ARQULE INC
Form 424B5
April 12, 2012

Filed Pursuant to Rule 424(b)(5)
Registration Nos. 333-166532 and 333-180635

PROSPECTUS SUPPLEMENT
(To Prospectus dated May 24, 2010)

7,150,000 Shares

Common Stock
$7.30 per share

We are selling 7,150,000 shares of our common stock.

We have granted the underwriters an option to purchase up to 1,072,500 additional shares.

Our common stock is listed on the Nasdaq Global Market under the symbol “ARQL.” The last reported sale price of our common stock on the Nasdaq Global Market on April 10, 2012 was $7.46 per share.

Investing in our common stock involves risks. See “Risk Factors” beginning on page S-7.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$ 7.300	$ 52,195,000
Underwriting Discount	$ 0.438	$ 3,131,700
Proceeds to ArQule (before expenses)	$ 6.862	$ 49,063,300

The underwriters expect to deliver the shares to purchasers on or about April 16, 2012 through the book-entry facilities of The Depository Trust Company.

Joint Book-Running Managers

Citigroup	Leerink Swann

Co-Managers

Lazard Capital Markets	RBC Capital Markets	Oppenheimer & Co.

April 11, 2012

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About this Prospectus Supplement

On May 5, 2010, we filed with the Securities and Exchange Commission (the "SEC") a registration statement on Form S-3 (File No. 333-166532) utilizing a shelf registration process relating to the securities described in this prospectus supplement, which registration statement became effective on May 24, 2010. Under this shelf registration process, we may, from time to time, sell up to $100,000,000 of our common stock and other securities, of which we sold $49,507,500 in January 2011, and of which this offering is a part.

We provide information to you about our common stock in two separate documents. This prospectus supplement describes the specific terms of this offering of our common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. If the information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus and any relevant free writing prospectus. Neither we nor the underwriters have authorized anyone to provide you with information different from that contained in this prospectus supplement and the accompanying prospectus and any relevant free writing prospectus. If you receive any information not authorized by us or the underwriters, you should not rely on it. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus or any relevant free writing prospectus is accurate as of any date other than its respective date.

We and the underwriters are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement, the accompanying prospectus or any free writing prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement, the accompanying prospectus or any free writing prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement, the accompanying prospectus and any free writing prospectus outside the United States. This prospectus supplement, the accompanying prospectus and any free writing prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement, the accompanying prospectus or any free writing prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

It is important for you to read and consider all of the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in these documents in making your investment decision. We include cross-references in this prospectus supplement and the accompanying prospectus to captions in these materials where you can find additional related discussions. The table of contents in this prospectus supplement provides the pages on which these captions are located.

The representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

In this prospectus, “ArQule,” “we,” “our,” “ours,” and “us” refer to ArQule, Inc., except where the context otherwise requires o
as otherwise indicated.

“ArQule”, the ArQule logo, and “AKIP” are our registered trademarks. Other service marks, trademarks and trade names appearing in this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Incorporation of Certain Documents by Reference

The SEC allows us to "incorporate by reference" the information we file with them, which means that we can disclose important information to you by referring you to these documents instead of having to repeat the information in this prospectus supplement. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede this information. Our periodic reports are filed with the SEC under SEC File Number 000-21429. We hereby incorporate by reference the following:

(1) our Annual Report filed on Form 10-K for the fiscal year ended December 31, 2011 filed with the SEC on March 1, 2012, as amended on April 10, 2012;

(2) our Current Reports on Form 8-K filed with the SEC on January 17, 2012; February 24, 2012, as amended February 27, 2012; and April 10, 2012; and

(3) the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on September 25, 1996, including any amendment or report filed for the purpose of updating such description.

In addition, all documents subsequently filed by the Company with the SEC pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), prior to the filing of a post-effective amendment that either indicates that all securities offered hereby have been sold or deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference in this prospectus supplement and to be a part hereof from the date of filing of such documents.

Unless specifically stated to the contrary, none of the information that we disclose under Items 2.02 or 7.01 of any Current Report on Form 8-K that we may from time to time furnish to the SEC will be incorporated by reference into, or otherwise included in, this prospectus supplement. All information incorporated by reference is part of this prospectus supplement, unless and until that information is updated and superseded by the information contained in this prospectus supplement, the accompanying prospectus, or any information later incorporated.

