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Preclinical Data on Proprietary AKT Inhibitor, ARQ 092, Demonstrating Effectiveness in the Treatment of Sickle Cell Disease Presented at the American Society of Hematology Annual Meeting

The study supports further exploration of ARQ 092 in sickle cell disease

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that preclinical data was presented on its proprietary AKT inhibitor, ARQ 092, in an oral presentation by the University of Illinois College of Medicine at the American Society of Hematology (ASH) Annual Meeting. The presentation highlighted preclinical studies of ARQ 092 in sickle cell disease (SCD). ARQ 092 is an orally available, selective pan-AKT inhibitor.

ARQ 092 Oral Presentation Highlights

Title: *Specific inhibition of AKT with ARQ 092, an orally-available selective allosteric AKT inhibitor, attenuates acute vaso-occlusive events in sickle cell disease*

- ARQ 092 inhibits activation, and effectively blocks heterotypic aggregation, of neutrophils and platelets in SCD patients *in vitro.*
- *Ex vivo* studies indicate that ARQ 092 inhibits activation of neutrophils and platelets isolated from SCD mice after oral administration.
- *In vivo* studies with SCD mice demonstrate that co-administration of hydroxyurea and ARQ 092 effectively attenuates acute vaso-occlusive events and improves survival.
- This study provides proof of concept in an established preclinical model and enables a clinical pathway for ARQ 092 in the treatment of SCD with or without hydroxyurea.

The presentation can be viewed at https://www.arqule.com/wp-content/uploads/ASH-2016-ARQ-092-in-Sickle-Cell-Disease-.pdf.

"SCD is a debilitating lifetime disease with a worldwide presence. A report from the American Society of Hematology shows that approximately 100,000 people suffer from this disease in the U.S." said Dr. Jaehyung Cho, PhD., of the University of Illinois College of Medicine. "Our research has been focused on identifying novel therapeutic targets to prevent and treat vaso-occlusive diseases. The work done at the University of Illinois, in collaboration with ArQule, shows the importance of the AKT pathway in inducing vaso-occlusive events during SCD and the beneficial effect of ARQ 092 in attenuating adhesive function of neutrophils and platelets in SCD mice. This work warrants further exploration of ARQ 092 in patients with SCD."

"Our AKT program, specifically ARQ 092, continues to progress with the phase 1 trial in Proteus syndrome sponsored by the National Institutes of Health (NIH) and with the recently approved Investigational New Drug (IND) application for expansion into the PROS family of rare over-growth diseases," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "The PI3K/AKT pathway has been implicated in multiple diseases including SCD. We would like to thank the University of Illinois College of Medicine for lending its expertise and helping to establish valuable proof of concept for ARQ 092 in this disease setting."

About the AKT Pathway and ARQ 092

ARQ 092 is an orally bioavailable, selective small molecule inhibitor of the AKT kinases. The AKT pathway when abnormally activated is implicated in multiple oncogenic processes such as cell proliferation and apoptosis. This pathway has emerged as a target of potential therapeutic relevance for compounds that inhibit its activity, which has been linked to a variety of cancers as well as to select non-oncology indications.

ARQ 092, the lead compound in ArQule's AKT program, has completed phase 1a clinical testing and has advanced into phase 1b expansion testing in cohorts of patients with endometrial cancer, lymphomas and tumors harboring either AKT or PI3K mutations. It is also in a phase 1 trial being conducted by the NIH for Proteus syndrome, a rare over-growth disease from the PROS family. Collaborators are exploring, in preclinical testing, other indications for ARQ 092 including sickle cell

disease.

About ArQule

ArQule is a biopharmaceutical company engaged in the research and development of targeted therapeutics to treat cancers and rare diseases. Our 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 lead product, in phase 3 clinical development, is tivantinib (ARQ 197), an oral, selective inhibitor of the c-MET receptor tyrosine kinase, for second-line treatment of hepatocellular carcinoma in partnership with Daiichi Sankyo in the West and Kyowa Hakko Kirin in Asia. 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 for multiple oncology indications as well as ultra-rare Proteus syndrome, in partnership with the National Institutes of Health (NIH); 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, into toxicology testing and plan to file an Investigational New Drug Application in early 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.

This press release contains forward-looking statements regarding certain pre-clinical experiments conducted by the Company's collaborators and the Company's clinical trials with ARQ 092. 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, including in SCD and Proteus syndrome, does not ensure that later stage or larger scale clinical trials will be successful. For example, ARQ 092 may not demonstrate promising therapeutic effect; in addition, the drug candidate 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 the compound that could lead the Company or its partners, including the National Institutes of Health, 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. Drug development involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. Positive pre-clinical data may not be supported in later stages of development. 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.

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