ARQULE INC
Form 8-K
January 24, 2011

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **January 19, 2011**

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):

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

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

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o 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 January 19, 2011, we announced a public offering of shares of our common stock. The following summary of our product candidates, clinical trials, pipeline and discovery platform appeared in our preliminary and final prospectus supplements. We also updated certain risk factors in connection with the offering and have reproduced the risk factors below.

Overview

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

ARQ 197: Lead Product Candidate

We are developing our lead product candidate, ARQ 197, with our partner, Daiichi Sankyo Co., Ltd. (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. (KHK). ARQ 197 is an inhibitor of the c-Met receptor tyrosine kinase that does not compete with ATP (adenosine triphospate). C-Met is a promising target for cancer therapy based on its multiple roles in cancerous cell proliferation, tumor spread, new blood vessel formation and resistance to certain drug therapy.

We are implementing a clinical development program designed to realize the broad potential of ARQ 197 as a well tolerated single agent and in combination with other anti-cancer therapies. We are conducting trials in a number of indications, including non-small cell lung cancer, liver cancer, colorectal cancer and germ cell tumors, and we are completing earlier-stage combination therapy trials that may provide data to support later-stage trials in additional indications.

Non-small cell lung cancer: Phase 2 trial

We presented Phase 2, proof-of-principle clinical data with ARQ 197 in its lead indication, non-small cell lung cancer, at the 2010 Annual Meeting of the American Society of Oncology (ASCO) in June 2010, with an update at the Annual Meeting of the European Society for Medical Oncology (ESMO) in October 2010. We believe the treatment benefit defined by improved progression-free survival (PFS), the primary endpoint in this trial, and by extended median overall survival (OS) observed in this trial would represent a meaningful clinical improvement over standard therapy if replicated in a Phase 3 trial. We are especially encouraged by the potential benefit for the large sub-group of non-squamous cell patients.

One hundred sixty-seven patients participated in this Phase 2, double blind, randomized signal generation trial. Patients were EGFR (epidermal growth factor receptor) inhibitor-naïve and

randomized one-to-one to receive either the combination of ARQ 197 plus erlotinib (an inhibitor of the EGFR tyrosine kinase marketed as Tarceva) or placebo plus erlotinib in second and third line settings.

Key findings from this trial include the following:

1. Progression-free survival (primary endpoint of the trial):

In the intent to treat (ITT) population (167 patients), ARQ 197, when used in combination with erlotinib, demonstrated a 66 percent improvement in PFS in patients with advanced, refractory non-small cell lung cancer over patients treated with erlotinib plus placebo. Median PFS was 16.1 weeks in the ARQ 197 plus erlotinib arm, compared with 9.7 weeks in the erlotinib plus placebo arm. The difference in PFS between the two arms did not achieve statistical significance (hazard ratio = 0.809) by applying a log-rank test. When adjusted for imbalances in the distribution of key prognostic factors, the difference in PFS was statistically significant (hazard ratio = 0.675) by applying a Cox regression analysis specified for secondary efficacy analyses. Improvement in median PFS was more pronounced in the pre-defined sub-group of patients with non-squamous histology (n = 117); median PFS was 18.9 weeks in the treatment arm versus 9.7 weeks in the control arm, which represents a 94% improvement. Based on an exploratory Cox regression analysis, the endpoint of PFS was met in the sub-group and achieved statistical significance (hazard ratio = 0.613).

2. Overall survival

Data showed that median OS in the ITT population (n = 167) was 36.6 weeks in the ARQ 197 plus erlotinib arm, compared with 29.4 weeks in the erlotinib plus placebo arm, an improvement of 24 percent (unadjusted hazard ratio = 0.88, p = 0.50). In the pre-defined sub-group of patients with non-squamous cell histology (n = 117), median OS was 43.1 weeks in the treatment arm, compared with 29.4 weeks in the placebo arm, an improvement of 47 percent (unadjusted hazard ratio = 0.72, p = 0.19). Based on an exploratory Cox regression analysis, the difference in median OS achieved statistical significance ($p < 0.05$) in this sub-group when adjusted for imbalances in key prognostic factors that included EGFR status and KRAS status, both of which favored the placebo arm.

3. Cross-over arm

The trial design included a cross-over arm to assess the impact of ARQ 197 plus erlotinib on patients who failed erlotinib monotherapy. Of the 23 cross-over patients who were evaluable for response, two had a partial response per Response Evaluation Criteria in Solid Tumors (RECIST) and nine had stable disease, for a disease control rate of 48 percent.

4. Anti-metastatic effect

Exploratory analyses showed that patients treated with ARQ 197 plus erlotinib had a median time to develop new metastases of 7.3 months, compared to 3.6 months for patients treated with erlotinib plus placebo (p=0.002). This effect was more pronounced among patients with non-

squamous cell histology, among whom the median time to develop new metastases was 11.0 months for patients treated with ARQ 197 plus erlotinib, compared with 3.6 months for those treated with erlotinib plus placebo (p=0.007).

5. Safety

No clinically relevant differences in adverse event rates were observed between the treatment and control arms. The most prevalent adverse events were mild in intensity and included rash, diarrhea and fatigue. The combination of ARQ 197 plus erlotinib was shown to be well tolerated, with manageable side effects similar to single agent profiles.

Non-small cell lung cancer: Phase 3 trial and Special Protocol Assessment

On January 12, 2011, we announced that the first patient was enrolled in the Phase 3 trial of ARQ 197 in combination with erlotinib for patients with non-squamous, non-small cell lung cancer who have received one or two prior systemic anti-cancer therapies. The Phase 3 trial is a randomized, double-blinded, controlled study of previously treated patients with locally advanced or metastatic, non-squamous NSCLC who will receive ARQ 197 plus erlotinib or placebo plus erlotinib. The primary objective is to evaluate OS in the ITT population. Secondary endpoints include OS in the subpopulation of patients with EGFR wild type, PFS in the ITT population, and further assessment of the safety of ARQ 197 in combination with erlotinib. Approximately 1,000 patients will be enrolled from 150 sites in the U.S., Canada, Europe, Russia, Australia and Latin America. There is a planned interim analysis after approximately 50% of survival events have occurred, and final data is expected in the middle part of 2013. As a result of the dosing of the first patient in this trial, we will receive a $25 million milestone payment from Daiichi Sankyo. Daiichi Sankyo is conducting the Phase 3 trial.

In October 2010, agreement was reached with the U.S. Food and Drug Administration (FDA) on a Special Protocol Assessment (SPA) for this trial. 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 ARQ 197. In addition, we continue to investigate and add to our understanding of the profile of ARQ 197 and its metabolites to better characterize their scope and effect as anti-cancer agents. Moreover, data on c-Met inhibition continue to be generated by us and others. Such findings should help to define additional clinical settings and patient populations that may benefit from c-Met inhibition therapy.