We will furnish to you at no cost, upon written or oral request, a copy of all of the documents that have been incorporated by reference in this prospectus, other than the exhibits to such documents unless the exhibits are specifically incorporated by reference but not delivered with this prospectus. Requests should be directed to:

William B. Boni, Vice President,
Investor Relations and Corporate Communications
ArQule, Inc.
19 Presidential Way
Woburn, MA 01801
(781) 994-0300
wboni@arqule.com

You should rely only on the information incorporated by reference or provided in this prospectus supplement and the accompanying prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus supplement and the accompanying prospectus is accurate as of any date other than the date on the front page of those documents.

Forward-Looking Statements

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in these documents include forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995. All statements that are not descriptions of historical fact are forward-looking statements based on estimates, assumptions and projections that are subject to risks and uncertainties. These statements can generally be identified by use of forward looking terminology such as “believes”, “expects”, “intends”, “may”, “will”, “plans”, “should”, “anticipates,” “potenti similar terminology. Although we believe that the expectations reflected in such forward looking statements are reasonable as of the date thereof, such expectations are based on certain assumptions regarding preclinical activities with our AKIP™ technology, the progress of other product development efforts including clinical trials, the prosecution of existing and efforts to execute new collaborative agreements, receipt of potential milestones and royalties under our collaborative agreements, government regulations, reliance on third parties to conduct clinical trials and perform research and analysis services, adequate financial resources, changes in economic and business conditions, and other factors relating to our growth. Such expectations may not materialize if product development efforts, including any necessary trials of our potential drug candidates, are delayed or suspended, if our compounds fail to demonstrate safety and efficacy, if positive early results are not repeated in later studies or in humans, if we or our partners fail to successfully commercialize our products, if planned acquisitions or negotiations with potential collaborators are delayed or unsuccessful, if we are unsuccessful at integrating acquired assets or technologies, or if other assumptions prove incorrect.

Factors that could cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those more fully described in the “Risk factors” section of this prospectus supplement and elsewhere in this prospectus supplement and in the reports we file with the SEC that are incorporated by reference into this prospectus supplement and the accompanying prospectus. We disclaim any intent or obligation to update any forward-looking statement to reflect events or circumstances after the date of this prospectus supplement except to the extent required by law.

Prospectus Supplement Summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. Because it is a summary, it does not contain all the information you should consider before investing in our common stock. You should carefully read this entire prospectus supplement and the accompanying prospectus, including the "Risk Factors" section contained in this prospectus supplement and the documents incorporated by reference, before making an investment decision.

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

Our Corporate Information

We are a Delaware corporation, incorporated in 1993. Our executive offices are located at 19 Presidential Way, Woburn, Massachusetts 01801, and our telephone number is (781) 994-0300. Our web site address is http://www.arqule.com. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

The Offering

Common stock offered by us	7,150,000 shares
Common stock to be outstanding after this offering	60,975,567 shares (or 62,048,067 shares if the underwriters' option to purchase additional securities is exercised in full)
Option to purchase additional securities	We have granted the underwriters an option to purchase up to 1,072,500 additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds of this offering to fund our research and development efforts, including clinical trials, for our proprietary candidates, and for general corporate purposes, including working capital. See “Use of Proceeds.”
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
NASDAQ Global Market Symbol	ARQL

The number of shares of our common stock to be outstanding after this offering is based on 53,825,567 shares of common stock outstanding as of December 31, 2011 and excludes:

- 6,547,443 shares issuable upon exercise of options outstanding as of December 31, 2011 at a weighted average exercise price of $5.34 per share, of which 3,952,607 were exercisable at December 31, 2011;
- 195,979 shares of restricted stock issuable upon vesting and a maximum of 390,000 performance based stock units at December 31, 2011;
- 4,663,745 shares of common stock available for future issuance under our employee and directors stock option plans; and

681,900 shares of common stock available for future issuance under our employee stock purchase plan.

Unless otherwise indicated, all information in this prospectus supplement assumes:

no exercise of the underwriters' option to purchase 1,072,500 additional shares of our common stock, and

no exercise of outstanding options or warrants to purchase shares of common stock.

Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described in this prospectus supplement and the accompanying prospectus and the other information in this prospectus supplement and the accompanying prospectus. If any of these risks occur, our business could be materially harmed, and our financial condition and results of operations could be materially and adversely affected. As a result, the price of our common stock could decline, and you could lose all or part of your investment.

