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ArQule Announces Interim Phase 2 Study Results for Tivantinib in Combination with Cetuximab in Patients with MET-High, KRAS Wild Type Colorectal Cancer Presented at ESMO World Congress on Gastrointestinal Cancer 2015

- Stage 1 endpoint of Objective Response Rate (ORR) met, study proceeding to Stage 2.
- Preliminary results support hypothesis that MET inhibition can reverse resistance to EGFR inhibitors.

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced interim data from an ongoing investigator-initiated Phase 2 clinical trial with tivantinib in combination with cetuximab in patients with MET-High, KRAS wild-type metastatic colorectal cancer (CRC) NCT01892527 who recently progressed on anti-EGFR antibodies. These data were presented on Friday, July 3rd at the European Society of Medical Oncology (ESMO) World GI 2015 (abstract number O-008) by Dr. Lorenza Rimassa, MD, Deputy Director, Medical Oncology Unit at Humanitas Cancer Center, in Rozzano (Milan, Italy).

"Considering that in CRC objective response rate (ORR) often correlates with overall survival (OS) benefit, the preliminary results obtained combining tivantinib with cetuximab are encouraging," said Dr. Rimassa. "Since all patients enrolled in this trial were MET-High and had recently progressed on a combination regimen including cetuximab or panitumumab, the data may support the hypothesis that MET inhibition can reverse resistance to EGFR inhibitors as well as the need for rigorous tissue collection procedures at enrollment to allow for a more robust correlative outcome assessment related to the MET pathway."

The primary endpoint of the trial is ORR in the biomarker defined population. Secondary study endpoints are progression-free survival (PFS), overall survival (OS) and safety. The ESMO World GI presentation included data from 21 patients enrolled in Stage 1 of this trial. One patient, still on therapy, experienced a complete response (CR) and 2 patients experienced durable confirmed partial responses (PRs). Stable disease was observed in 8 patients, including 2 short duration PRs, for an overall Disease Control Rate (CR + PR + SD) of 52.4%. Having met the Stage 1 endpoint (≥2 confirmed responses), the trial continued to Stage 2 and has recently completed enrollment.

Adverse events were in line with those historically reported, including skin toxicity attributed to cetuximab, and neutropenia attributed to tivantinib. Neutropenia was addressed timely with growth factors and dose adjustments.

The trial is a 2-stage, investigator-initiated study testing tivantinib plus cetuximab after recent progression on anti-EGFR antibodies. The trial is coordinated by the Humanitas Cancer Center in Milan, Italy. Stage 1 enrolled 21 patients, and Stage 2 recently completed enrollment of 20 additional patients. Final results from the 41 patients enrolled are expected by the end of 2015.

About Colorectal Cancer (CRC)

Colorectal cancer is the second leading cause of cancer-related deaths in the U.S. and is the third most common cancer in men and women. According to the National Cancer Institute, it is estimated that more than 132,000 new cases of colorectal cancer will be diagnosed in 2015, and an estimated 49,700 deaths from the disease will occur this year. The estimated incidence rate was 42.4 per 100,000 people during the period 2008-2012.

About MET and tivantinib (ARQ 197)

Tivantinib is an orally administered, selective inhibitor of MET, a receptor tyrosine kinase, which is currently in Phase 2 and Phase 3 clinical trials. In healthy adult cells, MET can be present in normal levels to support natural cellular function, but in cancer cells, MET can be inappropriately and continuously activated. When abnormally activated, MET plays multiple roles in aspects of human cancer, including cancer cell growth, survival, angiogenesis, invasion and metastasis. The activation of certain cell signaling pathways, including MET, has also been associated with the development of resistance to anti-EGFR (epidermal growth factor receptor) antibodies such as cetuximab and panitumumab.

Pre-clinical data have demonstrated that tivantinib inhibits MET activation in a range of human tumor cell lines and shows anti-tumor activity against several human tumor xenografts. In clinical trials to date, treatment with tivantinib has been generally well tolerated and has shown clinical activity in the tumors studied. Tivantinib has not yet been approved for any indication in any country.

In December 2008, ArQule and Daiichi Sankyo signed a license, co-development and co-commercialization agreement for tivantinib in the U.S., Europe, South America and the rest of the world, excluding Japan, China (including Hong Kong), South Korea and Taiwan.

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 human cancers. ArQule's lead product, in Phase 2 and Phase 3 clinical development, is tivantinib (ARQ 197), an oral, selective inhibitor of the c-MET receptor tyrosine kinase. The Company's pipeline includes: ARQ 092, designed to inhibit the AKT serine/threonine kinase; ARQ 087, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family; and ARQ 761, a Beta lapachone analog being evaluated as a promoter of NQ01-mediated programmed cancer cell necrosis. ArQule's current discovery efforts are focused on the identification of novel kinase inhibitors, leveraging the Company's proprietary library of compounds.

This press release contains forward-looking statements regarding the Company's clinical trials with tivantinib (ARQ 197). 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, tivantinib may not demonstrate promising therapeutic effect or appropriate safety profiles 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 or its partners and collaborators to fail to initiate or 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, the planned timing of initiation and completion of clinical trials for tivantinib is subject to the ability of the Company as well as Daiichi Sankyo, Inc., our development partner for tivantinib, and Kyowa Hakko Kirin, a licensee of tivantinib, 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 and our partners are utilizing a companion diagnostic to identify MET-high patients in the METIV-HCC JET-HCC and other trials. We may encounter difficulties in developing and obtaining approval for companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators or us to develop or obtain regulatory approval of the 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. 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. Moreover, with respect to partnered programs, even if certain compounds show initial promise, Daiichi Sankyo or Kyowa Hakko Kirin may decide not to license or continue to develop them, as the case may be. In addition, Daiichi Sankyo and Kyowa Hakko Kirin have certain rights to unilaterally terminate their agreements with ArQule. If either company were to do so, the Company might not be able to complete development and commercialization of the applicable licensed products on its own. 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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