Liver Cancer

Our therapeutic approaches to liver cancer include the use of ARQ 197 as both a single agent and in combination with an approved targeted therapy, sorafenib. Following the successful completion of safety testing with ARQ 197 as a single agent in cirrhotic patients with liver cancer, we have been enrolling patients in a randomized, double-blind, placebo controlled Phase 2 single agent trial and expect to substantially complete enrollment with approximately 100 patients in the first half of 2011. We have also been enrolling a cohort of patients in a Phase 1 ARQ 197-sorafenib combination safety trial, the final results of which we will evaluate prior to making a decision about initiating a Phase 2 trial with this combination in liver cancer.

Initial data from the Phase 1 safety trial with ARQ 197 as a single agent in liver cancer showed a manageable safety profile, with no drug-related worsening of liver function. A recommended Phase 2 dose of 360 milligrams (mg) twice daily (BID) was established, and preliminary anti-cancer activity was observed. At the 2010 Annual Meeting of ESMO, we presented further Phase 1 data describing a higher incidence of bone marrow toxicity in the liver cancer population than observed in previous ARQ 197 studies. A similar observation has been made in the Phase 2 single agent study, and as a result, we have reduced the starting dose of ARQ 197 to 240 mg BID in our Phase 2 trial. We continue to monitor the safety profile of ARQ 197 in patients with liver cancer, among whom underlying cirrhosis and compromised liver function may limit the body s ability to process ARQ 197 and thereby increase such toxicity.

We presented results from our ongoing Phase 1 ARQ 197-sorafenib combination safety trial, including a cohort of liver cancer patients (see Combination regimens below), at the ASCO and ESMO meetings. These data showed that the combination appears safe and well tolerated at full standard doses of each agent. Preliminary evidence of anti-cancer activity was also observed, indicating that the combination has therapeutic potential. Our decision to move forward in liver cancer with this combination will be predicated upon final analysis of data from the safety trial, as well as discussions with our partners and regulatory authorities.

Colorectal cancer

In February, 2010, Daiichi Sankyo initiated a Phase 1/2 clinical trial designed to evaluate the safety of ARQ 197 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. Following the successful completion of the Phase 1 safety run-in portion of the trial, the randomized, double-blind, placebo controlled Phase 2 portion of the trial was initiated in August 2010, comparing ARQ 197 in combination with irinotecan and cetuximab to placebo with the same two drugs. The primary objective of the Phase 2 trial is PFS, and secondary objectives include OS and overall response rate. Patient enrollment in this trial is proceeding.

Germ cell tumors

Daiichi Sankyo recently conducted a Phase 2, open label, signal generation trial with ARQ 197 as a single agent in approximately 25 patients in the niche indication of germ cell tumors. We have not observed a pre-determined, RECIST response rate among patients in this trial that would have supported our plan to move forward on a fast-to-market clinical development pathway. Consequently, we have elected to de-prioritize clinical development of ARQ 197 in this indication, consistent with our strategy to focus on the most promising indications within our clinical program.

C-Met-associated soft tissue sarcomas

We completed enrollment in a Phase 2, open label single agent trial with ARQ 197 among approximately 50 patients with c-Met associated soft tissue sarcomas in the first half of 2010. Patient recruitment in this trial was comparatively lengthy due to the rarity of these tumors. We and Daiichi Sankyo have decided not to move forward with a company-sponsored trial in this indication, based on an analysis of data to date. We are continuing to evaluate other clinical development options in these tumors that would leverage external resources, such as those available under a federally sponsored Cooperative Research and Development Agreement.

Combination regimens: ARQ 197 plus sorafenib and ARQ 197 plus gemcitabine

The ARQ 197 clinical program includes two Phase 1 open-label trials evaluating ARQ 197 in combination therapy regimens. The first combination, with sorafenib, is being tested in renal cell carcinoma, NSCLC, liver cancer, malignant melanoma and breast cancer. The second combination, with gemcitabine, is being tested in uterine, ovarian, bladder, NSCLC, pancreatic and breast cancer. Phase 2 development plans for both combination therapies will be based on final results observed in expanded cohorts of patients within the Phase 1 trials.

At the October 2010 ESMO meeting, interim data from the ARQ 197-sorafenib trial showed that this combination is well tolerated at full standard single agent doses and that the pharmacokinetic profile of ARQ 197 in this combination does not differ from the pharmacokinetic profile of ARQ 197 in monotherapy. Preliminary evidence of anti-cancer activity was observed, suggesting the therapeutic potential of this combination. Patients continue to be enrolled in this trial.

Interim data from the ARQ 197-gemcitabine combination trial was also presented at the ESMO meeting, showing that this combination was well tolerated at full standard single agent doses. Preliminary evidence of anti-cancer activity was observed, and expanded cohorts of patients with gemcitabine-sensitive tumor types are being enrolled. An increase in tumor growth inhibition was noted when dosing of these two compounds is alternated. Patients continue to be enrolled in this trial, although based on data observed to date, we do not plan to continue testing of this combination in pancreatic cancer.

Kyowa Hakko Kirin trials

Following the successful completion of a Phase 1 safety trial in Japan, KHK has initiated a Phase 2, single agent trial with ARQ 197 in gastric cancer. We received a $5 million milestone payment related to this clinical milestone in September 2010. Approximately 30 patients will be enrolled in this trial at clinical sites in Japan and Korea, and the primary objective is to determine disease control rate, defined as a combination of objective responses and stable disease.

Earlier Stage Product Candidates

Our product pipeline beyond ARQ 197 encompasses ARQ 621, an inhibitor of the Eg5 kinesin motor protein, and ARQ 736, an inhibitor of the RAF kinases, both of which are in Phase 1

clinical testing. We are also developing an inhibitor of Fibroblast Growth Factor Receptor based on our AKIP technology that is in pre-clinical development, for which we plan to file an Investigational New Drug application in 2011 or early 2012. Our strategy with this group of three product candidates is to generate pre-clinical and early clinical data beginning in 2010 and going through 2012 that will inform decisions to initiate Phase 2 testing with one or more of them either independently or on a partnered basis.

Discovery Platform

We are applying our drug discovery capabilities based on our proprietary ArQule Kinase Inhibitor Platform (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 also pursuing a drug discovery collaboration with Daiichi Sankyo that utilizes the capabilities of the AKIP technology to discover compounds that inhibit two such kinase targets in the field of oncology, and we are pursuing additional collaborations based on applications of AKIP . An expansion of our original collaboration with Daiichi Sankyo, announced in October 2010, established a third therapeutic target, with an option for a fourth, in the field of oncology, and it includes a two-year extension of the initial agreement through 2012.

Risk Factors

Risks related to our industry and business strategy

Development of our products is at an early stage and we may not successfully develop a drug candidate that becomes a commercially viable drug.

The discovery and development of drugs is inherently risky and involves a high rate of failure. Discovery and development of commercial drugs are relatively new to us. Our drug candidates and drug research programs are in early stages and require significant, time-consuming and costly research and development, testing and regulatory approvals.

