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Data on Proprietary BTK Inhibitor, ARQ 531, Demonstrating Inhibition of Wild Type and C481S Mutant BTK and Superiority to Ibrutinib in TCL1 Mouse Model Presented at the American Society of Hematology Annual Meeting

ARQ 531 demonstrates best-in-class potential as a reversible, non-covalent BTK inhibitor

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that preclinical data was presented on Bruton's tyrosine kinase (BTK) inhibitor, ARQ 531, in a poster presentation by The Ohio State University at the American Society of Hematology (ASH) Annual Meeting. The presentation highlighted preclinical studies of ARQ 531 in Chronic Lymphocytic Leukemia (CLL). ARQ 531 is an investigational, orally bioavailable, potent and reversible BTK inhibitor.

ARQ 531 Poster Presentation Highlights

Title: The Bruton's Tyrosine Kinase (BTK) Inhibitor ARQ 531 Effectively Inhibits Wild Type and C481S Mutant BTK and Is Superior to Ibrutinib in a Mouse Model of Chronic Lymphocytic Leukemia

- Multi-targeted inhibition of cytokine, chemokine, and BCR pathways by ARQ 531 decreases activation, migration, and viability of CLL cells.
- Unlike ibrutinib, ARQ 531 inhibits activation of C481S mutated BTK variants and maintains cytotoxicity in ibrutinib resistant clones.
- ARQ 531 demonstrates remarkable efficacy in an *in vivo* TCL1 adoptive transfer model, improving survival to a greater extent than ibrutinib and restoring granulocyte production.
- The company plans to complete preclinical studies and file an Investigational New Drug (IND) application in early 2017 to begin clinical testing later in the year.

The presentation can be viewed at https://www.arqule.com/wp-content/uploads/ASH-2016-ARQ-531-in-CLL.pdf.

"Irreversible kinase inhibitors directed at BTK have really changed the landscape of CLL but at extended follow up, we are beginning to see a subset of high risk patients who are relapsing," said Dr. Jennifer Woyach, M.D., of The Ohio State University College of Medicine. "Small molecules that target BTK that are not dependent upon the C481 site represent an exciting option for future clinical trials. We are excited to be working with ArQule on this project and look forward to initiating the first in man study with ARQ 531."

"We began our BTK discovery program in 2011 which ultimately lead to the selection of ARQ 531, a potent reversible inhibitor of both wild type and mutant BTK," said Dr. Giovanni Abbadessa, M.D., PhD., Vice President of Clinical Development, Translational Medicine and Medical Affairs at ArQule. "With the recent emergence in 2015 of BTK resistance we concentrated our efforts in this growing CLL patient population. We are pleased to be working with The Ohio State University to finish preclinical studies on this exciting program. We remain on track to file an IND application early next year."

About BTK and ARQ 531

ARQ 531 is an investigational, orally bioavailable, potent and reversible Bruton's tyrosine kinase (BTK) inhibitor. Biochemical and cellular studies have shown that ARQ 531inhibits both the wild type and C481S-mutant forms of BTK. The C481S mutation is a known emerging resistance mechanism for first generation irreversible BTK inhibitors. ARQ 531 has high oral bioavailability as well as good ADME, pharmacokinetic and metabolic properties. The company plans to file an IND for ARQ 531 in early 2017. BTK is a therapeutic target that has been clinically proven to inhibit B-cell receptor signaling in blood cancers.

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 preclinical experiments and planned clinical trials with ARQ 531. 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 results does not ensure that clinical trials will be successful. For example, ARQ 531 may not demonstrate promising therapeutic effect in man; in addition, and ARQ 531 may not exhibit an adequate safety profile in ongoing toxicology testing and may not demonstrate appropriate safety in planned, 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 these compounds 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. Drug development involves a high degree of risk. 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 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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ArQule, Inc.
Dawn Schottlandt, 781-994-0300
Sr. Director, Investor Relations/Corp. Communications
www.arqule.com

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