Risks related to our industry and business strategy

Development of our product candidates 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, tivantinib, is an inhibitor of the c-Met receptor tyrosine kinase. Our other proprietary clinical-stage product candidates, ARQ 621 and ARQ 736, are inhibitors of the Eg5 kinesin motor protein and the RAF kinases, respectively. ARQ 092 (licensed to Daiichi Sankyo) is an inhibitor of the AKT kinase. 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 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 tivantinib 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 tivantinib 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 tivantinib 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 tivantinib. 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 tivantinib or any other pre-clinical or clinical trials will be completed on schedule, or 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 have 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 SPA agreement with the FDA for the design of a Phase 3 trial of tivantinib in patients with 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 tivantinib. 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 tivantinib 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 seven IND applications, and we have initiated approximately 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 completed a Phase 3, or pivotal, clinical trial, registered a biomarker, 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 for which we are responsible. 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 trials. In particular, we will be relying principally on Daiichi Sankyo and Kyowa Hakko Kirin for the commercialization of tivantinib. 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 completed a Phase 2 clinical study and enrolled the first patient in the Phase 3 MARQUEE and ATTENTION trials in NSCLC in January and August 2011, respectively. 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 from a Phase 3 clinical study could cause the FDA to require that we repeat or conduct additional clinical studies. Furthermore, while we have obtained positive safety and efficacy results for tivantinib 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 December 31, 2011 we have incurred cumulative losses of approximately $409 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 recent years 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;

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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.

In addition to this offering, 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, 2011, we had federal NOL, state NOL, and research and development credit carryforwards of approximately $243 million, $171 million and $25 million respectively, which expire at various dates through 2031. 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, including this offering, increasing the ownership of certain stockholders 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 through 2011, 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 tivantinib and have enrolled patients in our Phase 3 non-small cell lung cancer trials being conducted by Daiichi Sankyo and Kyowa Hakko Kirin and Phase 1 clinical testing of ARQ 621, ARQ 736 and ARQ 092. We have never completed 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.

The requirements governing product licensing, pricing and reimbursement vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after product-licensing approval is granted. As a result, we may obtain regulatory approval for a drug candidate in a particular country, but then be subject to price regulations that reduce our profits from the sale of the product. In some foreign markets pricing of prescription pharmaceuticals is subject to continuing government control even after initial marketing approval. Varying price regulation between countries can lead to inconsistent prices and some re-selling by third parties of products from markets where products are sold at lower prices to markets where those products are sold at higher prices. Any practice of exploiting price differences between countries could undermine our sales in markets with higher prices and reduce the sales of our future products, if any.

Additionally, 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.

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 tivantinib, that are the subjects of our collaborations.

Our current collaborators, Daiichi Sankyo and Kyowa Hakko Kirin 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 tivantinib 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 Daiichi Sankyo and Kyowa Hakko Kirin, 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 tivantinib 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 tivantinib. 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 tivantinib, or our other product candidates. As a result, our financial results and the commercial prospects for tivantinib 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 Therapeutics, Inc., Curis, Inc., Cytokinetics, Inc., Deciphera Pharmaceuticals, Exelixis, Inc., Evotec AG, FORMA Therapeutics, Glaxo Smith Kline, Incyte Corporation, Infinity Pharmaceuticals, Inc., Onyx Pharmaceuticals, Inc., OSI Pharmaceuticals, Inc., Plexxikon, Inc., Roche and Telik, Inc. and many others.

With respect to tivantinib 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., AstraZeneca/Hutchison MediPharma, AVEO Pharmaceuticals, Inc., Bristol-Myers Squibb Company, Cephalon, Inc., Compugen Ltd., Exelixis, Inc., GlaxoSmithKline, Johnson & Johnson, Merck & Co., Inc., Methylgene Inc., Pfizer, Roche, Takeda 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.

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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.

Risks related to our common stock and the offering

Our stock price may be extremely volatile.

The trading price of our common stock has been highly volatile. We believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as:

adverse results or delays in clinical trials;

announcement of FDA approval or non-approval, or delays in the FDA review process, of our or our collaborators' product candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators' or our competitors' clinical trials;

announcement of new products by us or our competitors;

quarterly variations in our or our competitors' results of operations, including as a result of recognition of upfront licensing or other fees, the timing and amount of expenses incurred for clinical development, regulatory approval and commercialization of our product candidates;

litigation, including intellectual property infringement lawsuits, involving us;

financing transactions;

developments in the biotechnology and pharmaceutical industries;

the general performance of the equity markets and in particular the biopharmaceutical sector of the equity markets;

departures of key personnel or board members;

developments concerning current or future collaborations;

FDA or international regulatory actions affecting our industry generally; and

third-party reimbursement policies.