Our leading clinical-stage product candidate, ARQ 197, is based on inhibition of the c-Met receptor tyrosine kinase. Our other clinical-stage products, ARQ 621 and ARQ 736, are designed to inhibit the Eg5 kinesin motor protein and the RAF kinases, respectively. Although drugs have been approved that inhibit the activity of protein kinases and other enzymes and mitotic proteins such as tubulins, to our knowledge, no company has received regulatory approval for a drug based on the specific proteins targeted by any of our product candidates. Our approaches and scientific platforms may not lead to the development of approvable or marketable drugs.

In addition to our clinical-stage programs, we have a limited number of pre-clinical and research-stage programs in our pipeline. Our viability as a company depends, in part, on our ability to continue to create drug candidates for ourselves and our collaborators. Numerous significant factors will affect the success of our drug research and development efforts, including the biology and chemistry complexity involved, availability of appropriate technologies, the

7

uncertainty of the scientific process and the capabilities and performance of our employees. Our research and development capabilities may not be adequate to develop additional, viable drug candidates.

We must show the safety and efficacy of our product candidates through expensive, time consuming preclinical testing and clinical trials, the results of which are uncertain and governed by exacting regulations.

Our product candidates are in clinical or preclinical stages of development and may not prove to be sufficiently safe or effective in more advanced human clinical trials. We will need to conduct extensive further testing of all of our product candidates, expend significant additional resources and possibly partner emerging programs to realize commercial value from any of our product candidates.

Before obtaining regulatory approvals for the commercial sale of our products, we and our collaborative partners must demonstrate through preclinical studies (laboratory or animal testing) and clinical trials (human testing) that our proposed products are safe and effective for use in each target indication. This testing is expensive and time-consuming, and failure can occur at any stage. If we terminate a preclinical or clinical program, we will have expended resources in an effort that will not provide a return on our investment and missed the opportunity to have allocated those resources to potentially more productive uses.

Clinical trials must meet FDA and foreign regulatory requirements. We have limited experience in designing, conducting and managing the preclinical studies and clinical trials necessary to obtain regulatory approval for our product candidates in any country. We or our collaborative partners may encounter problems in clinical trials that may cause us or the FDA or foreign regulatory agencies to delay, suspend or terminate our clinical trials at any phase. These problems could include our inability to manufacture or obtain sufficient quantities of materials produced in accordance with current Good Manufacturing Practice, or cGMP, for use in our clinical trials, conduct clinical trials at our preferred sites, enroll a sufficient number of patients for our clinical trials at one or more sites, or begin or successfully complete clinical trials in a timely fashion, if at all. Furthermore, we, the FDA or foreign regulatory agencies may suspend clinical trials of our product candidates at any time if we or they believe the subjects participating in the trials are being exposed to unacceptable health risks as a result of adverse events occurring in our trials or if we or they find deficiencies in the clinical trial process or conduct of the investigation.

Acceptable results from initial preclinical studies and clinical trials of products under development are not necessarily indicative of results that will be obtained from subsequent or more extensive preclinical studies and clinical testing in humans. Clinical trials may not demonstrate sufficient safety and efficacy to obtain the required regulatory approvals or result in marketable products. Failure to adequately demonstrate the safety and efficacy of a product under development will delay and could prevent its regulatory approval.

A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after generating promising results in earlier trials.

Although it is part of our strategy to pursue clinical development to take advantage of available accelerated regulatory approval processes, there is no guarantee that our product candidates will show the evidence predictive of clinical benefit necessary to qualify for such regulatory treatment.

Delays in clinical testing could result in increased costs to us and delay our ability to obtain regulatory approval and commercialize our product candidates.

Clinical trials typically take several years to complete. The duration and cost of clinical trials will vary greatly depending on the nature, complexity, and intended use of the drug being tested. Even if the results of our clinical trials are favorable, the clinical trials of ARQ 197 and other product candidates will continue for several years and may take significantly longer than expected to complete. Delays in the commencement or completion of clinical testing for ARQ 197 or pre-clinical or clinical testing for any of our other product candidates could significantly affect our product development costs and business plan. In January 2011, our first patient was enrolled in the Phase 3 trial of ARQ 197 in combination with erlotinib for patients with non-squamous, non-small cell lung cancer who have received one or two prior systemic anti-cancer therapies. This trial is being conducted by Daiichi Sankyo, our collaborator in development of ARQ 197. Phase 3 clinical efficacy trials, in general, are significantly more complex and time-consuming and involve more patients than the Phase 1 and 2 clinical trials that have been completed to date. We do not know whether our Phase 3 clinical trials of ARQ 197 or any other pre-clinical or clinical trials be completed on schedule, if at all. At any time, a clinical trial can be placed on clinical hold or temporarily or permanently stopped for a variety of reasons, principally for safety concerns. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our product candidates, including the following:

- our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to provide additional information about formulation or manufacture of our product candidates or clinical trial design or to conduct additional clinical and/or pre-clinical testing or to abandon programs;

- we may experience delays related to reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, clinical investigators and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs, clinical investigators and trial sites;

- we may be unable to manufacture or obtain sufficient quantities of a product candidate for use in clinical trials;

- trial results may not meet the level of statistical significance required by the FDA or other regulatory agencies;

- enrollment in our clinical trials for our product candidates may be slower than we anticipate, resulting in significant delays;

- we, or regulators, may suspend or terminate our clinical trials if the participating patients are being exposed to unacceptable health risks;

- the effects of our product candidates on patients may not be the desired therapeutic effects or may include undesirable side effects or other characteristics that may delay or preclude regulatory approval or limit their commercial use, if approved; and

- the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of drugs based on our development platforms, which could lengthen the regulatory review process.

Completion and duration of clinical trials depends on, among other things, our ability to enroll a sufficient number of patients, which is a function of many factors, including:

- the incidence among the general population of diseases which contain therapeutic endpoints chosen for evaluation;

- the eligibility criteria defined in the protocol;

- the size of the patient population required for analysis of the trial s therapeutic endpoints;

- our ability to recruit clinical trial investigators and sites with the appropriate competencies and experience;

- our ability to obtain and maintain patient consents; and

- competition for patients by clinical trial programs for other treatments.

