ArQule Announces Clinical Proof-of-Concept Data from Ongoing Phase 1 Study of Reversible BTK Inhibitor, ARQ 531, in Patients with Relapsed/Refractory Hematologic Malignancies at the 2019 EHA Annual Meeting

June 14, 2019

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

-Four of six evaluable CLL patients, all with the BTK-C481S mutation, from cohort 7 (65 mg) experienced a Partial Response

-Partial Response also observed in the study's first Richter's Transformation patient

-Call with management and Dr. Jennifer Woyach, Principal Investigator, scheduled for today, June 14, at 8:00 am EDT to discuss these results

BURLINGTON, Mass.--(BUSINESS WIRE)--Jun. 14, 2019-- ArQule, Inc. (Nasdaq: ARQL) today announced preliminary results from the Company's phase 1 dose escalation study for ARQ 531, an orally bioavailable, potent and reversible dual inhibitor of both wild type and C481S-mutant Bruton's tyrosine kinase (BTK) in patients with relapsed or refractory hematologic malignancies at the 2019 European Hematology Association (EHA) Annual Meeting in Amsterdam, the Netherlands.

"The profile of ARQ 531 continues to strengthen, and we are delighted to be able to demonstrate such compelling clinical activity at a well-tolerated dose in patients who have already exhausted available therapies," commented Dr. Brian Schwartz, Chief Medical Officer of ArQule. "We are now focused on finalizing the recommended phase 2 dose and planning for the expansion of our clinical efforts with ARQ 531 into later stage trials across multiple indications as a single agent and as a combination therapy."

"ARQ 531 was selected and extensively tested preclinically to address the emerging therapeutic need for patients who have become resistant to covalent BTK inhibitors," commented Dr. Jennifer Woyach, Associate Professor of Medicine at The Ohio State University and the Principal Investigator of the study. "The data presented in this poster provide compelling clinical proof-of-concept for this novel class of reversible BTK inhibitors and was predicted by the preclinical studies published in Cancer Discovery[1] last year."

The reported data are from the ongoing phase 1, open label, single arm dose escalation study and include the first eight cohorts (n=34) at dose levels of 5, 10, 15, 20, 30, 45, 65 and 75 mg once a day in patients with relapsed or refractory chronic lymphocytic leukemia (CLL), small lymphocytic leukemia (SLL), Richter's Transformation, Waldenström macroglobulinemia and other B-cell Non-Hodgkin lymphomas. Cohort 8 (75 mg) enrollment is ongoing.

Key findings presented include the following:

- ARQ 531 is well-tolerated through 65 mg QD
- Pharmacokinetic data demonstrate a steady-state mean C_{min} of above 1 μM in patients receiving ≥45 mg QD. The plasma half-life ranges from 20-30 hours
- Pharmacodynamic data at doses above 20-30 mg QD is associated with complete pBTK inhibition and substantial CCL3 suppression
- Robust, dose-dependent, anti-tumor activity was observed
    - ORR of 66% (4 responses in 6 evaluable patients) was observed in heavily pretreated R/R CLL patients, all with the BTK-C481S mutation, from cohort 7
    - A partial response was observed in the first patient with Richter's Transformation, who had progressed on ibrutinib and R-CHOP, suggesting that ARQ 531's distinct MOA is amenable to target this highly unmet medical need
    - A Follicular Lymphoma patient remains a confirmed PR and has been on therapy approximately two years, providing valuable initial insights into long- term safety as well as durability of response

The poster at EHA presenting these data entitled, "*A Phase 1 Dose Escalation Study of ARQ 531 in Patients with Relapsed or Refractory B-Cell Lymphoid Malignancies*," is available on the company's website at www.arqule.com/publications-presentations/.

ArQule will host a conference call and webcast for investors on Friday, June 14, 2019 at 8:00 a.m. EDT to discuss the ARQ 531 clinical data. The live webcast can be accessed in the "Investors and Media" section of our website, www.arqule.com, under "Events & Presentations" or by clicking here. You may also listen to the call by dialing 1-800-239-9838 within the U.S. or 1-323-794-2551 outside the U.S. and providing conference ID 3110780. 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 dual inhibitor of both wild type and C481S-mutant BTK. The C481S-mutation is a known resistance mechanism for first generation irreversible BTK inhibitors. ARQ 531 has demonstrated a good safety profile, predictable PK, profound

pharmacodynamic effects and emerging signs of dose-proportional clinical activity in phase 1 clinical testing.

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 pipeline includes: ARQ 531, an orally bioavailable, potent and reversible dual 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 potent and selective inhibitor of the AKT serine/threonine kinase, in a planned registrational trial with cohorts in Proteus syndrome and PROS to initiate in 2019, and in phase 1b in combination with the hormonal therapy, anastrozole, in patients with advanced endometrial cancer; ARQ 751, a next generation highly potent and selective AKT inhibitor, in phase 1 for patients with AKT1 and PI3K mutations; and derazantinib, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in a registrational trial for iCCA in collaboration with Basilea and Sinovant. ArQule's current discovery efforts are focused on the identification and development of novel kinase inhibitors, leveraging the Company's proprietary library of compounds.

[1]Reiff *et al*. The BTK Inhibitor ARQ 531 Targets Ibrutinib-Resistant CLL and Richter Transformation. *Cancer Discovery*. 2018, 8:1300-1315

Forward Looking Statements
This press release contains forward-looking statements, including without limitation those regarding the current clinical trial with ARQ 531 and plans for future trials. 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 adequate 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 current or 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 or intellectual property, 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 diagnostic could delay or prevent approval of ARQ 531. 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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