This volatility and general market declines in our industry over the past several years have affected the market prices of securities issued by many companies, often for reasons unrelated to their operating performance, and may adversely affect the price of our common stock. In the past, securities class action litigation has often been instituted following periods of volatility in the market price of a company's securities. A securities class action suit against us could result in potential liabilities, substantial costs and the diversion of management's attention and resources, regardless of the outcome of the action.

Some of our existing stockholders can exert control over us, and their interests could conflict with the best interests of our other stockholders.

Due to their combined stock holdings, our principal stockholders (stockholders holding more than 5% of our common stock), acting together, may be able to exert significant influence over all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. In addition, this concentration of ownership may delay or prevent a change in control of our company, even when a change may be in the best interests of our stockholders. Furthermore, the interests of these stockholders may not always coincide with our interests as a company or the interests of other stockholders. Accordingly, these stockholders could cause us to enter into transactions or agreements that would not be widely viewed as beneficial.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent or deter attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and bylaws and Delaware law may discourage, delay or prevent an acquisition of our company, a change in control, or attempts by our stockholders to replace or remove members of our current Board of Directors. Because our Board of Directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

a Board of Directors having three classes of directors with a three-year term of office that expires as to one class each year, commonly referred to as a “staggered board”;

a prohibition on actions by our stockholders by written consent;

the inability of our stockholders to call special meetings of stockholders;

the ability of our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors;

limitations on the removal of directors; and

advance notice requirements for director nominations and stockholder proposals.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. As a result, it is difficult for a third party to acquire control of us without the approval of our Board of Directors and, therefore, mergers with and acquisitions of us that our stockholders may consider in their best interests may not occur.

Because we do not intend to pay dividends, stockholders will benefit from an investment in our common stock only if it appreciates in value.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain our future earnings, if any, to finance the expansion of our business and do not expect to pay any cash dividends in the

foreseeable future. As a result, the success of an investment in our common stock will depend entirely upon any future appreciation. There is no guarantee that our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

A substantial number of shares of our outstanding common stock may be sold in this offering, which could cause the price of our common stock to decline.

In this offering, assuming the underwriter's option to purchase up to 1,072,500 additional shares from us is exercised in full, we will sell 8,222,500 shares, or approximately 15.3% of our outstanding common stock as of December 31, 2011. This sale and any future sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could adversely affect the price of our common stock. We cannot predict the effect, if any, that market sales of those shares of common stock or the availability of those shares of common stock for sale will have on the market price of our common stock.

Future sales of our common stock may depress our stock price.

The market price of our common stock could decline as a result of sales of substantial amounts of our common stock in the public market after the closing of this offering, or the perception that these sales could occur. In addition, if our officers, directors or principal stockholders sell substantial amounts of our common stock (including shares issued upon the exercise of options and warrants) in the public market, the market price of our common stock could fall. These factors could make it more difficult for us to raise funds through future offerings of equity or equity-related securities at a time and price that we deem appropriate. There were 53,825,567 shares of common stock outstanding as of December 31, 2011. All of the shares sold in this offering and not held by our affiliates will be freely transferable without restriction or further registration under the Securities Act of 1933, as amended (the "Securities Act").

We had an aggregate of 5,345,645 shares of common stock remaining as of December 31, 2011 that have been registered or are freely tradable under an exemption from registration and are reserved for issuance upon exercise of options granted or reserved for grant under our stock option plan and our employee stock purchase plan. Stockholders can sell these shares in the public market upon issuance, subject to restrictions under securities laws. The number of shares we have reserved for issuance under our stock option plan may increase based on our issued and outstanding shares of common stock and we may increase the number of shares reserved for issuance under our employee stock purchase plan. We may register such additional shares in the future. In addition, some of our existing stockholders will be entitled to register their shares of common stock after this offering.

We have broad discretion in the use of the net proceeds from this offering, and we may not use these proceeds effectively.

We have not determined the specific allocation of the net proceeds of this offering. Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business or financial condition, cause the price of our common stock to decline and delay product development. In addition, our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Since the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on an offering price to the public of $7.30 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $6.01 per share in the net tangible book value of the common stock. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Use of Proceeds

Based on an offering price of $7.30 per share, we estimate that the net proceeds to us from this offering will be approximately $48.7 million (or approximately $56.1 million if the underwriters' option to purchase additional securities is exercised in full), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund our research and development efforts, including clinical trials for our proprietary candidates, and for general corporate purposes, including working capital. We may also use a portion of the net proceeds to acquire or invest in complementary businesses, technologies, drugs, drug candidates or other intellectual property, although we have no present commitments or agreements to do so.