We have reached a Special Protocol Assessment (SPA) agreement with the FDA for the design of a Phase 3 trial of ARQ 197 in patients with non-small cell lung cancer (NSCLC) of non-squamous histology. The SPA process is a procedure by which the FDA provides official evaluation and written guidance on the design and size of proposed protocols that are intended to form the basis for a New Drug Application. Final marketing approval depends on the results of the trial. The SPA may not be sufficient for the purpose of obtaining marketing approval for ARQ

197. Clinical trials may also be delayed or repeated as a result of ambiguous or negative interim results or unforeseen complications in testing. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities due to a number of factors, including:

- failure to design appropriate clinical trial protocols;

- failure by us, our employees, our CROs or their employees to conduct the clinical trial in accordance with all applicable FDA, DEA or other regulatory requirements or our clinical protocols;

- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

- discovery of serious or unexpected toxicities or side effects experienced by study participants or other unforeseen safety issues;

- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties; - lack of effectiveness of any product candidate during clinical trials;

- slower than expected rates of subject recruitment and enrollment rates in clinical trials;

- failure of our CROs or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;

- inability or unwillingness of medical investigators to follow our clinical protocols; and

- unfavorable results from on-going clinical trials and pre-clinical studies.

Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for ARQ 197 and our other product candidates may be harmed, which may have a material adverse effect on our business, results of operations, financial condition and prospects.

We have limited clinical development and commercialization experience.

We have limited experience conducting clinical trials and have never obtained regulatory approvals for any drug. To date, we have filed five IND applications, and we have initiated twenty Phase 1 clinical trials of which fourteen have been completed, and eleven Phase 2 clinical trials

of which seven have been completed. We have not conducted a Phase 3, or pivotal, clinical trial, filed an NDA or commercialized a drug. We have no experience as a company in the sale, marketing or distribution of pharmaceutical products and do not currently have a sales and marketing organization. Developing commercialization capabilities will be expensive and time-consuming, and could delay any product launch. We may not be able to develop a successful commercial organization. To the extent we are unable or determine not to acquire these resources internally, we will be forced to rely on third-party clinical investigators, clinical research

organizations, marketing organizations or our collaboration partners as we have done for our Phase 3 non-small cell lung cancer trial. If we were unable to establish adequate capabilities independently or with others, our drug development and commercialization efforts could fail, and we may be unable to generate product revenues.

We depend substantially on the successful completion of Phase 3 clinical trials for our product candidates. The positive clinical results obtained for our product candidates in Phase 2 clinical studies may not be repeated in Phase 3.

We have completed Phase 2 clinical studies and enrolled the first patient in our Phase 3 non-small cell lung cancer trial on January 12, 2011. However, we have never completed a Phase 3 clinical trial. Our product candidates are subject to the risks of failure inherent in pharmaceutical development. Before obtaining regulatory approval for the commercial sale of any product candidate, we and our collaborators must successfully complete Phase 3 clinical trials. Negative or inconclusive results of a Phase 3 clinical study could cause the FDA to require that we repeat it or conduct additional clinical studies. Furthermore, while we have obtained positive safety and efficacy results for ARQ 197 during our prior clinical trials, we cannot be certain that these results will be duplicated when our product candidates are tested in a larger number of patients in our Phase 3 clinical trials.

If our drug discovery and development programs do not progress as anticipated, our revenue and stock price could be negatively impacted.

We estimate the timing of a variety of preclinical, clinical, regulatory and other milestones for planning purposes, including when a drug candidate is expected to enter clinical trials, how soon patients will be recruited and enrolled in these trials, when a clinical trial will be completed and when an application for regulatory approval will be filed. We base our estimates on facts that are currently known to us and on a variety of assumptions, many of which are beyond our control. If we or our collaborators do not achieve milestones when anticipated, we will not receive the corresponding revenue, and our stock price could decline. In addition, our research and clinical testing may be delayed or abandoned if we or our competitors subsequently discover other compounds that show improved safety or efficacy compared to our product candidates, which could limit our ability to generate revenues, cause us to incur additional expense and cause the market price of our common stock to decline significantly.

Risks related to our financial condition

We have incurred significant losses since our inception and anticipate that we will incur significant continued losses for the next several years, and our future profitability is uncertain.

From our inception in 1993 through September 30, 2010 we have incurred cumulative losses of approximately $393 million. These losses have resulted principally from the costs of our research activities, acquisitions, enhancements to our technology and clinical trials. In the

past we derived our revenue primarily from license and technology transfer fees and payments for compound deliveries associated with our discontinued chemistry services operations; research and development funding paid under our agreements with collaboration partners; and to a limited extent, milestone payments.

We expect our expenses to increase significantly as we spend additional amounts to fund research, development, clinical testing and commercialization of our drug candidates. We currently have three product candidates in various stages of clinical development. As a result, we will need to generate significant additional revenues to achieve profitability.

To attain profitability, we will need to develop clinical products successfully and market and sell them effectively, either by ourselves or with collaborators. We have never generated revenue from the commercialization of our product candidates, and there is no guarantee that we will be able to do so. Even if were to generate product revenues and achieve profitability, we may not be able to maintain or increase profitability. Because of the numerous risks and uncertainties associated with the development of drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we fail to become profitable, or if we are unable to fund our continuing losses, we may be unable to continue our business.

We may need substantial additional funding and due to global capital and credit market conditions or for other reasons, we may be unable to raise capital when needed, or on terms favorable to us, which could force us to delay, reduce or eliminate our drug discovery, product development and commercialization activities.

Volatility and disruption in the global capital and credit markets in 2008 and 2009 have led to a tightening of business credit and investment capital in the United States and internationally. If global economic and financial market conditions deteriorate or remain weak for an extended period of time, our efforts to raise capital will face additional difficulties.

Developing drugs, conducting clinical trials, and commercializing products are expensive. Our future funding requirements will depend on many factors, including:

- the progress and cost of our ongoing and future collaborative and independent clinical trials and other research and development activities and our ability to share such costs of our clinical development efforts with third parties;

- the costs and timing of obtaining regulatory approvals;

- the costs of filing, prosecuting, maintaining, defending and enforcing any patent applications, claims, patents and other intellectual property rights;

- the cost and timing of securing manufacturing capabilities for our clinical product candidates and commercial products, if any;

13

- the costs and timing of commercializing our product candidates, including establishing or contracting for sales, marketing and distribution capabilities, if any such candidates receive regulatory approval for commercial sale; and

- the costs of any acquisitions of or investments in businesses, products and technologies.

We may seek the capital necessary to fund our operations through public or private equity offerings, debt financings, or collaboration and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders ownership interests will be diluted and the terms of such securities may include liquidation or other preferences that adversely affect our stockholders rights. Other debt-financing arrangements may require us to pledge certain assets and enter into covenants that would restrict certain business activities or our ability to incur further indebtedness. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently, or grant licenses on terms that are not favorable to us. There can be no assurance that sufficient funds will be available to us when required, on satisfactory terms, or at all. If we are unable to obtain additional funds when needed, we may have to delay, reduce the scope of or eliminate some of our development and commercialization programs, or obtain funds through other arrangements on unattractive terms, which could prevent us from successfully executing our business strategy.

We have federal and state net operating losses (NOL) and research and development credit carryforwards which, if we were to become profitable, could be used to offset/defer federal and state income taxes. Such carryforwards may not, under certain circumstances related to changes in ownership of our stock, be available to us.

