June 23, 2017

ArQule Presents Preclinical Data for BTK Inhibitor, ARQ 531, at the 22nd Annual Congress of the European Hematology Association (EHA)

In preclinical models ARQ 531 demonstrates potent anti-tumor activity in DLBCL

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that preclinical data for ARQ 531 in diffuse large B-cell lymphoma (DLBCL) *in vitro* and *in vivo* tumor models was presented at EHA Congress in Madrid, Spain. ARQ 531 is an investigational, orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant Bruton's tyrosine kinase (BTK).

The presentation titled "ARQ 531, A Reversible BTK Inhibitor, Demonstrates Potent Anti-Tumor Activity in ABC-DLBCL and GCB-DLBCL" can be viewed at https://www.arqule.com/wp-content/uploads/ARQ531_EHA_2017.pdf.

ARQ 531 Poster Presentation Highlights

- Preclinical data suggests ARQ 531 has the potential for broad clinical utility in a wide range of hematological malignancies and lymphomas.
- The signaling pathways evaluated show a distinct kinase inhibition profile that could be advantageous in treating lymphomas.
- ARQ 531, unlike other BTK inhibitors, has activity in both ABC-DLBCL and GCB-DLBCL preclinical models.
- A phase 1 trial with ARQ 531 in patients with B-cell malignancies refractory to other therapeutic options, including ibrutinib, is planned to commence by the third quarter of 2017.

"This data further strengthens a very comprehensive preclinical package for ARQ 531," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "While targeting ibrutinib resistant patients will be an initial, fast-to-market strategy for the clinical development of ARQ 531, the data presented at EHA clearly demonstrate the potential clinical utility of the drug beyond ibrutinib refractory cancers."

B-cell malignancies, like chronic lymphocytic leukemia, Waldenstrom's macroglobulinemia, DLBCL 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 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, 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.

Forward Looking Statements

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 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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