The amounts and timing of these expenditures will depend on a number of factors, such as the timing and progress of our research and development efforts, technological advances and the competitive environment for our drug candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, we will retain broad discretion over the use of these proceeds. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

Dilution

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering. Net tangible book value per share is equal to the amount of our total tangible assets, less total liabilities, divided by the number of shares of our common stock outstanding.

The net tangible book value of our common stock as of December 31, 2011 was approximately $29.7 million, or $0.55 per share. After giving effect to our sale of 7,150,000 shares of common stock we are offering through this prospectus supplement and the accompanying prospectus, at a public offering price of $7.30 per share, and after deducting underwriting discounts and commissions and estimated offering expenses, our net tangible book value as of December 31, 2011 would have been approximately $78.4 million, or $1.29 per share. This represents an immediate increase in net tangible book value of $0.74 per share to existing stockholders and an immediate dilution of $6.01 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Public offering price per share		$7.30
Net tangible book value per share as of December 31, 2011	$0.55	
Increase per share attributable to new investors	0.74	
As adjusted net tangible book value per share after giving effect to this offering		1.29
Dilution per share to new investors		$6.01

If the underwriters exercise the option to purchase additional securities granted by us in full, the as adjusted net tangible book value as of December 31, 2011 will increase to approximately $85.8 million, or $1.38 per share, representing an increase to existing stockholders of approximately $0.83 per share, and there will be an immediate dilution of approximately $5.92 per share to new investors.

The number of shares of our common stock in the calculations above are based on 53,825,567 shares outstanding as of December 31, 2011, assumes no exercise of the underwriters' option to purchase up to 1,072,500 additional shares of common stock from us, and excludes, as of that date:

- 6,547,443 shares issuable upon exercise of outstanding options at a weighted average exercise price of $5.34 per share; and
- 5,345,645 shares of common stock reserved for future issuance under our Equity Incentive Plan, Director's Plan and Employee Stock Purchase Plan.

Underwriting

Subject to the terms and conditions set forth in an underwriting agreement between us and the underwriters named below, for whom Citigroup Global Markets Inc. and Leerink Swann LLC are acting as representatives, we have agreed to sell to the underwriters, and the underwriters have severally agreed to purchase from us the number of shares of common stock listed next to its name in the following table:

Underwriter	Number of Shares
Citigroup Global Markets Inc.	3,038,750
Leerink Swann LLC	2,502,500
Lazard Capital Markets LLC	607,750
RBC Capital Markets, LLC	500,500
Oppenheimer & Company, Inc.	500,500
Total	7,150,000

The underwriters are committed to purchase all the common shares (other than those covered by the underwriters' option to purchase additional securities) offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers’ certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of $0.2628 per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional securities.

	Per Share	Without Option	With Option
Public offering price	$7.300	$52,195,000	$60,024,250
Underwriting discount	$0.438	$3,131,700	$3,601,455
Proceeds to ArQule (before expenses)	$6.862	$49,063,300	$56,422,795

Our total offering expenses, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discount, are estimated at approximately $205,000, net of certain of our expenses that Citigroup Global Markets Inc. has agreed to reimburse us for in connection with this offering, and are payable by us. In addition, upon the closing of this offering, we will pay to McNicoll, Lewis & Vlak LLC, or MLV, a financial advisory fee equal to $150,000. MLV is not acting as an underwriter in connection with this offering.

In no event will the total amount of compensation paid to the underwriters upon completion of this offering exceed 8.0% of the gross proceeds of this offering.

Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith.

Option to Purchase Additional Securities

If the underwriters sell more shares than the total number set forth in the table above, we have granted an option to the underwriters to purchase up to 1,072,500 additional shares at the public offering price, less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus. To the extent the option is excercised, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

No Sales of Similar Securities

We and our officers and directors have agreed, subject to certain exceptions, not to sell or transfer any common stock or securities convertible into, exchangeable for, or exercisable for common stock, other than the shares which we may sell in this offering, for 90 days after the date of this prospectus supplement without first obtaining the written consent of Citigroup Global Markets Inc. and Leerink Swann LLC. Specifically, we and these other individuals have agreed not to, nor to publicly disclose the intention to, directly or indirectly:

- offer, sell, issue, contract to sell, pledge or otherwise dispose of any common stock or securities convertible into common stock,
- enter into any swap, hedge or other agreement that transfers the economic consequence of owning common stock, or
- engage in short selling of the common stock (in the case of the individuals) or establishing or increasing a put equivalent position or liquidating or decreasing a call equivalent position in the common stock (in our case).

