ARQULE INC
Form 8-K
April 10, 2012

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

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Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934
Date of Report April 10, 2012

(Date of earliest event reported)

ARQULE, INC.
(Exact Name of Issuer as Specified in Charter)

Delaware	000-21429	04-3221586
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

19 Presidential Way
Woburn, MA
(Address of principal executive offices)

01801
(Zip code)

(781) 994-0300
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

¨ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

¨ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

¨ Pre-commencement communications pursuant to Rule 14d-2(b) under the

¨ Exchange Act (17 CFR 240.14d-2(b))
Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Section 8 — Other Events

Item 8.01 Other Events.

On April 10, 2012, we issued a press release announcing a proposed public offering of shares of our common stock. A copy of this press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference. The following summary of our product candidates, clinical trials, pipeline, discovery platform and significant events and milestones appeared in our preliminary prospectus supplement.

Overview

We are a clinical-stage biotechnology company engaged in the research and development of innovative cancer therapeutics. Our mission is to produce novel drugs with differentiated mechanisms of action that will extend the lives of our patients. These drugs target biological pathways implicated in a wide range of cancers. We employ technologies such as our ArQule Kinase Inhibitor Platform ("AKIP™") to design and develop drugs that have the potential to fulfill this mission.

Tivantinib (ARQ 197): Lead Product Candidate

We are developing our lead product candidate, tivantinib (ARQ 197), which has demonstrated anti-cancer activity across multiple types of tumors when administered in combination with approved cancer therapies and as a single agent. Tivantinib is an inhibitor of the c-Met receptor tyrosine kinase, or c-Met, a molecule that has emerged in recent years as an important target for cancer therapy based on its multiple roles in cancerous cell proliferation, tumor spread, new blood vessel formation and resistance to certain drug therapies.

Patients are currently being enrolled in two Phase 3 registration trials, the MARQUEE Phase 3 Trial and the ATTENTION Phase 3 Trial, of tivantinib for non-small cell lung cancer ("NSCLC") of non-squamous cell histology that cover global territories. In addition, recently generated, randomized Phase 2 data with tivantinib in hepatocellular carcinoma (HCC) are expected to form the basis of a decision this year regarding the possible initiation of Phase 3 clinical testing in this second disease indication.

Our partners for tivantinib include Daiichi Sankyo Co., Ltd., who we refer to as "Daiichi Sankyo," in the U.S., Europe, South America and the rest of the world, excluding Japan and certain other Asian countries, where we have licensed commercial rights to Kyowa Hakko Kirin Co., Ltd., who we refer to as "Kyowa Hakko Kirin." With these partners, we are implementing a clinical program in multiple tumor types that is designed to realize the broad therapeutic potential of tivantinib. Additionally, the National Institutes of Health ("NIH") has selected tivantinib for a number of independent investigator-sponsored trials supported by the NIH.

MARQUEE Phase 3 Trial in NSCLC

On January 12, 2011, we announced that the first patient had been enrolled in the Phase 3 MARQUEE trial of tivantinib in combination with erlotinib for patients with non-squamous NSCLC who have received one or two prior systemic anti-cancer therapies. The MARQUEE trial is a randomized, double-blinded, controlled study of previously treated patients with locally advanced or metastatic, non-squamous NSCLC who will receive tivantinib (360 milligrams twice daily) plus erlotinib or placebo plus erlotinib (an inhibitor of the epidermal growth factor, or EGFR, tyrosine kinase marketed as Tarceva™). The primary objective is to evaluate overall survival in the intent-to-treat population. Secondary endpoints include overall survival in the subpopulation of patients with EGFR wild type, progression free survival in the intent-to-treat population and further assessment of the safety of tivantinib in

combination with erlotinib.

Approximately 1,000 patients will be enrolled in MARQUEE from more than 200 sites in the U.S., Canada, Europe, Russia, Australia and Latin America. There is a planned interim analysis expected in the second half of 2012 after approximately 50% of survival events have occurred, and final data is expected in the middle part of 2013. Patient enrollment to date since the initiation of this trial is consistent with the timing of these anticipated milestones, and we expect to complete enrollment in mid-2012. As a result of the dosing of the first patient in this trial, in February 2011 we received a $25 million milestone payment from Daiichi Sankyo. Daiichi Sankyo, in collaboration with us, is conducting the Phase 3 trial.

