ArQule Announces Preclinical Data Demonstrating Potential of Miransertib (ARQ 092) to Treat PIK3CA-Driven Vascular Malformations at 2019 ASHG Annual Meeting

October 21, 2019

Treatment with miransertib prevents formation of new PIK3CA-driven vascular malformations and leads to regression of existing PIK3CA-driven vascular malformations in experimental mouse model

BURLINGTON, Mass.--(BUSINESS WIRE)--Oct. 21, 2019-- ArQule, Inc. (Nasdaq: ARQL), today announced preclinical data demonstrating the potential for miransertib (ARQ 092), it's pan-AKT inhibitor, to treat *PIK3CA* driven vascular malformations (VMs) in a poster at the 2019 American Society of Human Genetics Annual Meeting. Studies conducted in an experimental mouse model show that miransertib prevents the formation of PIK3CA-driven VMs and shows high efficacy in regressing vascular growth in already developed VMs.

"We are encouraged by these data generated by our collaborators at the Vascular Signaling Laboratory in Barcelona, as they further strengthen the therapeutic profile of miransertib in treating conditions characterized by overactive PIK3CA signaling," said Dr. Brian Schwartz, Chief Medical Officer of ArQule. "We are looking forward to continuing to examine the potential of miransertib to help patients with mutations in the PIK3CA/AKT pathway while at the same time focusing on enrolling our registrational MOSAIC (Miransertib in Overgrowth Syndromes in Adults and Children) trial of miransertib for the treatment of Proteus syndrome and PIK3CA-related Overgrowth Spectrum disorders, also known as PROS."

The poster presented today at ASHG details findings from studies of miransertib in an experimental mouse model that develops PIK3CA-driven VMs resembling those found in humans. Data show that miransertib prevents the formation of PIK3CA-driven VMs by suppressing vascular growth and endothelial cell proliferation. Treatment with miransertib was also found to lead to a regression in growth of already developed VMs, as measured by a significant reduction in retinal vascularity and endothelial cell number and proliferation.

VMs are painful, disfiguring lesions that can be present in any tissue and can lead to bleeding and obstruction of organs. The condition has an overall incidence of 1 in 5000, and no approved pharmacological options currently exist. Most VMs are caused by mutations in the *PIK3CA* or *TEK* gene, both of which lead to increased PIK3CA signaling through the PI3K/AKT pathway. Miransertib works by inhibiting *AKT*, thereby reducing the abnormal cell growth which results from increased PIK3CA signaling.

A copy of poster can be accessed by visiting the Publications & Presentations section of the ArQule website.

About MOSAIC

The MOSAIC (Miransertib in Overgrowth Syndromes in Adults and Children) trial is an international, multi-center, open-label study that will evaluate the objective response to miransertib in patients with Proteus syndrome (PS) and PIK3CA-related Overgrowth Spectrum disorders (PROS). The study will enroll approximately 30-35 patients with documented somatic mutations in the AKT1 or PIK3CA genes in the registrational cohorts for PS and PROS. Thirty to 35 additional patients will be enrolled in two other cohorts for patients under compassionate use or those ineligible to enter the registrational cohorts.

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 and 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 a single agent or in 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 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 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 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 1/2 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 registrational trial with cohorts in Proteus syndrome and PROS; ARQ 751, a next generation highly potent and selective AKT inhibitor, in phase 1 for patients with solid tumors 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 possibly pursuing VM and other indications driven by mutations in the PIK3CA pathway and the ongoing 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 preclinical or 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, 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 does not undertake any obligation to publicly update any forward-looking statements.

View source version on businesswire.com: https://www.businesswire.com/news/home/20191021005188/en/

Source: ArQule, Inc.

Corporate:
Kathleen Farren
Investor Relations & Executive Assistant to the CFO
ir@arqule.com

Media:
Cait Williamson, Ph.D.
LifeSci Public Relations
(646) 751-4366
cait@lifescipublicrelations.com