# ArQule Announces Publication of Clinical Data with Miransertib in Proteus Syndrome

February 25, 2019

Data support miransertib as a potential first systemic treatment for individuals affected by Proteus syndrome

BURLINGTON, Mass.--(BUSINESS WIRE)--Feb. 25, 2019-- ArQule, Inc. (Nasdaq:ARQL), today announced the publication of clinical pharmacodynamic, safety and efficacy data in patients with Proteus syndrome. These data, together with data already presented at ASHG last year, support miransertib's further development as a potential first systemic treatment for patients suffering from overgrowth diseases, such as Proteus syndrome. The study, published in the American Journal of Human Genetics, and led by the National Institutes of Health (NIH), demonstrated good target engagement, tolerability and reductions in lesion size and pain, especially in children.

Highlights from the study include:

- Generally well-tolerated safety profile
- Reductions in pAKT (activated AKT) in most patients
- Reductions in Cerebriform Connective Tissue Nevus (CCTN) lesions in size (measured with standardized photography) but also in firmness, depth of sulci and discomfort (by patient report)
- Reduction in pain intensity in all (3 of 3) children in the study

"These data are highly encouraging and support further investigation into the potential use of miransertib for this devastating condition," said Dr. Brian Schwartz, Chief Medical Officer at ArQule. "The reduction in CCTN lesions were particularly striking since these lesions are, in general, relentlessly progressive, and cause severe morbidity, ulcerations and intractable pain. We'd like to thank our academic collaborators and the patients and their families for their support and tremendous dedication to this cause."

The study is available online at: https://marlin-prod.literatumonline.com/pb-assets/journals/society/ajhg/AJHG2737.pdf

**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.

**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 Proteus**

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. 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.

*Forward Looking Statements*

*This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, including without limitation those regarding the current clinical trial with miransertib and the statement by Dr. Schwartz. 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 results from early stage clinical trials of miransertib are not necessarily indicative of results that will be obtained in subsequent trials and does not ensure that later stage or larger scale clinical trials will be successful.The results achieved in ongoing or later stage trials may not be sufficient to meet applicable regulatory standards or to justify further development. In addition, miransertib 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. 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. 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 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. Only a small number of research and development programs result in the commercialization of a product. Furthermore, the Company 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 disclaims any obligation to update the information contained in this press release as new information becomes available.*

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