The MARQUEE trial is being conducted under a Special Protocol Assessment ("SPA"), established following agreement reached with the U.S. Food and Drug Administration ("FDA") in October 2010. An SPA is an agreement establishing the design, endpoints and statistical analysis of a clinical trial intended to provide the necessary data, depending on the outcome of the trial, which could support the filing of a New Drug Application or NDA. Final marketing approval depends on the results of the trial.

We have incorporated into the SPA a broad genotyping and biomarker program designed to expand what is an evolving understanding of the biology of c-Met and of tivantinib. In addition, we continue to investigate and add to our understanding of the profile of tivantinib and its metabolites to better characterize their scope and effect as anti-cancer agents. These efforts include the generation and interpretation of clinical and pre-clinical data by us, our partners and third parties, which suggest potential anti-cancer activity in addition to c-Met inhibition. In this regard, certain preclinical experiments have demonstrated that tivantinib has activity against cells that harbor little or undetectable levels of c-Met, suggesting an additional mechanism or mechanisms in those settings, including mitotic arrest, or the possible involvement of cellular mechanisms and signaling pathways activated by c-Met. Although it is unclear what effect such activity may have in clinical settings, data from randomized, controlled clinical trials demonstrate that tivantinib has greater benefit for patients who have tested positive for high c-Met status while showing less activity in c-Met low populations. As a result, we believe that c-Met status remains the most significant biomarker for further development of the drug, and we, our partners and academic collaborators intend to focus on such patient populations in a number of tumor types. We will pursue these and future findings to inform our decisions regarding additional clinical settings and patient populations for tivantinib.

ATTENTION Phase 3 Trial in NSCLC

On August 9, 2011, Kyowa Hakko Kirin announced the dosing of the first patient in its Phase 3 ATTENTION trial in Asia of tivantinib and erlotinib in non-squamous NSCLC patients with wild-type EGFR. This trial will compare overall survival of patients treated with tivantinib and erlotinib to overall survival in patients treated with placebo and erlotinib. Approximately 460 patients will be enrolled at clinical centers in Japan, South Korea and Taiwan. The design of this trial is based on the results of clinical studies conducted by Kyowa Hakko Kirin in Japan and those conducted by Daiichi Sankyo and us in the U.S. and Europe. As a result of the dosing of the first patient in this trial, in August 2011 we received a $10 million milestone payment from Kyowa Hakko Kirin.

KRAS Mutation-Positive NSCLC Phase 2 Trial

In July 2011, we dosed the first patient in a Phase 2, randomized trial of tivantinib and erlotinib in NSCLC patients with a mutated form of the KRAS gene. We selected this patient population based on a strong signal of clinical benefit observed among KRAS-mutant patients who comprised a sub-group in our randomized Phase 2 NSCLC trial. This trial will compare progression-free survival of patients treated with tivantinib and erlotinib to progression-free survival of patients treated with single agent chemotherapy. Approximately 100 patients will be enrolled at 14 clinical sites in the U.S.

Hepatocellular Carcinoma ("HCC") Trials

Our therapeutic approaches to HCC include evaluating tivantinib as both a single agent and in combination with an approved targeted therapy, sorafenib. We recently completed enrollment of patients in a randomized, double-blind, placebo controlled, Phase 2 single agent trial in second-line HCC. On January 17, 2012, we announced the results of this trial, which demonstrated that treatment with tivantinib as single agent therapy produced a statistically significant 56 percent improvement in time-to-progression in the intent-to-treat population, the primary endpoint in this trial (hazard ratio = 0.64; log rank p-value = 0.04). Patients with higher levels of c-Met who were treated with tivantinib experienced pronounced benefit in prolonged time-to-progression.

The 107 patients in this trial had unresectable HCC and had experienced disease progression after first-line therapy or were unable to tolerate such therapy. Time-to-progression was defined as the time from patient randomization until objective tumor progression using RECIST (Response Evaluation Criteria in Solid Tumors) 1.1 criteria evaluated by central radiological review. We plan to present complete data from this trial, including secondary endpoint, sub-group and biomarker analyses, on June 2nd at the American Society of Clinical Oncologists' annual meeting.

