ArQule Presents Orphan Disease Clinical Data at the American Society of Human Genetics (ASHG) 2018 Annual Meeting for Its pan-AKT Inhibitor, Miransertib (ARQ 092)

October 19, 2018

Three poster presentations confirm miransertib's potential for treating patients with Proteus syndrome and PROS (PIK3CA-Related Overgrowth Spectrum)

BURLINGTON, Mass.--(BUSINESS WIRE)--Oct. 19, 2018-- ArQule, Inc. (Nasdaq:ARQL) today announced the presentation of preliminary clinical data on miransertib (ARQ 092) in three poster presentations at the American Society of Human Genetics (ASHG) 2018 Annual Meeting held from October 16 to 20, 2018 in San Diego. The data presented relate to patients affected by either Proteus syndrome or PROS who have been receiving miransertib as part of a clinical trial or in a compassionate use setting.

Two presentations feature data from two patients treated as part of ArQule's named patient/compassionate use program. Presentation highlights include:

1.Personalized medicine in rare diseases and cancer: A case report of a lasting response in a young teenage patient with Proteus syndrome and secondary ovarian cancer

- Treatment for the Proteus syndrome patient with concomitant relapsed ovarian cancer was administered at a dose level of 100mg and was well tolerated for over 19 months, resulting in a clinically significant/durable partial response of tumor and improvement of Proteus syndrome symptoms including improved mobility/bone changes

2.Severe PI3Kinase overgrowth syndrome treated with the AKT inhibitor miransertib

- Treatment for the PROS patient was well tolerated for over 25 months resulting in clinical stabilization and radiological improvement of disease

"Our understanding of the potential for miransertib to target and treat these rare and devastating diseases that arise due to genetic alterations of the PI3K/AKT pathway has grown significantly since we partnered with The National Human Genome Research Institute in 2015 to conduct the first clinical trial in Proteus syndrome," said Brian Schwartz, M.D., Chief Medical Officer of ArQule. "The data we are presenting at ASHG continues to highlight the promise of ArQule's precision medicine approach for both rare diseases and oncology. We remain deeply committed to advancing miransertib for rare PI3K/AKT pathway overgrowth diseases as rapidly as possible, as there are currently no approved therapeutics for these patients."

A third presentation features data from patients treated as part of ArQule's ongoing Phase 1/2, open label study of miransertib for the treatment of PROS. Study objectives include the evaluation of dosing schedule, safety, PK profile and preliminary efficacy of miransertib. Presentation highlights include:

3.An open-label, phase 1/2 study of miransertib (ARQ 092), an oral pan-AKT inhibitor, in patients (pts) with PIK3CA-related Overgrowth Spectrum (PROS): Preliminary results

- Preliminary evidence of clinical efficacy was demonstrated by improvements in disease related symptoms and objective radiologic and photographic measures
- Miransertib was well tolerated with a demonstrated manageable toxicity profile in patients as young as two years old
- The recommended dose of miransertib, defined as 15 mg/m^2 QD, with potential dose escalation to 25 mg/m^2 QD, provided appropriate inhibition of the activated PIK3CA pathway for long-term use without inhibition of growth in normal healthy cells

Peter Lawrence, President and Chief Operating Officer of ArQule said: "This initial presentation of clinical data from our Phase 1/2 study in PROS lays the foundation for potentially expanding the miransertib rare disease program beyond Proteus syndrome, for which the drug already has received Rare Pediatric Disease and Fast Track Designation. We look forward to continuing our productive discussions with regulators to define a pivotal trial design and rapidly advance miransertib."

All posters presented by ArQule at the ASHG 2018 Annual Meeting are available on the company's website at https://www.arqule.com/publications-presentations/.

About Miransertib
Miransertib (ARQ 092) is an orally available, selective, pan-AKT (protein kinase B) inhibitor that potently inhibits AKT1, 2 and 3 isoforms. 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 is currently in a Phase 1/2 company-sponsored study for PIK3CA-Related Overgrowth Spectrum (PROS), a Phase 1 study for ultra-rare Proteus syndrome conducted by the National Institutes of Health (NIH/NHGRI), and a Phase 1b study in combination with the hormonal therapy, anastrozole, in patients with advanced endometrial cancer with AKT and PI3K mutations. Miransertib has been granted Rare Pediatric Disease Designation and Fast Track Designation by the U.S. Food and Drug Administration (FDA), as well as Orphan Designation by the FDA and European Medicines Agency

in the rare overgrowth disease, Proteus syndrome.

About PROS
PROS is a term used to refer to a spectrum of rare diseases identified by somatic mutations in the PIK3CA gene, that result in excess growth in certain areas of the body. While the individual diseases that fall within the overgrowth spectrum have similar symptoms, each disease is defined by unique clinical characteristics. The implementation of genetic sequencing has led to the identification of the underlying genetic mutations that drive these overgrowth disorders, allowing for the development of medicines that target the specific causes of disease.

About Proteus Syndrome
Proteus syndrome is an ultra-rare condition characterized by the aberrant overgrowth of multiple tissues of the body. Patients with Proteus syndrome experience changes in the shapes of certain body structures over time, including abnormal, often asymmetric, massive growth (overgrowth) of the skeleton, skin, adipose tissue and central nervous system out of proportion to the rest of the body. Although patients may have minimal or no manifestations at birth, the disease develops and becomes apparent in early childhood (6-18 months) and rapidly progresses with intense growth in the first 10 years of life. The worldwide incidence is believed to be approximately one in a million. There are currently no approved medicinal treatments for Proteus syndrome, leaving patients with minimal treatment options to manage the disease and a mortality of 25% by age 22.

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 pipeline includes: ARQ 531, an 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; 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), and in Phase 1b in combination with the hormonal therapy, anastrozole, in patients with advanced endometrial cancer; ARQ 751, a next generation AKT inhibitor, in Phase 1 for patients with AKT1 and PI3K mutations; Derazantinib, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in a registrational trial for iCCA; 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. 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 regarding the planned clinical development of miransertib, including statements regarding its rapid advancement in overgrowth diseases. 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 early clinical results does not ensure that later-stage clinical trials will be successful. For example, miransertib may not demonstrate sufficient therapeutic effect in man; in addition, it may not exhibit an adequate safety profile in planned 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 miransertib 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 are utilizing diagnostic tests to identify patients in the Phase 1/2 trial with miransertib in PROS diseases and expect to utilize diagnostic tests in other clinical trials with miransertib. We or our collaborators may need to develop and register these or other diagnostic tests as companion diagnostics with the FDA. We or our collaborators may encounter difficulties in developing and obtaining regulatory approval for companion diagnostics, including issues relating to access to certain technologies, selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators or us to develop or obtain regulatory approval of companion diagnostics could delay or prevent approval of our product candidates. Drug development involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. 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.

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