the Commemorative Medal for the 125th Anniversary of the Confederation of Canada in recognition of his significant contribution to his community and country.

#### Jacqueline Le Saux

A seasoned Canadian health care legal executive who has held senior positions at large and small public and private life science companies. Jacqueline's legal experience is focused on securities, pharmaceutical regulatory and intellectual property law. As a Vice President, Legal in both public and private companies Ms. Le Saux has led multiple financings, mergers and acquisitions and product licensing transactions.



### **Clinical Advisory Board**

Dr. Petter Bjornstad, M.D.

University of Colorado Denver School of Medicine Barbara Davis Center.

**Dr. Richard Johnson, M.D** Professor of Medicine and the Chief of the Renal Division and Hypertension at the University of CO.

**Dr. Anjay Rastogi, M.D., Ph.D.** Professor and Clinical Chief of Nephrology at the David Geffen School of Medicine at UCLA, Los Angeles, CA.

**Dr. Federico Maese, M.D.** Cardiology Specialist in Red Oak, TX.

**Dr. Henk ter Keurs, M.D.** Professor of Cardiac Sciences, Medicine at the University of Calgary.

#### Dr. Charles Edelstein, M.D., Ph.D.

Professor of Medicine and Nephrologist at the University of Colorado. Dr. Edelstein is board certified in Nephrology and has a doctoral degree (PhD) in Internal Medicine. He did his Internal Medicine residency and Nephrology fellowship at University of Stellenbosch and University Cape Town Medical School, respectively. His academic research focuses on both therapeutic studies in animal models of polycystic kidney disease (PKD) as well as acute kidney injury (AKI) and biomarkers of AKI. Dr. Edelstein is a world leader in PKD research and PKD care and has received an award for the WSCI Outstanding Investigator Award and is a former president of the Western Section of the American Federation of Clinical Research and International Society of nephrology member and American Society of Nephrology Advisory Committee Member.



### Designed to Slow the Decline in Renal Function

- XRx-008 in progressive kidney disease designed to decrease uric acid & attenuate loss of filtering capacity of kidneys.
- A potential therapeutic option to maintain and extend kidney health can redefine kidney disease treatment in the future.
- JYNARQUE® effect focuses on minimizing cyst/kidney volume. The FDA approvable endpoint is based upon slowing loss of filtering capacity of kidneys.

#### End-Stage Renal Disease (ESRD) A Life Altering Event

- 4 hour dialysis 3 times per week
- Loss of ability to work full time
- Dependence on family
- Pain and declining health are constant burden
- Shortened survival only 50% of patients survive two years



Days after eGFR fell below15 ml/min