ArQule Announces Preliminary Results from Its Phase 1/2 Study of Miransertib (ARQ 092), in Patients with PIK3CA-related Overgrowth Spectrum (PROS) and Proteus syndrome (PS) in an Oral Presentation at the European Society of Human Genetics Conference

June 17, 2019

Encouraging preliminary safety and clinical activity data confirm miransertib's potential for treating PS and PROS patients

Registrational study, MOSAIC (Miransertib in Overgrowth Syndromes in Adults and Children), expected to begin enrollment in Q3 2019

BURLINGTON, Mass.--(BUSINESS WIRE)--Jun. 17, 2019-- ArQule, Inc. (Nasdaq:ARQL) today announced preliminary results from the company's phase 1/2 study of its pan-AKT inhibitor, miransertib (ARQ 092), in patients with PIK3CA-related Overgrowth Spectrum (PROS) and Proteus syndrome (PS) in an oral presentation at the European Society of Human Genetics Conference in Gothenburg, Sweden.

"The results presented from our ongoing phase 1/2 study highlight the potential for miransertib to provide a molecularly targeted treatment for patients with rare PI3K/AKT driven overgrowth diseases," said Dr. Brian Schwartz, Chief Medical Officer of ArQule. "We have been committed to rapidly advancing miransertib for patients with these devastating diseases since collaborating with The National Human Genome Research Institute in 2015 and are now poised to start the registrational study, MOSAIC, in the third quarter of this year. We are thrilled with the preliminary safety and clinical activity data and look forward to continued clinical progress for the program."

Dr. Chiara Leoni, an Investigator on the study from the Fondazione Policlinico Universitario Agostino Gemelli, said, "The precision medicine approach of the study has led to very encouraging preliminary results with the observed safety and tolerability profile, along with clinically meaningful improvement in disease related symptoms in patients. In addition, the majority of patients have had stable disease while on treatment, demonstrating the potential of miransertib to halt disease progression. The ability to attain durable treatment responses with a manageable safety profile is an important step forward for this patient population that currently has no medicinal treatment options, and I look forward to advancing the registrational MOSAIC study in the coming months."

The reported interim data are from the phase 1/2 study, an international, multi-center, open-label 2-part study evaluating miransertib in patients with PS and PROS. The first part of the study is evaluating the safety, tolerability, PK profile and preliminary evidence of clinical activity of miransertib at different dose levels. MOSAIC, the registrational part of the study, is expected to begin patient enrollment in Q3 2019.

Key findings presented include:

- Recommended initial dose for the registrational study was defined as 15mg/m^2 QD with subsequent maximum dose increase to 25mg/m^2
- A manageable safety profile was observed in patients as young as 2 years old, with mostly Grade 1 or 2 AEs
- Improvement in disease related symptoms and performance status as measured by Karnofsky/Lansky scale was reported in the majority of patients
- The majority of patients demonstrated improvement or no disease progression extending beyond 1 year on treatment

The presentation, *Preliminary results from the company's phase 1/2 study of its pan-AKT inhibitor, miransertib (ARQ 092), in patients with PIK3CA-related Overgrowth Spectrum (PROS) and Proteus syndrome (PS)*, is available on the company's website at www.arqule.com/publications-presentations/.

About Miransertib
Miransertib (ARQ 092) is an orally available, selective, pan-AKT (protein kinase B) inhibitor that potently inhibits AKT 1, 2 and 3 isoforms. Additionally, it binds both the active and inactive forms of AKT which directly inhibits and prevents membrane localization, respectively. Dysregulation of AKT has been implicated in a variety of rare overgrowth diseases and cancers; however, there are currently no approved inhibitors of AKT. AKT inhibitors, either as single agent or combination therapy, show significant promise in molecularly defined patient populations. Miransertib has been granted Rare Pediatric Disease Designation for Proteus syndrome by the U.S. Food and Drug Administration (FDA) as well as Orphan Drug Designation by both the FDA and European Medicines Agency. Fast Track Designation has been granted by the FDA for PROS.

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 pipeline includes: ARQ 531, an orally bioavailable, potent and reversible dual inhibitor of both wild type and C481S-mutant BTK, in phase 1 for patients with B-cell malignancies refractory to other therapeutic options; miransertib (ARQ 092), a potent and selective inhibitor of the AKT serine/threonine kinase, in a planned registrational trial with cohorts in Proteus syndrome and PROS to initiate in 2019, and in phase 1b in combination with the hormonal therapy, anastrozole, in patients with advanced endometrial cancer; ARQ 751, a next generation highly potent and selective AKT inhibitor, in phase 1 for patients with AKT1 and PI3K mutations; and derazantinib, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in a registrational trial for iCCA in collaboration with Basilea and Sinovant. ArQule's current discovery efforts are focused on the identification and

development of novel kinase inhibitors, leveraging the Company’s proprietary library of compounds.

Forward Looking Statements

This press release contains forward-looking statements, including without limitation those regarding the ongoing phase 1/2 study with miransertib and the planned MOSAIC registrational study in Proteus syndrome and PROS. 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 from those set forth in this press release. Positive information about early stage clinical trial results does not ensure that later stage or larger scale clinical trials will be successful. For example, miransertib may not demonstrate adequate therapeutic effect; in addition, it may not demonstrate an appropriate 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 current or later stage trials may not be sufficient to meet applicable regulatory standards or to justify further development. Problems or delays may arise prior to the initiation of planned clinical trials, during clinical trials or in the course of developing, testing or manufacturing 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 or its collaborators’ view of data or require additional data or information or additional studies. In addition, the planned timing of completion of clinical trials is subject to the ability of the Company and, in certain cases, its collaborators to enroll patients, enter into agreements with clinical trial sites and investigators, and overcome technical hurdles and other issues related to the conduct of the trials for which each of them is responsible. There is a risk that these issues may not be successfully resolved. 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, financial condition 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.

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