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ArQule Announces First Patient Dosed in Phase 1 Trial of BTK Inhibitor, ARQ 531, for B-cell Malignancies

Trial is enrolling patients refractory to standard of care, including ibrutinib

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that the first patient has been dosed in a phase 1a/b trial with its BTK inhibitor, ARQ 531, in patients with B-cell malignancies refractory to other approved therapies. The trial can enroll up to 120 patients. ARQ 531 is an investigational, orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant Bruton's tyrosine kinase (BTK).

The phase 1 trial is designed to enroll patients with B-cell malignancies including B-cell lymphomas, chronic lymphocytic leukemia, and Waldenstrom's macroglobulinemia. The phase 1a portion of the trial will be a dose escalation study open to all refractory patients, with the aim of establishing a recommended dose. Upon completion of the phase 1a trial, the company plans to begin the phase 1b portion of trial that will consist of a number of expansion cohorts including patients with the C481S mutation who are refractory to other approved therapies. The goal of the phase 1b portion would be to establish proof of concept and early signs of activity.

"There is a clear clinical need to address the refractory population in B-cell malignancies, particularly those with the BTK C481S mutation," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "Our clinical strategy is to rapidly identify a recommended dose and then begin to enroll a number of expansion cohorts including one dedicated to patients with the C481S mutation."

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. A phase 1 trial commenced in 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 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 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 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), as well as in multiple oncology indications; 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, in phase 1 for patients with B-cell malignancies refractory to other therapeutic options. 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.

Forward Looking Statements

This press release contains forward-looking statements regarding preclinical experiments and 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 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 ARQ 531 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. 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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