ArQule Presents Clinical and Preclinical Data for ARQ 751 at the 30th EORTC/AACR/NCI Symposium

November 16, 2018

Three poster presentations demonstrate ARQ 751's potential as both a monotherapy and in combination with other anti-cancer agents

BURLINGTON, Mass.--(BUSINESS WIRE)--Nov. 16, 2018-- ArQule, Inc. (Nasdaq: ARQL) today announced the presentation of clinical and preclinical data on ARQ 751 in three poster presentations at the 30th EORTC/AACR/NCI Symposium held from November 13 to 16, 2018 in Dublin, Ireland. The data presented highlight clinical data from ARQ 751-101, a Phase 1 study in adult patients with refractory and/or metastatic tumors that harbor AKT, PI3K or PTEN genetic alterations, and preclinical data on ARQ 751 in combination with other agents.

Clinical data highlights and key conclusions include:

1. *A Phase 1 Dose Escalation Study of ARQ 751 in Adult Patients with Advanced Solid Tumors with AKT1, 2, 3 Genetic Alterations, Activating PI3K Mutations, PTEN-null, or Other Known Actionable PTEN Mutations*

- ARQ 751 demonstrated manageable toxicity at doses from 5 mg QD to 75 mg QD, and the recommended Phase 2 dose was determined to be 75 mg QD
- Evidence of clinical activity was observed with two partial responses in ER+/PR+/HER2- stage IV breast cancer patients, one with PTEN C296fs*2 mutation, one with PIK3CA H1047R mutation, 11 patients had stable disease
- The data support continued development of ARQ 751 as a monotherapy or in combination with other anti-cancer agents due to its manageable safety profile and preliminary evidence of biological activity

"ARQ 751, as a highly specific allosteric AKT inhibitor, holds great potential in treating patients with solid tumors harboring mutations in the AKT/PI3K/PTEN pathways," said Brian Schwartz, M.D., Chief Medical Officer of ArQule. "The presented data are very encouraging and demonstrate both preliminary signs of clinical activity and a favorable safety profile while also determining the recommended Phase 2 dose. At ArQule, we are committed to developing genetically targeted cancer treatments to provide effective new treatment options for patients, particularly those with advanced or relapsed disease, and look forward to advancing the ARQ 751 clinical program."

Preclinical data highlights include:

2. Combination of the AKT inhibitor ARQ 751 with Immune Checkpoint Inhibitor and Other Therapeutic Agents

- In preclinical cellular models, ARQ 751 exerted greater anti-proliferative and biochemical effects when in combination with multiple therapeutic agents including an ER antagonist, aromatase inhibitor, androgen receptor antagonist and a BTK inhibitor
- In an *in vivo* colon cancer animal model, ARQ 751 in combination with an anti-PD-1 antibody exhibited superior anti-tumor activity compared to single agents

3.Miransertib and ARQ 751 exhibit superior cell-death-inducing properties compared to other AKT inhibitors and can overcome resistance to other allosteric AKT inhibitors

- ArQule's AKT inhibitors, miransertib and ARQ 751 showed superior activity in comparison to other allosteric and ATP-competitive AKT inhibitors currently in clinical development
- Miransertib and ARQ 751 have the potential to overcome some mechanisms of resistance to AKT inhibitors
- Miransertib and ARQ 751 in combination with ATM inhibition demonstrated synergistic effects

Dr. Shubham Pant, MD, Associate Professor in the Department of Investigational Cancer Therapeutics at MD Anderson Cancer Center, said "AKT inhibitors have significant potential to treat a broad range of solid tumors in molecularly defined patient populations. The presented data show that ARQ 751 exhibits unique properties that differentiate it from other AKT inhibitors. It is our hope that by combining ARQ 751 with a broad spectrum of therapeutic agents, including hormonal agents, we could provide new opportunities for combinatorial interventions in oncology."

All posters presented by ArQule at the EORTC/AACR/NCI Symposium are available on the company's website at https://www.arqule.com/publications-presentations/.

About ARQ 751
ARQ 751 is an orally bioavailable, selective small molecule inhibitor of the AKT serine/threonine kinase. The AKT pathway when abnormally activated is implicated in multiple oncogenic processes such as cell proliferation and apoptosis. This pathway has emerged as a target of potential therapeutic relevance for compounds that inhibit its activity, which has been linked to a variety of cancers as well as to select non-oncology indications. ARQ 751 is currently in a Phase 1 study in adult patients with refractory and/or metastatic tumors that harbor genetic alterations along the AKT pathway.

About Miransertib
Miransertib (ARQ 092) is an orally bioavailable, selective, pan-AKT (protein kinase B) inhibitor that potently inhibits AKT1, 2 and 3 isoforms.

Dysregulation of AKT has been implicated in a variety of rare overgrowth diseases and cancers; however, there are currently no approved inhibitors of AKT. AKT inhibitors, either as single agent or combination therapy, show significant promise in molecularly defined patient populations. Miransertib is currently in a Phase 1/2 company-sponsored study for PIK3CA-Related Overgrowth Spectrum (PROS), a Phase 1 study for ultra-rare Proteus syndrome conducted by the National Institutes of Health (NIH/NHGRI), and a Phase 1b study in combination with the hormonal therapy, anastrozole, in patients with advanced endometrial cancer with AKT and PI3K mutations. Miransertib has been granted Rare Pediatric Disease Designation and Fast Track Designation by the U.S. Food and Drug Administration (FDA), as well as Orphan Designation by the FDA and European Medicines Agency in the rare overgrowth disease, Proteus syndrome.

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 regarding the planned clinical development of miransertib and ARQ 751, the Company's AKT inhibitors. 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 early clinical results does not ensure that later-stage clinical trials will be successful. For example, miransertib and ARQ 751 may not demonstrate sufficient therapeutic effect in man; in addition, neither agent 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 miransertib 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. In addition, we are utilizing diagnostic tests to identify patients in the trials with miransertib and ARQ 751 and expect to utilize diagnostic tests in other clinical trials with these agents. We or our collaborators may need to develop and register these or other diagnostic tests as companion diagnostics with the FDA. We or our collaborators may encounter difficulties in developing and obtaining regulatory 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. 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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