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FDA Grants Rare Pediatric Disease Designation to ArQule's Miransertib (ARQ 092) for the Treatment of Proteus Syndrome

BURLINGTON, Mass.--(BUSINESS WIRE)-- ArQule, Inc. (Nasdaq: ARQL) today announced that the U.S. Food and Drug Administration (FDA) has granted Rare Pediatric Disease Designation to miransertib (ARQ 092) for the treatment of Proteus syndrome. Under the FDA's rare pediatric disease priority review voucher program, the sponsor may be eligible for a voucher that can be used to obtain priority review for a subsequent human drug application if it meets relevant statutory requirements associated with the program, including FDA approval of the drug in this indication. The FDA previously granted Orphan Drug Designation to miransertib for the treatment of Proteus syndrome, a rare disease characterized by overgrowth of the skeleton, skin, adipose tissue and central nervous system. Miransertib is an orally available, selective pan-AKT inhibitor.

"The FDA's granting of the Rare Pediatric Disease Designation and Orphan Drug Designation underscores the unmet medical need in Proteus syndrome and the potential for miransertib to address this unmet need," said Dr. Brian Schwartz, M.D., Head of Research and Development and Chief Medical Officer at ArQule. "We plan to work closely with the FDA and clinical experts, including Dr. Leslie G. Biesecker, M.D. Chief of the Medical Genomics and Metabolic Genetics Branch at the National Human Genome Research Institute who discovered the relevance of AKT in Proteus syndrome, to define a regulatory path forward."

ArQule is enrolling a phase 1/2 trial for Overgrowth Diseases, including Proteus syndrome and PROS, driven by either the AKT or PI3K mutation. The phase 1 portion of the trial is enrolling six patients in a dose escalation cohort. An additional 10 patients will be enrolled in an expansion cohort as part of the phase 2 portion of the trial. In parallel with the company sponsored phase 1/2 trial, ArQule will continue to provide miransertib on a named patient basis to those patients unable to travel to a clinical trial site due to severe disease.

About the AKT Pathway and Miransertib (ARQ 092)

Miransertib (ARQ 092) is an orally bioavailable, selective small molecule inhibitor of the AKT 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.

Dysregulation of AKT is also a driver of certain rare proliferative disorders. For example, the E17K mutation of AKT1 causes Proteus syndrome, a rare non-cancerous segmental overgrowth disorder, and the analogous PIK3CA-Related Overgrowth Spectrum (PROS) is caused by genetic alterations in the PI3K pathway. Miransertib has been shown preclinically and clinically to inhibit AKT and PI3K cell signaling and therefore may provide the potential for much-needed treatment options for patients with these diseases.

Miransertib, the lead compound in ArQule's AKT program, has completed phase 1a clinical testing and has advanced into phase 1b expansion testing in cohorts of patients with endometrial cancer, lymphomas and tumors harboring either AKT or PI3K mutations. A company sponsored phase 1/2 trial is being conducted in the U.S. and E.U. for Overgrowth Diseases, including PROS and Proteus syndrome. Miransertib is also in a phase 1 trial being conducted by the NIH for Proteus syndrome. Collaborators are exploring in preclinical testing other indications for miransertib, including sickle cell disease.

About Proteus Syndrome

According to the patient advocacy and support group, the Proteus syndrome Foundation (http://www.proteus-syndrome.org/), the condition was named for Proteus, the Greek god who could transform his shape. Patients experience changes in the shapes of certain body structures over time, including abnormal, often asymmetric, massive growth (overgrowth) of the skeleton, skin, adipose tissue and central nervous system out of proportion to the rest of the body, which may appear normal. Although patients may have minimal or no manifestations at birth, the disease develops and becomes apparent in early childhood (6-18 months) and rapidly progresses with intense growth in the first ten years of life. It is primarily a childhood-onset disease.

Proteus syndrome is a rare condition with an incidence of less than one in one million people worldwide. Only a few hundred individuals have been reported in the medical literature. At this time, there are more than 120 documented cases worldwide,

but because not all cases are documented, it is not known how many people have this disease. The incidence of Proteus syndrome classifies it as a rare disorder, defined by the National Organization of Rare Diseases (NORD) as any disease affecting fewer than 200,000 Americans.

About Overgrowth Disease

Overgrowth Disease is a term used to refer to a spectrum of rare diseases identified by somatic mutations, often of the PI3K or AKT1 pathway, that result in excess growth in certain areas of the body. While the individual diseases that fall within the overgrowth spectrum have similar symptoms, each disease is defined by unique characteristics. Diseases that are part of the overgrowth spectrum include PROS diseases (PIK3CA Rare Overgrowth Spectrum) and Proteus syndrome. Each disease on its own is rare, sometimes ultra-rare, often only impacting an estimated one in a million people worldwide.

As an example, CLOVES (Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, Spinal/skeletal anomalies and/or scoliosis) is a disease that is part of the PROS family of diseases. According to the CLOVES Foundation (www.clovesfoundation.org), CLOVES is an extremely rare progressive overgrowth disorder, affecting approximately 200 people worldwide. The symptoms vary from mild soft tissue tumors to Vascular Malformations encompassing the spine or internal organs. CLOVES is closely linked to other overgrowth disorders like M-CM (Macrocephaly-Capillary Malformation) Syndrome, Klippel-Trénaunay-Weber syndrome, and 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 proprietary pipeline includes: Derazantinib (ARQ 087), a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in phase 2 for iCCA and in phase 1b for multiple oncology indications; 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), as well as in multiple oncology indications; ARQ 751, a next generation AKT inhibitor, in phase 1 for patients with AKT1 and PI3K mutations; 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. In addition, we have advanced ARQ 531, an investigational, 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. ArQule's current discovery efforts are focused on the identification and development of novel kinase inhibitors, leveraging the Company's proprietary library of compounds. You can follow us on Twitter and LinkedIn.

Forward Looking Statements

This press release contains forward-looking statements regarding the Company's clinical trials with miransertib and the possible awarding of a rare pediatric disease priority review voucher for Proteus syndrome. 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. For example, miransertib must first receive marketing approval from FDA and meet all relevant statutory requirements prior to its possibly receiving the rare pediatric disease priority review voucher for Proteus syndrome. Positive information about pre-clinical, and early stage clinical trial results, including in Proteus syndrome, does not ensure that later stage or larger scale clinical trials will be successful. Miransertib 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 during clinical trials or in the course of developing, testing or manufacturing the compound that could lead the Company or its partners, including the National Institutes of Health, 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. Drug development involves a high degree of risk. 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 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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