# Thryv Therapeutics Announces Significant Progress Across all Programs within its SGK1 Inhibitor Portfolio and the Closing of a Convertible Note Financing with Investissement Québec

- **Long QT Syndrome: Completion of dosing in the WAVE-1 drug induced Long QT Syndrome study enables enrollment of in-patient, safety cohort of Long QT Syndrome patients.**
- **Oncology: New in vivo data with Thryv's lead oncology compound in combination with standard of care or added to standard of care following development of tumor resistance, demonstrated rapid tumor regression in Anaplastic Thyroid Carcinoma.**
- **A-Fib: US IND being prepared following encouraging findings from atrial fibrillation and anti-fibrotic model in obese mice with insulin resistance.**
- **$5 million convertible note financing by Investissement Québec, with an option to invest an additional $8 million at close of Series B.**

**Montreal, Quebec – June 6, 2023** – Thryv Therapeutics Inc. announced today the closing of a USD $5,000,0000 convertible note investment by Investissement Québec (IQ). Under certain conditions, the convertible note can be repaid or converted into equity at the company's next equity financing round, and includes an option for IQ to invest up to an additional $8,000,000 in the next equity financing round. The proceeds of the convertible note will be used to immediately accelerate Thryv's portfolio programs.

"While we await results from our initial proof of efficacy study this summer in Long QT Syndrome, we are able to accelerate a number of pipeline initiatives thanks to this new investment from IQ. The financing provides maximum flexibility to move forward on a number of fronts. We remain on track to obtain data from the WAVE-1 initial proof of efficacy in drug-induced Long QT Syndrome study this summer," said Paul Truex, Chairman and CEO.

The IQ convertible note Investment enables Thryv to commence a safety study in Long QT Syndrome Type 2 and Type 3 patients nine months earlier than planned. The study will enroll up to 12 Long QT Syndrome patients at the same clinical safety pharmacology unit previously used for Thryv's WAVE-1 study. This effort will allow the pivotal Long Qt Syndrome studies to be conducted remotely without patients having to travel to centralized hospitals for assessments – a limitation of previous trials.

Thryv has generated highly encouraging new in vivo animal data with its lead oncology compound demonstrating tumor regression in treatment resistant anaplastic thyroid carcinomas. This new data, coupled with helpful feedback from the US Food and Drug Administration regarding Thryv's

initial clinical plan, will allow the company to submit its Investigational New Drug Application (IND) this summer.

Finally, the company's atrial fibrillation preclinical program will now be completed six months early to allow for submission of an IND later this year. Thryv plans to initiate additional non-clinical studies in models of atrial fibrillation and heart failure later this year which will enable proof of concept studies to start in late 2024.

**About Long QT Syndrome**

Long QT Syndrome (LQTS) is a rare genetic condition that causes an elongation between the Q and T waves during a heartbeat. The lengthening of the interval can lead to unexpected and life-threatening arrhythmias called torsades de pointes. These arrhythmias are generally in response to exercise and stress. Data suggests that SGK1 is a prime target for shortening the QT interval and for regulating heart rhythm in LQTS Types 1, 2, and 3, which account for approximately 90% of all people with LQTS. Scientists and collaborators at Thryv have demonstrated that treatment of cellular and animal models of LQTS with SGK1 inhibitors can substantially reduce the potential for a prolonged QT interval. Studies have demonstrated a direct correlation between the length of increase in the QT interval and the risk of sudden death in LQTS patients, and shortening this interval would result in a reduction of sudden death and other cardiac arrhythmias.

**About Anaplastic Thyroid Cancer**

Anaplastic Thyroid Cancer (ATC) is a rare, aggressive thyroid cancer that represents less than 2% of thyroid cancer cases and represents a major unmet medical need. However, most patients present at stage IV with a median survival of 5 months, and a one-year overall survival rate of only 20% with current standard of care Mekinist® and Taflinar®.

Several groups have identified SGK1 to be upregulated and promote an AKT independent maintenance of PI3K/mTOR signaling. This continued signaling via SGK1 can be targeted to address resistance to the standard of care in this aggressive form of cancer. Recent preclinical and animal data generated by Thryv Therapeutics has demonstrated that, in addition to synergizing with PI3K, AKT, and mTOR inhibitors, SGK1 inhibition can also synergize with BRAF and MEK inhibitors, in various cancer cell lines with oncogenic mutations in KRAS or BRAF, as well as delay and overcome resistance to these inhibitors *in vivo*. Additionally, a previous study determined that SGK activity was critical for the proliferation of several ATC cancer cell lines regardless of their oncogenic drivers (BRAF, PIK3CA, RAS, PTEN).

Altogether, these results suggest that SGK1 is involved in the regulation of the crosstalk between the RAS/MAPK and PI3K/mTOR pathways and could represent a novel approach to address current resistance to therapies targeting these pathways, including Anaplastic Thyroid Cancer.

**About Atrial Fibrillation**

Atrial fibrillation is a global problem with worldwide prevalence of over 37 million cases, which is expected to further increase 60% by 2050. Obesity and metabolic diseases represent significant risk factors for the development of atrial fibrillation and are partially responsible for the increasing prevalence of atrial fibrillation. Fibrosis, inflammation, and ion channel alteration have been implicated in the pathogenesis of obesity-related atrial fibrillation and SGK1 is believed to play a contributory role to this disruption in normal cardiac function.

Data from an obese mouse model with insulin resistance has demonstrated upregulation of SGK1 activity in the mouse atria and plays a role in the adverse pathological mechanisms associated with atrial arrhythmogenesis. Inhibition of SGK1, both genetically and now for the first time, pharmacologically with a Thryv SGK1 inhibitor, demonstrated a reduction in fibrotic signaling and a reduction in NLRP3 inflammasome expression, and resulted in reduced atrial fibrillation. With the recent success of SGLT2 inhibitors, which have also demonstrated reduced fibrotic signaling and inflammasome expression, possibly via SGK1-mediated pathways, Thryv is accelerating its efforts to bring a potent SGK1 inhibitor forward for the treatment and prevention of obesity-related paroxysmal atrial fibrillation where additional therapeutic options are needed.

**About Thryv Therapeutics Inc.**

Thryv Therapeutics Inc. (previously LQT Therapeutics Inc.) is a privately owned 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.