# Thryv Therapeutics Announces Positive Results from the WAVE 1 Proof of Concept Study in Long QT Syndrome. LQT-1213 Rapidly and Meaningfully Reduces QT Interval in Individuals with Prolonged QT induced by Dofetilide.

**Montreal, Quebec – August 25th, 2023** – Thryv Therapeutics Inc. today announced positive results of the WAVE 1 Proof of Concept clinical study evaluating LQT-1213 for the reduction of QTcF in individuals with dofetilide-induced long QT. LQT-1213 is a potent and selective inhibitor of Serum Glucocorticoid inducible Kinase 1 (SGK-1), which is implicated in QTc prolongation.

Long QT Syndrome, or LQTS, is a disorder of the heart's electrical system causing the lower chambers of the heart to contract and release too slowly. LQTS can be either congenital or acquired. Congenital LQTS is a set of rare orphan diseases in which people are genetically predisposed to chronic prolongation of their QTc interval (commonly more than 480 milliseconds), leading to increased risk of torsades de pointes, a lethal cardiac arrhythmia that causes sudden cardiac death. Acquired Long QT may develop from the administration of therapies which block electrical pathways in the heart, leading to a similar mechanistic prolongation of QT and risk of sudden cardiac death.

In the WAVE 1 study, mean reductions in QT from baseline (measured as QTcF) were statistically significant beginning at the two-hour time-point on day four of LQT-1213 dosing. In a predefined subset of individuals who experienced larger dofetilide-induced prolongation of QTcF, individuals treated with LQT-1213 achieved more robust, clinically meaningful reductions of QT consistent with scientific evidence of SGK-1 activation in LQTS. LQT-1213 was well tolerated with no serious adverse events or treatment related study discontinuations. No QTcF over-shortening was observed in the study. There were no observed changes in ECG morphology, heart rate, or blood pressure. The company plans to present full data from the study at an upcoming scientific meeting.

"Over the past few years, our research has continued to validate the pathogenic role of SGK-1 in rare arrythmias. We now have the first in human evidence of the benefits of targeting this activated kinase to reduce prolonged QTc," commented Philip Sager, MD, Chief Medical Officer of Thryv Therapeutics. "With this initial safety and efficacy data in hand, clinical testing can commence in people with Congenital Long QT Syndrome Types 2 and 3, where chronic and substantial QTc prolongation can lead to lethal ventricular arrhythmias."

In preclinical studies of dofetilide-induced long QT or in experiments utilizing stem cells from individuals with congenital Long QT Syndrome Type 2 and Type 3, LQT-1213 reproducibly and

markedly reduced the QTc and APD and, in some cases, fully corrected pathogenic prolongation without any instances of over-shortening.

“Serum and glucocorticoid regulated kinase (SGK) activity is upregulated in patient-specific induced pluripotent stem cell–derived cardiomyocytes stemming from Long QT Syndrome,” commented Saumya Das, MD, PhD, and Principal Scientific and Medical Advisor of Thryv Therapeutics. “Activation of SGK-1 in the heart markedly increases the late sodium current preferentially leading to prolongation of the action potential duration and an increased propensity to develop arrhythmias. This latest data builds further on our understanding of the potential for SGK-1 inhibition to provide a new option for individuals with Long QT Syndrome.”

Part two of the WAVE 1 study is currently enrolling a small cohort of patients with congenital Long QT Syndrome Types 2 and 3. The company anticipates finalizing the results of part one of this study in the coming weeks and discussing the path to registration with the US FDA in early 2024. Pivotal studies in patients with congenital Long QT Syndromes are anticipated to begin in 2024.

“My daughter’s journey with Long QT Syndrome Type 3 ended abruptly and tragically in December of 2022. Isla had a very aggressive form of Long QT and despite multiple interventions, shocks from her defibrillator, and unapproved medicines, she was a happy girl who touched the lives of so many. I’m beyond happy to know that help is on the way, and I know she would be too,” commented David Hutton of Bury, United Kingdom. David is a founder and trustee of Team 1C, a charity dedicated to raising funds to help parents and families with healthcare costs. David’s daughter, Isla, passed away at the age of six and a half. She was diagnosed with Long QT Syndrome Type 3 at birth.

**About WAVE 1**

Part one of the WAVE 1 crossover study included twenty-three (23) trial completers who received high dose dofetilide, which prolongs QTc and acutely imitates congenital Long QT Syndrome. During the two eight-day clinical study periods individuals received doses of dofetilide and either placebo or three increasing doses of LQT-1213 in a crossover design. Rigorous QTc analyses were performed on days four, six, and eight. Changes in study participants’ QTc on day four, six and eight were compared to their own placebo time periods throughout the course of the study.

Part two of the WAVE 1 clinical study is currently enrolling a small cohort of individuals with genetically proven Congenital Long QT Syndrome Type 2 and Type 3. This study will provide information about the safety of LQT-1213 before initiation of clinical studies in congenital LQTS

patients. More about the WAVE 1 (part 1 and 2) can be found at https://www.clinicaltrials.gov/study/NCT05906732.

**About Long QT Syndrome**

Congenital Long QT Syndrome (LQTS) is a rare genetic condition that causes a prolongation between the beginning of the ECG QRS complex and the end of the T wave, representing cardiac repolarization. The lengthening of the interval can lead to unexpected and life-threatening arrhythmias called torsades de pointes. Studies have demonstrated a direct correlation between the length of the QTc interval and the risk of sudden cardiac death in LQTS patients. Shortening this interval would result in a reduction of sudden death, syncope, and cardiac arrhythmias in patients with Congenital Long QT Syndrome. More information about Long QT Syndrome can also be found at www.sads.org.

**About Thryv Therapeutics**

Thryv Therapeutics Inc. is a privately owned, clinical stage company based in Montreal, Quebec, Canada. Thryv Therapeutics is pioneering a precision medicine approach to treat genetic and drug-induced Long QT Syndromes, atrial fibrillation, and resistant cancers with potent and selective inhibitors of Serum Glucocorticoid inducible Kinase. For more information, please visit www.thryvtrx.com.