As of December 31, 2009, we had federal NOL, state NOL, and research and development credit carryforwards of approximately $179 million, $117 million and $21 million respectively, which expire at various dates through 2030. Such carryforwards could potentially be used to offset certain future federal and state income tax liabilities. Utilization of carryforwards may be subject to a substantial annual limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended, as well as similar state provisions due to ownership changes that have occurred previously or that could occur in the future. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. We undertook a detailed study of our NOL and research and development credit carryforwards in the fourth quarter of 2009 to determine whether such amounts are likely to be limited by Section 382. As a result of this analysis and a review of ownership changes in 2010, we currently do not believe Sections 382 s limitations will significantly impact our ability to offset income with available NOL and research and development credit carryforwards. However, future ownership changes under Section 382 may limit our ability to fully utilize these tax benefits.

Any limitation may result in expiration of a portion of the carryforwards before utilization. If we were not able to utilize our carryforwards, we would be required to use our cash resources to pay taxes that would otherwise have been offset, thereby reducing our liquidity.

Risks related to regulatory approval

Our product candidates are subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which would adversely affect our ability to commercialize products. We have only limited experience in regulatory affairs.

Our product candidates, as well as the activities associated with their research, development and commercialization, are subject to extensive regulation by the FDA in the United States and by comparable authorities in other countries, for example EMA in the E.U. These regulations govern or influence the manufacturing, assessment of benefit and risk, safety, labeling, storage, records and marketing of these products.

Failure to obtain regulatory approval for a product candidate would prevent us from commercializing that product candidate. We have not applied for or received regulatory approval to market any of our product candidates in any jurisdiction and have only limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved.

The regulatory process requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, the results of later trials may not confirm the positive results of earlier preclinical studies or trials. Delays or rejections may also be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval phases of our product candidates may cause delays in the approval or rejection of an application. We are currently in Phase 1 and Phase 2 clinical testing of ARQ 197 and have enrolled a patient in our Phase 3 non-small cell lung cancer trail being conducted by Daiichi Sankyo and Phase 1 clinical testing of ARQ 621 and ARQ 736. We have never conducted a Phase 3, or pivotal, clinical trial, nor have we filed or prosecuted the applications necessary to gain regulatory approvals.

A company first must conduct preclinical studies in the laboratory and in animal models to gain preliminary information on a candidate compound s activity and to identify potential safety problems. Preclinical studies must be conducted in accordance with applicable regulations of the relevant regulatory authority (e.g. the FDA in the United States, the EMA in E.U.). The results of these studies are submitted as a part of an IND application with the FDA or a CTA application with the appropriate regulatory authority outside of the United States. The regulatory agency involved must review the data in the application before human clinical trials of an investigational drug can commence. If the regulatory authority does not object, a drug developer can begin clinical trials after expiration of a specified statutory period following submission of

the application. Notwithstanding that the regulatory authority does not respond during the thirty-day, post-submission review period, the regulatory authority may at any time re-evaluate the adequacy of the application and require additional information about any aspect of the IND or CTA application and corresponding clinical trial, e.g. preclinical testing, drug formulation and manufacture, dosing regimens and drug administration or potential safety risk. Before a new marketing application can be filed with the FDA or other regulatory authority, the product candidate must undergo extensive clinical trials. Any clinical trial may fail to produce results satisfactory to the regulatory authority, typically for lack of safety or efficacy or for safety risks. For example, the regulatory authority could determine that the design of a clinical trial is inadequate to produce reliable results or convincing results.

Even if our drug candidates obtain regulatory approval, we and our collaborators will be subject to ongoing government regulation.

Even if regulatory authorities approve any of our drug candidates, the manufacture, marketing and sale of these drugs will be subject to strict and ongoing regulation. Compliance with such regulations may consume substantial financial and management resources and expose us and our collaborators to the potential for other adverse circumstances. For example, a regulatory authority can place restrictions on the sale or marketing of a drug in order to manage the risks identified during initial clinical trials or after the drug is on the market. A regulatory authority can condition the approval for a drug on costly post-marketing follow-up studies. Based on these studies, if a regulatory authority does not believe that the drug demonstrates a clinical benefit to patients or an acceptable safety profile, it could limit the indications for which a drug may be sold or revoke the drug s marketing approval. In addition, identification of certain side effects either during clinical trials or after a drug is on the market may result in reformulation of a drug, additional preclinical and clinical trials, labeling changes, termination of ongoing clinical trials or withdrawal of approval. Any of these events could delay or prevent us from generating revenue from the commercialization of these drugs and cause us to incur significant additional costs.

Even if we or our collaborators bring products to market, we may be unable to price our products effectively or obtain adequate reimbursement for sales of our products, which would have an adverse effect on our revenues.

Third party payors, such as government and private insurance plans, frequently require companies to provide rebates and predetermined discounts from list prices and are increasingly challenging the prices charged for pharmaceuticals and other medical products. Our products may not be considered cost-effective, and reimbursement to the patient may not be available or be sufficient to allow the sale of our products on a competitive basis. We, or our collaborators, may not be able to negotiate favorable reimbursement rates for our products. If we, or our collaborators, fail to obtain an adequate level of reimbursement for our products by third-party payors, sales of the drugs would be adversely affected or there may be no commercially viable market for the products.

We face potential liability related to the privacy of health information we obtain from research institutions.

Most health care providers, including research institutions from which we or our collaborators obtain patient information, are subject to privacy regulations promulgated under the Health Insurance Portability and Accountability Act of 1996, or HIPAA. Although we are not directly regulated by HIPAA, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a health care provider or research institution that has not satisfied HIPPA s disclosure standards. In addition, certain state privacy laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our use and dissemination of individuals health information. Moreover, patients about whom we or our collaborators obtain information, as well as the providers who share this information with us, may have contractual rights that limit our ability to use and disclose the information. Claims that we have violated individuals privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Risks related to collaborations

Part of our business strategy involves collaborative out-licensing of our drug candidates while retaining commercialization or co-promotional rights in parts of the world. We may not be able to find collaborators or successfully form suitable collaborations to further our drug development and commercialization efforts.

We have sought and may seek collaborators for our drug development and commercialization efforts. We may enter into these collaborations to obtain external financing for drug development and to obtain access to drug development and commercialization expertise. The availability of partners depends on the willingness of pharmaceutical and biotechnology companies to collaborate in drug discovery activities. Only a limited number of pharmaceutical and biotechnology companies would fit our requirements. The number could decline further through consolidation, or the number of collaborators with interest in our drugs could decline. If the number of our potential collaborators were to decline, the remaining collaborators may be able to negotiate terms less favorable to us.