In addition, during such 90-day restriction period, we have agreed not to file a registration statement with the Securities and Exchange Commission relating to the common stock.

The lock-up restrictions described in the immediately preceding paragraph do not apply:

with respect to us:

- to the shares of our common stock to be sold in this offering,
- in connection with the exercise of an option or warrant or the conversion of a security outstanding as of the date of the underwriting agreement, of which the underwriters have been advised in writing, or
- to the issuance of common stock options or stock-based awards (or the issuance of shares of common stock on the exercise of those awards) to eligible participants pursuant to employee benefit plans disclosed in this prospectus supplement, the accompanying prospectus, or in documents incorporated by reference herein or therein, or

with respect to our officers and directors:

- to transfers of shares of common stock or any security convertible into common stock as a bona fide gift,
- to transfers of shares of common stock to any trust for the benefit of the officer or director or his or her immediate family; transfers of shares of common stock by will or intestate succession upon the death of such a person.

provided that in the case of any transfer or distribution described in the preceding bullets, (i) each donee, transferee or distributee agrees in writing to the same restrictions set forth above, and (ii) no filing under section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the 90-day restricted period;

to the entry into any trading plan established pursuant to Rule 10b5-1 of the Exchange Act, provided that no sales or other dispositions may occur under such plan until the expiration of the restricted period; and

to the sale of shares of common stock pursuant to any contract, instruction or plan that complies with Rule 10b5-1 and was existing on the date of the lock-up agreement and are related to options that are set to expire during the lock-up period.

The 90-day restricted period in all of the agreements is subject to extension if (i) during the last 17 days of the restricted period we issue an earnings release or material news or a material event relating to us occurs or (ii) prior to the expiration of the restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the lock-up period, in which case the restrictions imposed in these lock-up agreements shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make for these liabilities.

Nasdaq Global Market Listing

Our shares are listed on the Nasdaq Global Market under the symbol “ARQL.”

Price Stabilization and Short Positions

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters’ option to purchase additional shares, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.

- “Covered” short sales are sales of shares in an amount up to the number of shares represented by the underwriters’ option to purchase additional shares.
- “Naked” short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters’ option to purchase additional shares.

Covering transactions involve purchases of shares either pursuant to the underwriters’ option to purchase additional shares or in the open market after the distribution has been completed in order to cover short positions.

- To close a naked short position, the underwriters must purchase shares in the open market after the distribution has been completed. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

- To close a covered short position, the underwriters must purchase shares in the open market after the distribution has been completed or must exercise the option to purchase additional shares. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the underwriters' option to purchase additional shares.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

In addition, in connection with this offering, some of the underwriters (and selling group members) may engage in passive market making transactions in the shares on the Nasdaq Global Market, prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than those independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker's average daily trading volume in the shares during a specified period and must be discontinued when that limit is reached. Passive market making may cause the price of the shares to be higher than the price that otherwise would exist in the open market in the absence of those transactions. If the underwriters commence passive market making transactions, they may discontinue them at any time.

Electronic Offer, Sale and Distribution of Shares

A prospectus supplement in electronic format may be made available on the websites maintained by one or more underwriters or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations. Other than the prospectus supplement in electronic format, the information on the underwriters' websites and any information contained in any other website maintained by the underwriters is not part of this prospectus supplement or the registration statement of which this prospectus supplement forms a part.

Conflicts of Interest

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates have in the past performed commercial banking, investment banking and advisory services for us from time to time for which they have received customary fees and reimbursement of expenses and may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus supplement may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus supplement. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus supplement and the accompanying prospectus are only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a "relevant person"). This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia (''Corporations Act'')) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission (''ASIC''). This document has not been lodged with ASIC and is only directed to certain categories of

exempt persons. Accordingly, if you receive this document in Australia:

(a) you confirm and warrant that you are either:

(i) a ‘‘sophisticated investor’’ under section 708(8)(a) or (b) of the Corporations Act;

(ii) a ‘‘sophisticated investor’’ under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant’s certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