At the start of the Phase 2 trial, patients were randomized to receive tivantinib at 360 milligrams twice daily or placebo. Due to the rate of neutropenia, or an abnormally low count of white blood cells that help fight infections, the tivantinib dose was reduced to 240 milligrams twice daily for all patients. Adverse events were reported at similar rates in the treatment and placebo arms, except for a higher incidence of fatigue and hematologic events, including neutropenia and anemia, in tivantinib-treated patients. The incidence of these types of events declined following dose reduction.

We continue to monitor the safety profile of tivantinib in patients with HCC, among whom underlying cirrhosis and compromised liver function may limit the body's ability to process tivantinib and thereby increase such toxicity. Among these patients, the recommended dose of tivantinib in HCC is 240 milligrams twice daily. The 360 milligram dose and the 240 milligram dose performed similarly with regard to efficacy in the intent-to-treat population.

We presented data from our ongoing Phase 1 tivantinib-sorafenib combination trial at the 2011 Annual Meeting of ASCO on June 6, 2011 that included cohorts of patients with HCC. These data reflected anti-cancer activity in this cohort, as measured by stable disease and duration of therapy. We plan to present final data in expanded cohorts of these patients in 2012 or early 2013.

Colorectal Cancer Trial

In February 2010, Daiichi Sankyo initiated a Phase 1/2 clinical trial designed to evaluate the safety of tivantinib administered in combination with irinotecan and cetuximab in approximately 150 patients with metastatic colorectal cancer who possess the wild-type form of the KRAS gene. Data from the Phase 1 safety run-in portion of this trial were presented at the ASCO 2011 Gastrointestinal Cancers Symposium in January 2011, showing that this combination was well tolerated and demonstrated encouraging anti-tumor activity in patients with relapsed metastatic

colorectal cancer. Following the successful completion of Phase 1, the randomized, double-blind, placebo controlled Phase 2 portion of the trial was initiated in August 2010, comparing tivantinib in combination with irinotecan and cetuximab to placebo with the same two drugs. The primary objective of the Phase 2 trial is progression-free survival, and secondary objectives include overall survival and overall response rate. Patient enrollment in this trial has been completed, and data is expected to be available in the second half of 2012 or early 2013.

Combination Regimen Trials

The tivantinib clinical program includes two Phase 1 open-label trials evaluating tivantinib in combination therapy regimens. The first combination, with sorafenib, is being tested in NSCLC, HCC, renal cell carcinoma ("RCC"), malignant melanoma and breast cancer. The second combination, with gemcitabine, was tested in uterine, ovarian, bladder, NSCLC, pancreatic and breast cancer. Any potential plans for the further development of these combination therapies will be based on analysis of final results observed in expanded cohorts of patients within the Phase 1 trials.

We presented interim data from both combination trials at the 2011 Annual Meeting of ASCO on June 6, 2011. The tivantinib-sorafenib trial included cohorts of patients with HCC, melanoma and RCC, in whom preliminary evidence of anti-cancer activity was observed. Dosing in the cohort of HCC patients included both 360 milligrams twice daily and 240 milligrams twice daily, with the lower dose administered to patients with more compromised liver function. We expect to have final data in expanded cohorts of these patients in 2012.

National Institutes of Health Program

The National Cancer Institute ("NCI"), through its Cancer Therapy Evaluation Program ("CTEP"), has selected tivantinib for study under a Cooperative Research and Development Agreement ("CRADA"). The CRADA provides financial support for a number of independent investigator-sponsored clinical trials that will examine the safety and spectrum of tivantinib's anti-tumor activity, including new potential indications based on the profile of tivantinib and the role of c-Met in different diseases. Additionally, it provides support for pre-clinical studies designed to expand the basic understanding and development of tivantinib, including exploration of its potential activity beyond c-Met inhibition. Patient enrollment is ongoing with tivantinib as a single agent and in combinations with other anti-cancer therapies in a number of CRADA-sponsored trials. These include Phase 2 single agent trials in prostate cancer (randomized), multiple myeloma and breast cancer, with trial protocols in other indications under review. In addition, trials with tivantinib are ongoing or planned in combination with other agents, including pazopanib, bevacizumab and temsirolimus.