We face significant competition in seeking drug development collaborations, both from other biotechnology companies and from the internal capabilities and compound pipelines of the pharmaceutical and biotechnology companies themselves. This competition is particularly intense in the oncology field. Our ability to interest such companies in forming co-development and commercialization arrangements with us will be influenced by, among other things:

- the compatibility of technologies;
- the potential partner s acceptance of our approach to drug discovery;
- the novelty, quality and commercial potential of any drug candidate we may succeed in developing; and
- our ability, and collaborators perceptions of our ability, to achieve intended results in a timely fashion, with acceptable quality and cost.

17

Even if we are able to gain the interest of potential drug development partners, the negotiation, documentation and implementation of collaborative arrangements are complex and time-consuming. Collaborations may not be available on commercially acceptable terms and, if formed, may not be commercially successful or, if successful, may not realize sufficient benefit for us. If we are unable to form collaborations, we may not gain access to the financial resources and industry expertise necessary to develop and commercialize drug products or successfully market any products we develop on our own and, therefore, be unable to generate revenue from our products. In addition, our past, existing and future collaboration terms contain or will likely contain, limitations on classes of chemical compounds or biological targets that we may explore outside those collaborations for our own use.

Our success depends in part on the efforts of our current and possible future collaborators, who will likely have substantial control and discretion over the continued development and commercialization of drug candidates, including ARQ 197, that are the subjects of our collaborations.

Our current collaborators, Kyowa Hakko Kirin and Daiichi Sankyo have, and future collaborators will have significant discretion in determining the efforts and amount of resources that they dedicate to our collaborations. Our collaborators may determine not to proceed with clinical development or commercialization of a particular drug candidate for a number of reasons that are beyond our control, even under circumstances where we might have continued such a program. In addition, our rights to receive milestone payments and royalties from our collaborators will depend on our collaborators abilities to establish the safety and efficacy of our drug candidates, obtain regulatory approvals and achieve market acceptance of products developed from our drug candidates. We may also depend on our collaborators to manufacture clinical scale quantities of some of our drug candidates and, possibly, for commercial scale manufacture, distribution and direct sales. Our collaborators may not be successful in manufacturing our drug candidates or successfully commercializing them.

We face additional risks in connection with our existing and future collaborations, including the following:

- our collaborators may develop and commercialize, either alone or with others, products that are similar to or competitive with the products that are the subject of the collaboration with us;

- our collaborators may underfund, not commit sufficient resources to, or conduct in an unsatisfactory matter the testing, marketing, distribution or other development of our drug candidates;

- our collaborators may not properly maintain or defend our intellectual property rights or they may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our intellectual property or proprietary information or expose us to potential liability;

- our collaborators may encounter conflicts of interest, changes in business strategy or other business issues which could adversely affect their willingness or ability to fulfill their obligations to us (for example, pharmaceutical and biotechnology companies historically have re-evaluated their priorities following mergers and consolidations, which have been common in recent years in these industries); and

- disputes may arise between us and our collaborators delaying or terminating the research, development or commercialization of our drug candidates, resulting in significant litigation or arbitration that could be time-consuming and expensive, or causing collaborators to act in their own self-interest and not in the interest of our stockholders;

- we might not have the financial or human resources to meet our obligations or take advantage of our rights under the terms of our existing and future collaborations; and

- our existing collaborators may exercise their respective rights to terminate without cause their collaborations with us, in which event, we might not be able to complete development and commercialization of ARQ 197 and other drug candidates on our own.

We may not receive any further milestone, royalty or license payments under our current collaborations.

Although we have received license fees and other payments to date under our current drug development collaborations with Kyowa Hakko Kirin and Daiichi Sankyo, we may not receive any royalty payments or additional license and milestone fees under such agreements. Our receipt of any future milestone, royalty or license payments depends on many factors, including whether our collaborators want or are able to continue to pursue potential drug candidates, intellectual property issues, unforeseen complications in the development or commercialization process, and the ultimate commercial success of the drugs.

Risks related to relationships with third party vendors

We rely heavily on third parties such as contract research organizations, to conduct clinical trials and perform research and analysis services for us. If third parties upon which we rely do not perform as contractually required or expected, we may not be able to develop further, obtain regulatory approval for or commercialize our product candidates.

We do not have the ability or the human resources to perform all of the testing or conduct all of the clinical trials that are necessary in connection with the development of our product candidates. We are using third-party clinical research organizations, or CROs, to oversee many of our ongoing clinical trials and expect to use the same or similar organizations for certain of our future clinical trials. Our reliance on these third parties reduces our control over these activities. We may face delays outside of our control if these parties do not perform their obligations in a timely or competent fashion or if we are forced to change service providers or if

the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or for other reasons. These risks are heightened if we conduct clinical trials outside of the United States, where it may be more difficult to ensure that studies are conducted in compliance with FDA requirements. Any third party that we hire to conduct clinical trials may also provide services to our competitors, which could compromise the performance of their obligations to us. If we experience significant delays in the progress of our clinical trials and in our plans to file NDAs, the commercial prospects for product candidates could be harmed and our ability to generate product revenue would be delayed or prevented.

If the third parties we rely upon to conduct, supervise and monitor our clinical studies perform in an unsatisfactory manner, it may harm our business.

We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our ongoing clinical programs for ARQ 197 and our other product candidates, as well as the execution of nonclinical studies. We control only certain aspects of our CROs activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with the FDA s current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA may determine that our Phase 3 clinical trials do not comply with cGCPs. In addition, our Phase 3 clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of ARQ 197. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat the Phase 3 clinical trials, which would delay the regulatory approval process. Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may allow our potential competitors to access our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize ARQ 197, or our other product candidates. As a result, our financial results and the commercial prospects for ARQ 197 and any future product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We have limited manufacturing experience. Currently, we primarily rely on third parties to provide sufficient quantities of our product candidates to conduct pre-clinical and clinical studies. In the future, we may rely on our collaborators for drug supply. We have no control over our manufacturers , suppliers and collaborators compliance with manufacturing regulations, and their failure to comply could interrupt our drug supply.

To date, our product candidates have been manufactured in relatively small quantities for preclinical and clinical trials. We have no experience in manufacturing any of our product candidates on a large scale and have contracted with third party manufacturers to provide material for clinical trials and to assist in the development and optimization of our manufacturing processes and methods. Our ability to conduct clinical trials and commercialize our product candidates will depend on the ability of such third parties to manufacture our products on a large scale at a competitive cost and in accordance with cGMP and other regulatory requirements. Significant scale-up of manufacturing may result in unanticipated technical challenges and may require additional validation studies that the FDA must review and approve. If we are not able to obtain contract cGMP manufacturing on commercially reasonable terms, obtain or develop the necessary materials and technologies for manufacturing, or obtain intellectual property rights necessary for manufacturing, we may not be able to conduct or complete clinical trials or commercialize our product candidates. There can be no assurance that we will be able to obtain such requisite terms, materials, technologies and intellectual property necessary to successfully manufacture our product candidates for clinical trials or commercialization. Our product candidates require precise, high-quality manufacturing. The failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

The facilities used by our contract manufacturers may undergo inspections by the FDA for compliance with cGMP regulations before our product candidates produced there can receive marketing approval. If these facilities do not satisfy cGMP requirements in connection with the manufacture of our product candidates, we may need to conduct additional validation studies, or find alternative manufacturing facilities, either of which would result in significant cost to us as well as a delay of up to several years in obtaining approval for any affected product candidate. In addition, after approval of a product candidate for commercial use, our contract manufacturers and any alternative contract manufacturer we may utilize will be subject to ongoing periodic inspection by the FDA and corresponding state and foreign agencies for compliance with cGMP regulations, similar foreign regulations and other regulatory standards. We do not have control over our contract manufacturers compliance with these regulations and standards. Any failure by our third-party manufacturers or suppliers to comply with applicable regulations could result in sanctions being imposed (including fines, injunctions and civil penalties), failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecution.