(iii) a person associated with the company under section 708(12) of the Corporations Act; or

(iv) a ‘‘professional investor’’ within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

(b) you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Chile

The shares are not registered in the Securities Registry (Registro de Valores) or subject to the control of the Chilean Securities and Exchange Commission (Superintendencia de Valores y Seguros de Chile). This prospectus and other offering materials relating to the offer of the shares do not constitute a public offer of, or an invitation to subscribe for or purchase, the shares in the Republic of Chile, other than to individually identified purchasers pursuant to a private offering within the meaning of Article 4 of the Chilean Securities Market Act (Ley de Mercado de Valores) (an offer that is not "addressed to the public at large or to a certain sector or specific group of the public").

Notice to Prospective Investors in France

Neither this prospectus supplement nor any other offering material relating to the shares described in this prospectus supplement has been submitted to the clearance procedures of the Autorité des Marchés Financiers or of the competent authority of another member state of the European Economic Area and notified to the Autorité des Marchés Financiers. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus supplement nor any other offering material relating to the shares has been or will be:

released, issued, distributed or caused to be released, issued or distributed to the public in France; or

used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

to qualified investors (investisseurs qualifiés) and/or to a restricted circle of investors (cercle restreint d'investisseurs), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code monétaire et financier;

to investment services providers authorized to engage in portfolio management on behalf of third parties; or

in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French Code monétaire et financier and article 211-2 of the General Regulations (Règlement Général) of the Autorité des Marchés Financiers, does not constitute a public offer (appel public à l'épargne).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code monétaire et financier.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus supplement have not been registered under the Securities and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan, except (i) pursuant to an exemption from the registration requirements of the Securities and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures

and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

Legal Matters

The validity of the securities offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Arnold & Porter LLP, Washington, DC. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, NY, is counsel for the underwriters in connection with this offering.

Experts

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus supplement and the accompanying prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2011 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Where You Can Find More Information

This prospectus supplement and the accompanying prospectus are part of a certain registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document.

Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and special reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's web site at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

PROSPECTUS

ARQULE, INC.

UP TO $100,000,000 OF OUR

COMMON STOCK

PREFERRED STOCK

WARRANTS

We may offer from time to time up to $100,000,000 in total of:

- shares of our common stock,
- shares of our preferred stock,
- warrants to purchase shares of common stock or preferred stock, or
- any combination of our common stock, preferred stock or warrants.

We may offer the common stock, preferred stock and warrants (collectively, the "securities") separately or together, in separate series, in amounts, at prices and on terms to be set forth in one or more supplements to this prospectus. When we decide to issue securities, we will provide you with the specific terms and the public offering price of the securities in prospectus supplements. You should read this prospectus and the prospectus supplements carefully before you invest. This prospectus may not be used to offer or sell securities unless accompanied by a prospectus supplement.

Our common stock is quoted on the NASDAQ Global Market and traded under the symbol "ARQL." We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents in the applicable prospectus supplement.

Our principal executive offices are located at 19 Presidential Way, Woburn, Massachusetts 01801-5140 and our telephone number is (781) 994-0300.

An investment in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 3 for information regarding certain material factors that you should consider in connection with an investment in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 24, 2010

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ARQULE, INC.

SUMMARY

This summary contains a general summary of the information contained in this prospectus. It may not include all the information that is important to you. You should read the entire prospectus, the prospectus supplement delivered with the prospectus, and the documents incorporated by reference before making an investment decision.

We are a clinical-stage biotechnology company formed as a Delaware corporation in 1993 engaged in the research and development of innovative cancer therapeutics. Our mission is to produce novel medicines with differentiated mechanisms of action that target the 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.

Our products and programs span a continuum of research and development ranging from drug discovery to advanced clinical testing. They are based on our understanding of biological processes that lead to the proliferation and metastasis of cancer cells, combined with our ability to generate product candidates possessing certain pre-selected, drug-like properties and designed to act specifically against cancer cells. We believe that these qualities, when present from the earliest stages of product development, increase the likelihood of producing safe, effective and marketable drugs.