Gastric Cancer Trial Conducted by Kyowa Hakko Kirin

Following the completion of a Phase 1 safety trial in Japan, Kyowa Hakko Kirin initiated a Phase 2, single agent trial with tivantinib in gastric cancer. We received a $5 million payment related to this clinical milestone in September 2010. Approximately 30 patients were enrolled in this trial at clinical sites in Japan and S. Korea, and the primary objective was to determine disease control rate, defined as a combination of objective responses and stable disease. We believe data from this trial will be presented by Kyowa Hakko Kirin later this year

Earlier Stage Product Candidates: ARQ 621, ARQ 736, ARQ 087, ARQ 761 and ARQ 092

Our proprietary early clinical-stage product pipeline encompasses ARQ 621, an inhibitor of the Eg5 kinesin motor protein, ARQ 736, an inhibitor of the RAF kinases, and ARQ 761, an activator of the E2F-1 damage response/checkpoint pathway. We have completed a Phase 1 trial with ARQ 621 and are in the later stages of conducting a Phase 1 trial with ARQ 736, while ARQ 761 is the subject of an investigator-sponsored Phase 1 clinical trial. Our pre-clinical pipeline includes ARQ 087, an inhibitor of fibroblast growth factor receptor ("FGFR") based on our AKIP™ technology for which we may file an Investigational New Drug application in 2012.

Our strategy with these product candidates is to generate pre-clinical and early clinical data that will inform decisions regarding possible initiation of Phase 2 testing with one or more of them either independently or on a partnered basis. Eg5 is not yet validated as a therapeutic target, and we are seeking additional scientific evidence that the class of Eg5 inhibitors merits further clinical testing. The barriers to entry in the field of RAF kinase inhibitors have become more difficult as vemurafinib has been recently approved for the treatment of late-stage melanoma patients with the BRAF V600 mutation, and additional members of this class are marketed or in development. ARQ 761 is a second-generation compound from our E2F-1 DNA damage response/checkpoint pathway, the rights to which we retain following the termination of a license to Roche.

Our partnered early stage product pipeline includes ARQ 092, an AKT inhibitor discovered through our AKIP™ collaboration with Daiichi Sankyo. On November 10, 2011, Daiichi Sankyo and we announced the execution of a license agreement for the development of ARQ 092, the first compound to emerge from this collaboration. The license agreement provides exclusive rights to Daiichi Sankyo for the development, manufacturing and marketing of ARQ 092 on a worldwide basis. Under this agreement, we received a $10 million upfront fee from Daiichi Sankyo in November 2011, as well as support for an ongoing Phase 1 clinical trial that we are conducting in the U.S. The agreement provides for up to $265 million in potential development and sales milestone payment, as well as tiered, double-digit royalties on net sales.

Discovery Platform

We have discovered a novel binding mode of tivantinib to its target that effects inhibition of the c-Met receptor kinase without competing with adenosine triphosphate ("ATP") for binding to that kinase. We have completed a research program with the objective of querying the human kinome (consisting of 518 human kinase genes) for similar binding sites, and we have identified comparable sites in approximately 270 kinases, some having roles in different therapeutic areas, leading to the establishment of our proprietary drug discovery platform, AKIP™.

We believe that this platform allows our scientists to rationally design novel kinase inhibitors that encompass new chemical spaces and provide for an expanding intellectual property estate. We are applying our drug discovery capabilities based on AKIP™ to generate novel, selective and potent compounds that target the inactive form of kinases. We have assessed AKIP™'s potential to target multiple kinases in oncology and other therapeutic areas, and we are generating and validating compounds that inhibit these kinase targets.

We are pursuing a drug discovery collaboration with Daiichi Sankyo that utilizes the capabilities of the AKIP™ technology to discover compounds for as many as three such kinase targets in the field of oncology (including AKT), with an option for a fourth, in the field of oncology. We are also pursuing additional collaborations based on applications of AKIP™ in multiple therapeutic areas.

Significant Events and Milestones

Section 9 – Financial Statements and Exhibits

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No. 99.1 Text of press release announcing offering of common stock dated April 10, 2012.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ARQULE, INC.
(Registrant)

/s/ Peter S. Lawrence
Peter S. Lawrence
President and Chief Operating Officer

April 10, 2012

8