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ArQule Announces Dosing in a Registrational Trial of FGFR Inhibitor, Derazantinib, for Treatment of Intrahepatic Cholangiocarcinoma

The trial is being conducted with a biomarker assay to identify FGFR2 fusions

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced dosing of the initial patients in a registrational trial with its FGFR inhibitor, derazantinib (ARQ 087) in FGFR2 fusion driven second-line intrahepatic Cholangiocarcinoma (iCCA). The trial is planned to enroll up to 100 iCCA patients and provides an opportunity for a conditional approval as part of a fast-to-market strategy. Derazantinib is a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family.

The open-label single-arm trial will be recruiting initially in the U.S. and subsequently in Europe with objective response rate (ORR) as the primary endpoint. Derazantinib will be dosed orally once a day at 300 mg. FGFR2 fusion status will be determined by a break apart FISH assay. An interim analysis will be performed after the first 40 patients have been enrolled and evaluated for response.

"iCCA is a rare and difficult disease to treat," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "The durable response rate of 21% we observed in the phase 1/2 iCCA FGFR2 fusion driven trial has lead us to design the first registrational trial with a biomarker for this patient population. We are happy to report that recruitment is off to a great start with four patients already dosed."

Patients with advanced iCCA who relapse after first-line multi-agent chemotherapy have limited treatment options with poor prognosis. In recent years, FGFR2 fusions have been recognized as a potential iCCA-specific therapeutic target. The company has been granted orphan drug designation by the U.S. Food and Drug Administration and European Medicines Agency for derazantinib in this indication.

About Intrahepatic Cholangiocarcinoma

Cholangiocarcinoma (CCA) is the most common biliary malignancy and the second most common hepatic malignancy after hepatocellular carcinoma (HCC)[1]. Depending on the anatomic location, CCA is classified as intrahepatic (iCCA), perihilar (pCCA), and extrahepatic (eCCA). iCCA originates from the intrahepatic biliary ductal system and forms an intrahepatic mass. The average age adjusted incidence rate for iCCA is approximately one in 100,000 per year in the United States and Europe[2,3].

About FGFR and Derazantinib (ARQ 087)

Derazantinib is a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor ("FGFR") family with demonstrated efficacy in FGFR2 genetic alterations. The FGFR pathway is disrupted in several ways in human cancer, thus providing numerous therapeutic targets for an inhibitor of this pathway. Derazantinib has demonstrated *in vivo* inhibition of tumor growth and downstream signaling in tumors whose growth is driven by FGFR.

Signals of single agent activity with this drug were observed in phase 1a testing. Phase 1b expansion cohorts with derazantinib include patients with cholangiocarcinoma and adrenocortical tumors, as well as those with FGFR translocations, amplifications and mutations. Clinical development of derazantinib advanced into phase 2 for intrahepatic cholangiocarcinoma (iCCA) in patients with FGFR2 fusions following the observation of two confirmed responses in this patient population in the phase 1 portion of the program and a registrational trial is being conducted in this same patient population.

About ArQule

ArQule is a biopharmaceutical company engaged in the research and development of targeted therapeutics to treat cancers and rare diseases. ArQule's mission is to discover, develop and commercialize novel small molecule drugs in areas of high unmet need that will dramatically extend and improve the lives of our patients. Our clinical-stage pipeline consists of five drug candidates, all of which are in targeted, biomarker-defined patient populations, making ArQule a leader among companies our size in precision medicine. ArQule's proprietary pipeline includes: Derazantinib, a multi-kinase inhibitor

designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in a registrational trial for iCCA and in phase 1b for multiple oncology indications; Miransertib (ARQ 092), a selective inhibitor of the AKT serine/threonine kinase, in a phase 1/2 company sponsored study for Overgrowth Diseases, in a phase 1 study for ultra-rare Proteus syndrome conducted by the National Institutes of Health (NIH), as well as in multiple oncology indications; ARQ 751, a next generation AKT inhibitor, in phase 1 for patients with AKT1 and PI3K mutations; and ARQ 761, a β-lapachone analog being evaluated as a promoter of NQO1-mediated programmed cancer cell necrosis, in phase 1/2 in multiple oncology indications in partnership with the University of Texas Southwestern Medical Center. In addition, we have advanced ARQ 531, an investigational, orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant BTK, in phase 1 for patients with B-cell malignancies refractory to other therapeutic options. ArQule's current discovery efforts are focused on the identification and development of novel kinase inhibitors, leveraging the Company's proprietary library of compounds. You can follow us on Twitter and LinkedIn.

Forward Looking Statements

This press release contains forward-looking statements regarding the Company's clinical trials with derazantinib. These statements are based on the Company's current beliefs and expectations, and are subject to risks and uncertainties that could cause actual results to differ materially. Positive information about pre-clinical and early stage clinical trial results does not ensure that later stage or larger scale clinical trials will be successful. For example, derazantinib may not demonstrate promising therapeutic effect. In addition, derazantinib may not demonstrate an acceptable safety profile in current or later stage or larger scale clinical trials as a result of known or as yet unanticipated side effects. The results achieved in later stage trials may not be sufficient to meet applicable regulatory standards or to justify further development. Problems or delays may arise during clinical trials or in the course of developing, testing or manufacturing derazantinib that could lead the Company to discontinue its development. Even if later stage clinical trials are successful, unexpected concerns may arise from subsequent analysis of data or from additional data. Obstacles may arise or issues may be identified in connection with review of clinical data with regulatory authorities. Regulatory authorities may disagree with the Company's view of the data or require additional data or information or additional studies. In addition, we plan to develop and use a companion diagnostic to identify patients with FGFR2 fusions and possibly other fusions for our future derazantinib clinical trials. We intend to outsource the development of such companion diagnostics to one or more third party collaborators. There can be no assurance that we will successfully enter into an agreement or agreements with any such collaborators; in addition, any such collaborator may encounter difficulties in developing and obtaining approval for such companion diagnostic, including issues relating to selectivity/specificity, analytical validation, reproducibility, concordance or clinical validation. Any delay or failure to develop or obtain regulatory approval of such companion diagnostic could delay or prevent approval of derazantinib. Drug development involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. Furthermore, ArQule may not have the financial or human resources to successfully pursue drug discovery in the future. For more detailed information on the risks and uncertainties associated with the Company's drug development and other activities, see the Company's periodic reports filed with the Securities and Exchange Commission. The Company does not undertake any obligation to publicly update any forward-looking statements.

[1] Welzel TM, et al. Impact of classification of hilar cholangiocarcinomas (Klatskin tumors) on the incidence of intra- and extrahepatic cholangiocarcinoma in the United States. *J Natl Cancer Inst.* **2006**; *98*(12),873-875.

[2] National Cancer Institute: Surveillance, Epidemiology, and End Results

[3] rarecarenet.eu

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