Materials necessary to manufacture our product candidates currently under development may not be available on commercially reasonable terms, or at all, which may delay our development and commercialization of these drugs.

Some of the materials necessary for the manufacture of our product candidates currently under development may, from time to time, be available either in limited quantities, or from a limited number of manufacturers, or both. We and/or our collaborators need to obtain these materials for our clinical trials and, potentially, for commercial distribution when and if we obtain marketing approval for these compounds. Suppliers may not sell us these materials at the time we need them or on commercially reasonable terms. If we are unable to obtain the materials needed for the conduct of our clinical trials, product testing and potential regulatory approval could be delayed, adversely impacting our ability to develop the product candidates. If it becomes necessary to change suppliers for any of these materials or if any of our suppliers experience a shutdown or disruption in the facilities used to produce these materials, due to technical, regulatory or other problems, it could significantly hinder or prevent manufacture of our drug candidates and any resulting products.

Risks related to competition

The drug research and development industry is highly competitive, and we compete with some companies that have a broader range of capabilities and better access to resources than we do.

The pharmaceutical and biotechnology industries are characterized by rapid and continuous technological innovation. We compete with companies worldwide that are engaged in the research and discovery, licensing, development and commercialization of drug candidates, including, in the area of small molecule anti-cancer therapeutics, biotechnology companies such as Ariad Pharmaceuticals, Inc.; Array BioPharma Inc.; Astex Therapeutics; Cell Genesys, Inc.; Cell Therapeutics, Inc.; Curis, Inc.; Exelixis, Inc.; Idera Pharmaceuticals, Inc.; Infinity Pharmaceuticals, Inc.; Onyx Pharmaceuticals, Inc.; OSI Pharmaceuticals, Inc.; Oxigene, Inc.; Pharmacopeia, Inc.; Plexxikon, Inc. Telik, Inc.; and Vertex Pharmaceuticals, Inc. and many others.

With respect to ARQ 197 specifically, we are aware of a number of biotechnology and pharmaceutical companies that are or may be pursuing approaches to c-Met inhibition, including Amgen Inc.; AVEO Pharmaceuticals, Inc.; Bristol-Myers Squibb Company; Cephalon, Inc.; Compugen Ltd.; Eli Lilly & Company; Exelixis, Inc.; Genentech, Inc.; GlaxoSmithKline; Johnson & Johnson; Merck & Co., Inc.; Methylgene Inc.; Pfizer Inc., Roche, Schering-Plough; and Supergen Inc. and others.

Even if we are successful in bringing products to market, we face substantial competitive challenges in effectively marketing and distributing our products. Companies and research institutions, including large pharmaceutical companies with much greater financial resources and more experience in developing products, conducting clinical trials, obtaining FDA and foreign regulatory approvals and bringing new drugs to market are developing products within the field

of oncology. Some of these entities already have competitive products on the market or product candidates in more advanced stages of development than we do. By virtue of having or introducing competitive products on the market before us, these entities may gain a competitive advantage. In addition, there may be product candidates of which we are not aware at an earlier stage of development that may compete with our product candidates. Some of our competitors have entered into collaborations with leading companies within our target markets.

We are in a rapidly evolving field of research. Consequently, our technology may be rendered non-competitive or obsolete by approaches and methodologies discovered by others, both before and after we have gone to market with our products. We also face competition from existing therapies that are currently accepted in the marketplace and from the impact of adverse events in our field that may affect regulatory approval or public perception.

We anticipate that we will face increased competition in the future as new companies enter the market and advanced technologies become available. If we are unable to successfully compete in our chosen field, we will not become profitable.

We may not be able to recruit and retain the scientists and management we need to compete.

Our success depends on our ability to attract, retain and motivate highly skilled scientific personnel and management, and our ability to develop and maintain important relationships with leading academic institutions, clinicians and scientists. We are highly dependent on our senior management and scientific staff, and the loss of the services of one or more of our other key employees could have an adverse effect on the successful completion of our clinical trials or the commercialization of our product candidates.

We compete intensely with pharmaceutical and biotechnology companies, including our collaborators, medicinal chemistry outsourcing companies, contract research and manufacturing organizations, and academic and research institutions in the recruitment of scientists and management. The shortage of personnel with experience in drug development could lead to increased recruiting, relocation and compensation costs, which may exceed our expectations and resources. If we cannot hire additional qualified personnel, the workload may increase for both existing and new personnel. If we are unsuccessful in our recruitment efforts, we may be unable to execute our strategy.

Risks related to intellectual property

Our patents and other proprietary rights may fail to protect our business. If we are unable to adequately protect our intellectual property, third parties may be able to use our technology which could adversely affect our ability to compete in the market.

To be successful and compete, we must obtain and protect patents on our products and technology and protect our trade secrets. Where appropriate, we seek patent protection for certain aspects of the technology we are developing, but patent protection may not be available for some of our product candidates or their use, synthesis or formulations. The patent position of biotechnology firms is highly uncertain, involves complex legal and factual questions, and has

recently been the subject of much litigation. No consistent policy has emerged from the U.S. Patent and Trademark Office or the courts regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology patents. In addition, there is a substantial backlog of biotechnology patent applications at the U.S. Patent and Trademark Office. As a consequence of these factors, the approval or rejection of patent applications may take several years.

We do not know whether our patent applications will result in issued patents. In addition, the receipt of a patent might not provide much practical protection. If we receive a patent with a narrow scope it will be easier for competitors to design products that do not infringe our patent. We cannot be certain that we will receive any additional patents, that the claims of our patents will offer significant protection for our technology, or that our patents will not be challenged, narrowed, invalidated or circumvented.

Competitors may interfere with our patent protection in a variety of ways. Competitors may claim that they invented the claimed invention before us. Competitors may also claim that we are infringing on their patents and that, therefore, we cannot practice our technology as claimed under our patents. Competitors may also contest our patents by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our issued patents are not valid for a number of reasons. If a court agrees, our patents could be narrowed, invalidated or rendered unenforceable, or we may be forced to stop using the technology covered by these patents or to license the technology from third parties. As a company, we have no meaningful experience with competitors interfering with our patents or patent applications and therefore may not have the experience we would need to aggressively protect our patents should such action become necessary.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our product candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement.

