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ArQule Presents Phase 1/2 Clinical Data with ARQ 087 in Intrahepatic Cholangiocarcinoma at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting

83% disease control rate observed in intrahepatic cholangiocarcinoma FGFR2 positive patients

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that data from a phase 1/2 trial with fibroblast growth factor receptor (FGFR) inhibitor, ARQ 087, presented at ASCO demonstrate a meaningful clinical benefit to intrahepatic cholangiocarcinoma (iCCA) patients harboring FGFR2 fusions. The data show a robust response rate and prolonged duration of therapy for these patients well in excess of that reported for second-line chemotherapy. These data support future development of ARQ 087 as second-line treatment, and a registrational phase 3 trial in iCCA FGFR2 fusion positive patients is planned to begin in the third quarter of 2017. ARQ 087 is a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family.

The presentation titled "ARQ 087, an oral pan-Fibroblast Growth Factor Receptor (FGFR) inhibitor, in patients with advanced intrahepatic cholangiocarcinoma (iCCA) with FGFR2 genetic aberrations" can be viewed at https://www.arqule.com/wp-content/uploads/ARQ-087-101_Poster_ASCO-2017.pdf.

ARQ 087 Results from Phase 1/2 iCCA Trial Presented at ASCO

- The data is comprised of 35 iCCA patients harboring FGFR2 genetic alterations, of which 29 patients were FGFR2 fusion positive. All 29 of these patients were evaluable for this data presentation.
- The objective response rate for iCCA FGFR2 fusion positive patients was 21% (six partial responses) and the disease control rate was 83% (six partial responses and 18 patients with stable disease). Patients were evaluated using Standard RECIST (Response Evaluation Criteria in Solid Tumors).
- Clinical benefit was observed in 72% of FGFR2 fusion positive patients defined as partial response (six patients) and stable disease (15 patients) for at least 16 weeks.
- The median duration of therapy observed in iCCA FGFR2 fusion positive patients was 182 days. In these same patients, the median duration of front-line chemotherapy was 119 days.
- ARQ 087 showed a manageable safety profile with mostly Grade 1 and 2 adverse events.
- Nine patients with FGFR2 fusions are on-going in the trial.

"Clinical evidence is accumulating on the role of FGFR inhibitors in cholangiocarcinoma and other FGFR driven tumors such as urothelial and gastric cancers," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "We are encouraged to see that both the response rate and disease control rate were consistent throughout the trial. Patients with iCCA often have a poor prognosis for front-line treatment with chemotherapy, and there are no currently approved second-line therapeutic options."

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 ARQ 087 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 ARQ 087

ARQ 087 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. ARQ 087 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 ARQ 087 include patients with cholangiocarcinoma and adrenocortical tumors, as well as those with FGFR translocations, amplifications and mutations. Clinical development of ARQ 087 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 phase 3 registrational trial is planned to begin in the third quarter of 2017 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 four 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: ARQ 087, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in phase 2 for iCCA and in phase 1b for multiple oncology indications; ARQ 092, a selective inhibitor of the AKT serine/threonine kinase, in phase 1/2 company sponsored study for Overgrowth Diseases, in phase 1 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, through toxicology testing and plan to initiate a phase 1 trial by the third quarter of 2017. 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 ARQ 087. 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, ARQ 087 may not demonstrate promising therapeutic effect; in addition, these drugs may not demonstrate appropriate safety profiles 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 these compounds that could lead the Company to discontinue 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 and possibly other fusions for our future ARQ 087 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 ARQ 087. 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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