

## Quark Pharmaceuticals RNAi Drug Succeeds in Phase 2 Study to Prevent Acute Kidney Injury Following Cardiac Surgery

- ***QPI 1002 Meets Primary & Multiple Secondary Endpoints***
- ***A statistically significant reduction in AKI incidence following cardiac surgery was demonstrated***
- ***First multicenter Phase 2 clinical study with an investigational drug for the prevention of AKI to meet primary endpoint***
- ***QPI-1002 appears to be well tolerated with no safety issues identified***

Fremont, CA – July 27, 2017 – Today, Quark Pharmaceuticals, Inc. announced successful completion of a randomized, double-blinded, placebo-controlled multicenter Phase 2 trial of QPI-1002, a synthetic chemically modified siRNA acting to temporarily reduce p53 expression, for the prophylaxis of acute kidney injury (AKI) following cardiac surgery (QRK-209; NCT02610283).

The study included 341 subjects of age 45 or greater undergoing cardiac surgery and at risk for AKI, randomized in a 1:1 ratio to QPI-1002 or placebo. The primary endpoint for the study, the proportion of subjects developing AKI through Day 5, based on the Acute Kidney Injury Network (AKIN) classification, was achieved, with QPI-1002 treatment significantly reducing the incidence of AKI.

The QPI-1002 treatment effect observed in the overall study population was consistent in predefined subgroups of subjects including those with chronic kidney disease (CKD), diabetes, and high-risk patients who underwent multiple cardiovascular surgical procedures. A statistically significant treatment effect was also seen for AKI defined by the RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) classification.

QPI-1002 appeared to be well tolerated in the study. QPI-1002 had similar rates of adverse events compared to placebo, with the most common events occurring in both treatment groups being those typically seen following cardiovascular surgery including pleural effusions, respiratory and infectious complications.

These trial findings support continued development of QPI-1002 for the prevention and amelioration of AKI associated with cardiac surgery in patients at risk for whom no approved therapy exists to date. Quark believes that QRK-209 study, enrolling hundreds of patients, is the first well-controlled clinical trial to achieve the primary endpoint of reduction of AKI. The data from this study will be submitted for presentation at an upcoming medical congress.

“Quark is developing QPI-1002 in a variety of indications associated with ischemia-reperfusion renal injury,” stated Dr. Shai Erlich, CMO and President Quark US Operations. “We are excited about the QRK-209 study results which reinforce the positive effect of QPI-1002 as previously reported in a randomized, double-blind, placebo-controlled multicenter

Phase 2 study (QRK-006b; NCT00802347) where QPI-1002 was shown to reduce the incidence and severity of delayed graft function (DGF) in patients undergoing renal transplantation[1]. The results of these two studies validate Quark's vertically integrated Discovery-to-Development Platform and supports Quark as a leader in the field of siRNA therapeutics. QPI-1002 is currently being evaluated in a Phase 3 clinical study (QRK-306; NCT02610296) for the reduction of DGF incidence and severity."

"AKI is one of the major complications following cardiac surgery and is associated with increased hospitalization, development of chronic kidney disease and higher post-surgical mortality. There is currently no approved treatment for the prevention of AKI," observed Dr. Bruce A. Molitoris, Distinguished Professor of Medicine and Cellular and Integrative Physiology Indiana University School of Medicine and past president of the American Society of Nephrology. "The results of the Quark QRK-209 study are encouraging and bring us closer to having a treatment that would reduce AKI incidence which represents a significant advance in patient care."

### **About Acute Kidney Injury (AKI)**

AKI is a serious clinical condition that complicates approximately 5% of hospital admissions and up to 30% of admissions to intensive care units. In patients undergoing major cardiovascular surgery, post-surgical AKI develops within hours to days as a result of ischemic conditions caused by reduced local blood flow to the kidneys during surgery and so-called reperfusion injury following restoration of the blood flow. The rate of AKI development in most patients undergoing cardiovascular surgery is low, but the rate can be as high as 22-39% (depending upon AKI definition) in high-risk patients. The 30-day mortality rate following onset of AKI after surgery is greater than 50%[2]. The prognosis among patients requiring dialysis after cardiac surgery is poor, with an increased mortality risk exceeding 60%, however, the risk of short and long term mortality is increased up to 4-fold in patients who develop non-dialysis requiring AKI compared to patients with normal renal function after cardiac surgery[3]. AKI is an unmet medical need, with no specific treatment available.

### **About QPI-1002**

QPI-1002 is the first systemic siRNA drug to enter human clinical trials and to complete several well-controlled clinical studies with efficacy endpoints that were conducted in hundreds of patients. It is an investigational drug designed to temporarily inhibit the expression of the pro-apoptotic gene, p53, to protect normal cells from death stemming from acute tissue injury. Preclinical studies have shown that p53-targeted siRNAs can protect kidneys from ischemia-reperfusion injury in a variety of clinically relevant animal models. QPI-1002 has been granted Orphan Drug designation in the USA and Europe for prophylaxis of delayed graft function following kidney transplantation. Under an August 2010 agreement, Novartis has an exclusive worldwide license option for the development and commercialization of QPI-1002.

### **About Quark Pharmaceuticals, Inc.**

Quark Pharmaceuticals, Inc is one of the world leaders in discovery and development of novel siRNA therapeutics. Such therapeutics act via engaging a natural mechanism of inhibition of target gene expression, RNA interference (RNAi). The Company's fully integrated drug discovery and development platform spans from therapeutic target identification to drug development. In addition to QPI-1002, Quark has clinical development programs in several ophthalmology indications as well as a rich pre-clinical pipeline.

Quark is headquartered in Fremont, California and operates a research facility in Ness-Ziona, Israel.

For additional information please visit: [www.quarkpharma.com](http://www.quarkpharma.com)

[1]Am Jour Trans vol14 S3 p153 abstract #2967

[2] Cardiorenal Med 2013;3:178-199, (DOI:10.1159/000353134)

[3] The Annals of Thoracic Surgery 93.1 (2012): 337–347. PMC. Web. 6 Sept. 2015