ArQule Achieves Clinical Milestone in MiT Trial with ARQ 197

Confirmed tumor response in clear cell sarcoma leads to expanded trial

WOBURN, Mass.--(BUSINESS WIRE)--ArQule, Inc. (NASDAQ: ARQL) today announced the expansion of its Phase 2 trial with ARQ 197, a proprietary, orally administered small molecule inhibitor of the c-Met receptor tyrosine kinase, in MiT (Microphthalmia Transcription Factor)-associated tumors based on the achievement of a partial response, as defined by RECIST (Response Evaluation Criteria in Solid Tumors), in a patient with clear cell sarcoma.

"We are delighted to observe this first objective response in a cohort of patients affected by a molecularly-linked group of tumor types for which there is no effective treatment," said Paolo Pucci, chief executive officer of ArQule. "We are especially pleased for the patient, who is continuing on treatment. Based on the achievement of the protocol-defined endpoint of an objective response in the first stage of this trial, we are proceeding to the second stage, optimizing it further by implementing a higher dose of ARQ 197, 360 milligrams (mg) twice daily (b.i.d.). In parallel, we are preparing to initiate discussions with regulatory authorities to determine the optimal clinical pathway to prove the utility of this compound in sarcomas."

MiT tumors, which include clear cell sarcoma (CCS), alveolar soft part sarcoma (ASPS) and translocation-associated renal cell carcinoma (RCC), are linked biologically through a common chromosomal abnormality that is responsible for the over-expression of c-Met resulting in the development of these tumors. Tumors with this abnormality are resistant to current therapies and, in the absence of successful surgical resection, are invariably fatal.

During the first stage of the study, 23 patients were enrolled and treated with 120 mg of ARQ 197 b.i.d. To date, fourteen of these patients are evaluable for efficacy. In addition to the patient with the confirmed partial response, ten of the evaluable patients have demonstrated stable disease. Preliminary data from the first stage will be presented at the Connective Tissue Oncology Society meeting scheduled in November, 2008.

"This objective clinical response builds upon the strong pre-clinical rationale for this trial, including data which showed that knockout of MiT expression by shRNA suppressed c-Met expression and impeded the growth of human clear cell sarcoma cells in vitro and in vivo," said Dr. George Demetri, Director of the Ludwig Center at the Dana-Farber/Harvard Cancer Center, the clinical site leading this trial. "This finding led us to develop a clinical trial in patients with MiT-associated tumors using ArQule's c-Met inhibitor, ARQ 197, which had previously shown anti-cancer activity, including objective tumor responses, as well as the ability to inhibit the c-Met protein in tumor biopsies from patients treated with the drug. We continue to follow several patients enrolled in the first stage of this trial, and we look forward to enrolling additional patients in the second stage of the MiT program."

ArQule is completing its scientific, regulatory and commercial analyses related to the overall Phase 2 development program for ARQ 197. The Company plans to communicate additional details regarding this program this month.

About ARQ 197 and c-Met

ARQ 197 is a selective inhibitor of c-Met, a receptor tyrosine kinase. When abnormally activated, c-Met plays multiple roles in aspects of human cancer, including cancer cell growth, survival, angiogenesis, invasion and metastasis. Pre-clinical data have demonstrated that ARQ 197 inhibits c-Met activation in a wide range of human tumor cell lines, including clear cell sarcoma, and shows anti-tumor activity against several human tumor xenografts. In clinical studies to date, treatment with ARQ 197 has been well tolerated and has resulted in tumor responses and prolonged stable disease across broad ranges of tumors and doses.

ArQule has licensed rights to develop and commercialize ARQ 197 in Japan and parts of Asia to Kyowa Hakko Kirin Co., Ltd. (Kyowa). Other than the rights licensed under the agreement with Kyowa, ArQule retains all worldwide rights to ARQ 197.

About ArQule

ArQule is a biotechnology company engaged in the research and development of next-generation, small-molecule cancer therapeutics. The Company's targeted, broad-spectrum products and research programs are focused on key biological processes that are central to cancer. ArQule's lead product, which is in clinical-stage development, is ARQ 197, an inhibitor of the c-Met receptor tyrosine kinase. An additional clinical-stage program includes compounds that activate the cell's DNA damage response mechanism mediated by the E2F-1 transcription factor. The Company's most advanced pre-clinical

development programs are focused on compounds that inhibit the Eg5 kinesin spindle protein and the BRAF kinase. ArQule's discovery efforts are focused on the identification of novel kinase inhibitors that are potent, selective and do not compete with ATP (adenosine triphosphate), an energy source for cells.

This press release contains forward-looking statements regarding the Company's Phase 1 and Phase 2 clinical trials with ARQ 197 and other candidates in earlier stages of development, including statements related to potential outcomes from increased dosing, perceived safety, perceived clinical benefit, including disease stabilization, and changes to existing studies. 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 and early stage clinical trial results does not ensure that later stage or larger scale clinical trials will be successful. For example, ARQ 197 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. Problems or delays may arise during clinical trials or in the course of developing, testing or manufacturing these compounds that could lead the Company or Kyowa to discontinue development. Even if later stage clinical trials are successful, the risk exists that unexpected concerns may arise from analysis of data or from additional data or that obstacles may arise or issues be identified in connection with review of clinical data with regulatory authorities or that regulatory authorities may disagree with the Company's view of the data or require additional data or information or additional studies. In addition, the planned timing of initiation and completion of clinical trials for ARQ 197 are subject to the ability of the Company to enroll patients, enter into agreements with clinical trial sites and investigators, and other technical hurdles and issues that may not be resolved. Drug development involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. Positive pre-clinical data may not be supported in later stages of development. 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 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.

Source: ArQule, Inc.