ArQule Presents Results from Ongoing Phase 1 Dose Escalation Study of its Reversible BTK Inhibitor, ARQ 531

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BURLINGTON, Mass.--(BUSINESS WIRE)--Jun. 15, 2018-- ArQule, Inc. (Nasdaq:ARQL) today is presenting preliminary results from the Company's Phase 1 dose escalation study for ARQ 531, an orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant Bruton's tyrosine kinase (BTK) in patients with relapsed or refractory hematologic malignancies at the 23rd Congress of European Hematological Association (EHA) in Stockholm, Sweden.

"Preliminary data from our Phase 1 dose escalation trial highlights the potential of ARQ 531 to become a new therapeutic option for patients with B-cell malignancies," commented ArQule Chief Medical Officer and Head of Research and Development, Brian Schwartz, M.D. "There is a significant unmet need for patients with relapsed or refractory B-cell malignancies, in particular those with C481S-mediated resistance to irreversible BTK inhibitors such as ibrutinib. We are especially encouraged by the early signs of anti-tumor activity observed in the first three cohorts."

The reported data from the ongoing Phase 1, open label, single arm dose escalation 3+3 study are from the first three cohorts at dose levels of 5 (n=3), 10 (n=4) and 15 mg (n=4) in patients with relapsed or refractory chronic lymphocytic leukemia (CLL), small lymphocytic leukemia (SLL), Waldenstrom's macroglobinemia and B-cell Non-Hodgkin lymphoma.

ARQ 531 demonstrated preliminary anti-tumor activity at all dose levels, resulting in an observed tumor reduction of 35% at 5mg, 33% at 10mg, and 29% at 15mg doses. The 29% tumor reduction in the 15mg cohort was achieved after 8 weeks of treatment in a patient with the BTK C481S-mutation, after 5 prior systemic regimens including ibrutinib and venetoclax, with treatment still ongoing. Overall treatment duration ranged from 1 to 46 weeks with 4 of 11 patients treated still ongoing.

ARQ 531 was well tolerated at all three dose levels, supporting continued dose escalation. No dose limiting toxicities or ARQ 531-related Grade 3 or greater adverse events were observed, and the maximum tolerated dose has not been reached.

The half-life of ARQ 531 was between 22-27 hours suggesting the potential for sustained target inhibition and supporting a once daily dosing regimen with preliminary pharmacokinetics showing increases in exposure that are approximately dose proportional.

The poster, A Phase 1 Dose Escalation Study of ARQ 531 in Selected Patients with Relapsed or Refractory Hematologic Malignancies, is available on ArQule's website, www.arqule.com, under "Publications and Presentations": https://www.arqule.com/publications-presentations/.

About BTK and ARQ 531

Bruton's tyrosine kinase, BTK, is a therapeutic target that has been clinically proven to inhibit B-cell receptor signaling in blood cancers. ARQ 531 is an orally bioavailable, potent and reversible 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 resistance mechanism for first generation irreversible BTK inhibitors. In preclinical studies, ARQ 531 has demonstrated good oral bioavailability as well as favorable pharmacokinetic, pharmacodynamic and metabolic properties.

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 pipeline includes: ARQ 531, an 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; Miransertib (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), and in Phase 1b in combination with the hormonal therapy, anastrozole, in patients with advanced endometrial cancer; ARQ 751 a next generation AKT inhibitor, in Phase 1 for patients with AKT1 and PI3K mutations; Derazantinib, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in a registrational trial for iCCA; 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. 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, including without limitation those regarding current 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 from those set forth in this press release. Positive information about early stage clinical trial results does not ensure that later stage or larger scale clinical trials will be successful. For example, ARQ 531 may not demonstrate promising therapeutic effect; in addition, it may not demonstrate an appropriate safety profile 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 prior to the initiation of planned clinical trials, during clinical trials or in the course of developing, testing or manufacturing 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 or its collaborators' view of data or require additional data or information or additional studies. In addition, the planned timing of completion of clinical trials is subject to the ability of the Company and, in certain cases, its collaborators to enroll patients, enter into agreements with clinical trial sites and investigators, and overcome technical hurdles and other issues related to the conduct of the trials for which each of them is responsible. There is a risk that these issues may not be successfully resolved. In addition, we expect to utilize diagnostic tools in ongoing and future biomarker-guided clinical trials with ARQ 531. We or our collaborators may encounter difficulties in developing and obtaining approval for companion diagnostics, including issues relating to access to certain technologies, selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators or us to develop or obtain regulatory approval of companion diagnostics could delay or prevent approval of our product candidates. 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, financial condition 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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