Drug candidates we develop that are approved for commercial marketing by the FDA would be subject to the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act. The Hatch-Waxman Act provides companies with marketing exclusivity for varying time periods during which generic versions of a drug may not be marketed and allows companies to apply to extend patent protection for up to five additional years. It also provides a means for approving generic versions of a drug once the

marketing exclusivity period has ended and all relevant patents have expired. The period of exclusive marketing, however, may be shortened if a patent is successfully challenged and defeated, which could reduce the amount of revenue we receive for such product.

Agreements we have with our employees, consultants and collaborators may not afford adequate protection for our trade secrets, confidential information and other proprietary information.

In addition to patent protection, we also rely on copyright and trademark protection, trade secrets, and know-how. It is unclear whether our trade secrets and know-how will prove to be adequately protected. To protect our trade secrets and know-how, we require our employees, consultants and advisors to execute agreements regarding the confidentiality and ownership of such proprietary information. We cannot guarantee, however, that these agreements will provide us with adequate protection against improper use or disclosure of confidential information and there may not be adequate remedies in the event of unauthorized use or disclosure. Our employees, consultants or advisors may unintentionally or willfully disclose our information to competitors. In addition, in some situations, these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors had or have previous employment or consulting relationships. Like patent litigation, enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time-consuming and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing than our federal and state courts to protect trade secrets. Furthermore, others may independently develop substantially equivalent knowledge, methods and know-how. Our failure or inability to protect our proprietary information and techniques may inhibit or limit our ability to compete effectively or exclude certain competitors from the market.

Our success will depend partly on our ability to operate without infringing upon or misappropriating the proprietary rights of others.

There are many patents in our field of technology and we cannot guarantee that we do not infringe on those patents or that we will not infringe on patents granted in the future. If a patent holder believes a product of ours infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology.

If we do not prevail in litigation or if other parties have filed, or in the future should file, patent applications covering products and technologies that we have developed or intend to develop, we may have to obtain licenses from third parties, which may not be available on commercially reasonable terms, or at all, and may require us to pay substantial royalties or grant a cross-license to some of our patents to another patent holder. Additionally, we may have to change the formulation of a product candidate so that we do not infringe third- party patents. Such reformulation may be impossible to achieve or which may require substantial time and expense. If we are unable to cost-effectively redesign our products so they do not infringe a patent, we may be unable to sell some of our products. Any of these occurrences will result in lost revenues and profits for us.

The drug research and development industry has a history of patent and other intellectual property litigation, and we may be involved in costly intellectual property lawsuits.

The drug research and development industry has a history of patent and other intellectual property litigation, and we believe these lawsuits are likely to continue. Legal proceedings relating to intellectual property would be expensive, take significant time and divert management s attention from other business concerns. We face potential patent infringement suits by companies that control patents for drugs or potential drugs similar to our product candidates or other suits alleging infringement of their intellectual property rights. There could be issued patents of which we are not aware that our products and their use, whether as single agents or in combination with other products, infringe or patents that we believe we do not infringe that we are ultimately found to infringe. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patent applications can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that we infringe with our drug candidates or resulting products, and their use as single agents or in combination with other products. In addition, technology created under our research and development collaborations may infringe the intellectual property rights of third parties, in which case we may not receive milestone or royalty revenue from those collaborations.

If we do not prevail in an infringement lawsuit brought against us, we might have to pay substantial damages and we could be required to stop the infringing activity or obtain a license to use the patented technology or redesign our products so as not to infringe the patent. We may not be able to enter into licensing arrangements at a reasonable cost or effectively redesign our products. Any inability to secure licenses or alternative technology could delay the introduction of our products or prevent us from manufacturing or selling products.

Risks related to employees and facilities

Our operations could be interrupted by damage to our laboratory facilities.

Our operations are dependent upon the continued use of our specialized laboratories and equipment in Woburn, Massachusetts. Catastrophic events, including fires or explosions, could damage our laboratories, equipment, scientific data, work in progress or inventories of chemical compounds and biological materials and may materially interrupt our business. We employ safety precautions in our laboratory activities in order to reduce the likelihood of the occurrence of these catastrophic events; however, we cannot eliminate the chance that such an event will occur. Rebuilding our facilities could be time consuming and result in substantial delays in our development of products and in fulfilling our agreements with our collaborators.

Security breaches may disrupt our operations and adversely affect our operating results.

Our network security and data recovery measures may not be adequate to protect against computer viruses, break-ins, and similar disruptions from unauthorized tampering with our computer systems. The misappropriation, theft, sabotage or any other type of security breach

with respect to any of our proprietary and confidential information that is electronically stored, including research or clinical data, could have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our research and development equipment and assets could have a material adverse impact on our business, operating results, and financial condition.

Risks related to product liability

If our use of chemical and biological materials and hazardous materials violates applicable laws or causes personal injury, we may be liable for damages.

Our drug discovery activities, including the analysis and synthesis of chemical compounds, involve the controlled use of chemicals, including flammable, combustible, toxic and radioactive materials that are potentially hazardous if misused. Federal, state and local laws and regulations govern our use, storage, handling and disposal of these materials. These laws and regulations include the Resource Conservation and Recovery Act, the Occupational Safety and Health Act, local fire and building codes, regulations promulgated by the Department of Transportation, the Drug Enforcement Agency and the Department of Energy, the Department of Health and Human Services, and the laws of Massachusetts where we conduct our operations. We may incur significant costs to comply with these laws and regulations in the future and current or future environmental laws and regulations may impair our research, development and production efforts. Notwithstanding our extensive safety procedures for handling and disposing of materials, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of an accident, our business could be disrupted and we could be liable for damages. Our liability may exceed our insurance coverage and our total assets and have a negative impact on our financial condition and results of operations.

We may be exposed to potential liability related to the development, testing or manufacturing of compounds we develop and our insurance coverage may not be sufficient to cover losses.

We are developing, clinically testing and manufacturing potential therapeutic products for use in humans. In connection with these activities, we could be liable if persons are injured or die while using these drugs. We may have to pay substantial damages and/or incur legal costs to defend claims resulting from injury or death, and we may not receive expected royalty or milestone payments if commercialization of a drug is limited or ended as a result of such claims. We have product liability and clinical trial insurance that contains customary exclusions and provides coverage per occurrence at levels, in the aggregate, which we believe are customary and commercially reasonable in our industry given our current stage of drug development. Our product liability insurance does not cover every type of product liability claim that we may face or loss we may incur and may not adequately compensate us for the entire amount of covered claims or losses or for the harm to our business reputation. Also, we may be unable to maintain

our current insurance policies or obtain and maintain necessary additional coverage at acceptable costs, or at all.

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 January 19, 2011.

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

January 24, 2011