ArQule Announces Clinical Data from Ongoing Phase 1 Study of Reversible BTK Inhibitor, ARQ 531, in Patients with Relapsed/Refractory Hematologic Malignancies at the 2018 ASH Annual Meeting

December 3, 2018

-ARQ 531 demonstrates anti-tumor activity and favorable safety profile

-Dose escalation to continue

- Call with management scheduled for 12/3 at 9:00 ET to discuss the results

BURLINGTON, Mass.--(BUSINESS WIRE)--Dec. 3, 2018-- ArQule, Inc. (Nasdaq: ARQL) yesterday presented 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 2018 American Society of Hematology (ASH) Annual Meeting in San Diego.

Dr. Brian Schwartz, Chief Medical Officer of ArQule commented, "We are encouraged by the pace at which this trial is progressing and by the level of target engagement we are observing as we continue to dose escalate. Four out of the five heavily pretreated CLL patients enrolled in the last two cohorts with the BTK-C481S mutation have experienced tumor shrinkage."

"These data provide further evidence of ARQ 531's potential to become a new therapeutic option for patients with B cell malignancies," commented Paolo Pucci, Chief Executive Officer of ArQule. "There is significant unmet need for patients with relapsed or refractory B-cell malignancies in particular those with the C481S-mediated resistance to irreversible BTK inhibitors such as ibrutinib."

The reported data are from the ongoing Phase 1, open label, single arm dose escalation 3+3 study and include the first six cohorts (n=20) at dose levels of 5, 10, 15, 20, 30 and 45 mg once a day in patients with relapsed or refractory chronic lymphocytic leukemia (CLL), small lymphocytic leukemia (SLL), Waldenstrom's macroglobinemia and B-cell Non-Hodgkin lymphomas.

Key findings presented include the following:

- ARQ 531 has demonstrated a manageable safety profile with no dose-limiting toxicities observed to date
- Pharmacokinetic data are nearly dose proportional with a mean plasma half-life that supports QD dosing
- Pharmacodynamic biomarkers for cohorts 4 through 6 showed profound pBTK inhibition
- Anti-tumor activity, with reduction of tumor burden, was observed in 9 out of 20 patients
    - At the first assessment of tumor response, 80% of the ibrutinib refractory, heavily pretreated CLL patients (4 out of 5) in the highest dose cohorts (30 and 45 mg) experienced tumor shrinkages
    - Four out of 5 lymphoma patients derived benefit with shrinkages between 27 and 58%, including 1 PR in a Follicular Lymphoma patient who began at 5 mg, was dose escalated to 15 and then 45 mg, and remains on therapy after 70 weeks
- The study is on-going and dose escalation continues

The presented poster, *A Phase 1 Dose Escalation Study of ARQ 531 in Selected Patients with Relapsed or Refractory Hematologic Malignancies*, is available on the company's website at https://www.arqule.com/publications-presentations/.

The Company will hold a conference call and webcast today at 9:00 a.m. ET to discuss these results. The live webcast can be accessed in the "Investors and Media" section of our website, www.arqule.com, under "Events & Presentations." You may also listen to the call by dialing (877) 868-1831 within the U.S. or (914) 495-8595 outside the U.S. A replay will be available two hours after the completion of the call and can be accessed in the "Investors & Media" section of our website, www.arqule.com, under "Events and 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.

Forward Looking Statements

This press release contains forward-looking statements, including without limitation those regarding the current clinical trial 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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