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ArQule Receives Clearance of Investigational New Drug Application from the FDA for Proprietary Reversible BTK Inhibitor, ARQ 531

Plan to initiate a phase 1 trial by Q3 of 2017

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that it has received clearance from the U.S. Food and Drug Administration (FDA) for the Investigational New Drug (IND) application to conduct a phase 1 clinical trial with ARQ 531 in patients with B-cell malignancies who are refractory to other therapeutic options. ARQ 531 is an investigational, orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant Bruton's tyrosine kinase (BTK).

ArQule plans to initiate a phase 1a/b dose escalation and signal generation trial by Q3 of 2017. The phase 1a portion will be a dose escalation study open to patients with B-cell malignancies, with the aim of establishing a recommended dose. Upon completion of the phase 1a trial, the company plans to begin a phase 1b trial in a number of expansion cohorts that will include patients with the C481S mutation who are refractory to other therapies. The goal would be to establish target engagement and early proof of concept.

"Given the emerging data on BTK resistance and the extensive preclinical work the team at The Ohio State University have done with ARQ 531, we are looking forward to moving this drug from the bench to the bedside," said Dr. Jennifer Woyach, M.D., of The Ohio State University College of Medicine. "A clear need is emerging for a BTK inhibitor that addresses resistance."

"There is an emerging body of evidence that is defining the potential clinical need related to BTK resistance, and new molecules are needed to treat patients who have developed resistance," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "We have been working with The Ohio State University in the preclinical development of ARQ 531, and we are looking forward to extending that partnership into clinical testing."

B-cell malignancies, like chronic lymphocytic leukemia, Waldenstrom's macroglobulinemia, diffuse large B-cell lymphoma and mantle cell lymphoma are driven by BTK. The only approved BTK inhibitor, ibrutinib, is irreversible and makes a covalent bond with the C481 residue of the targeted protein. Although ibrutinib has demonstrated excellent responses in patients with elevated B-cell receptor signaling, clinical resistance has been observed, and the BTK C481S mutation is emerging as a predominant mechanism of resistance. As a reversible inhibitor, ARQ 531 does not require interaction with the C481 residue, a binding site essential for irreversible ibrutinib binding to BTK, thus positioning ARQ 531 as a targeted therapy for patients harboring C481S-mutant BTK who have developed resistance to irreversible BTK inhibitors.

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 531 inhibits 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. In preclinical studies ARQ 531 has demonstrated high oral bioavailability as well as good ADME, pharmacokinetic and metabolic properties. The company plans to initiate a phase 1 trial by the third quarter of 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. 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 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, through toxicology testing and plan to initiate a phase 1 trial by the third quarter of 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, it may not exhibit an adequate safety profile 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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