Our lead product is ARQ 197, a non-adenosine triphosphate ("ATP")-competitive inhibitor of the c-Met receptor tyrosine kinase ("c-Met"). C-Met is a promising target for cancer therapy, as evidence suggests that it plays a key role in cancerous cell proliferation, tumor spread, new blood vessel formation and drug resistance. Our ongoing Phase 2 clinical trial program with ARQ 197 encompasses six tumor types, including non-small cell lung cancer, c-Met-associated soft tissue sarcomas, pancreatic adenocarcinoma, hepatocellular carcinoma, germ cell tumors and colorectal cancer. On March 31, 2010, we announced the results of our Phase 2 trial with ARQ 197 in non-small cell lung cancer. We believe the data from this trial provide a signal of efficacy, together with a safety profile showing that ARQ 197 was well tolerated when combined with another tyrosine kinase inhibitor (erlotinib). With our partner, Daiichi Sankyo Co. Ltd. ("Daiichi Sankyo"), we will consider further analyses of these results, as well as related discussions with regulatory authorities, to optimize ongoing and future trials of ARQ 197.

We have licensed commercial rights to ARQ 197 for human cancer indications to Daiichi Sankyo in the United States, Europe, South America and the rest of the world, excluding certain Asian countries, where we have licensed commercial rights to Kyowa Hakko Kirin Co., Ltd. ("Kyowa Hakko Kirin"). Our agreements with these partners provide for possible future milestone payments, royalties on product sales, and development funding, in addition to significant payments that we have already received.

Our proprietary pipeline is directed toward molecular targets and biological processes with demonstrated roles in the development of human cancers. The most advanced candidate in this pipeline is ARQ 621, an inhibitor of the Eg5 kinesin motor protein that is in Phase 1 clinical testing. Additional pipeline assets include ARQ 501 and ARQ 761, activators of the cell's DNA damage response mechanism that we plan to develop further on a partnered basis. We are also pursuing pre-clinical development of an inhibitor of the B-RAF kinase that is in toxicology testing leading to a potential investigational new drug submission in 2010.

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Securities We are Offering

We may offer any of the following securities from time to time:

shares of our common stock;

shares of our preferred stock;

warrants to purchase shares of our preferred stock or common stock; or

any combination of our common stock, preferred stock, or warrants.

When we use the term "securities" in this prospectus, we mean any of the securities we may offer with this prospectus, unless we say otherwise. The total dollar amount of all securities that we may issue will not exceed $100,000,000. This prospectus, including the following summary, describes the general terms that may apply to the securities; the specific terms of any particular securities that we may offer will be described in a separate supplement to this prospectus.

Common Stock. We may offer shares of our common stock. Our common stock currently is listed on the NASDAQ Global Market under the symbol "ARQL."

Preferred Stock. We may offer our preferred stock in one or more series. For any particular series we offer, the applicable prospectus supplement will describe the specific designation; the aggregate number of shares offered; the rate and periods, or manner of calculating the rate and periods, for dividends, if any; the stated value and liquidation preference amount, if any; the voting rights, if any; the terms on which the series will be convertible into or exchangeable for other securities or property, if any; the redemption terms, if any; and any other specific terms.

Warrants. We may offer warrants to purchase our common stock and preferred stock. For any particular warrants we offer, the applicable prospectus supplement will describe the underlying security; the expiration date; the exercise price or the manner of determining the exercise price; the amount and kind, or the manner of determining the amount and kind, of any security to be delivered by us upon exercise; and any other specific terms. We may issue the warrants under warrant agreements between us and one or more warrant agents.

Units. We may offer units comprised of our common stock, preferred stock and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

Listing. If any securities are to be listed or quoted on a securities exchange or quotation system, the applicable prospectus supplement will say so.

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the specific risks set forth under the caption "Risk Factors" in the applicable prospectus supplement before making an investment decision. The risks and uncertainties described in the prospectus supplement are not the only ones we face. Additional risks and uncertainties that we are unaware of or that we believe are not material at the time could also materially adversely affect our business, financial condition or results of operations. In any case, the value of our common stock, preferred stock or warrants could decline, and you could lose all or part of your investment. You should also refer to the other information contained in this prospectus or incorporated herein by reference, including our consolidated financial statements and the notes to those statements and the risks and uncertainties described in Item 1A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2009. See also the information contained under the heading "Special Note Regarding Forward Looking Statements" immediately below.

SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement contains and incorporates by reference certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements also may be included in other statements that we make. All statements that are not descriptions of historical facts are forward-looking statements, based on management's estimates, assumptions and projections that are subject to risks and uncertainties. These statements can generally be identified by the use of forward-looking terminology such as "believes," "expects," "intends," "may," "will," "should," or "anticipates" or similar terminology. Although we believe that the expectations reflected in our forward-looking statements are reasonable as of the date made, actual results could differ materially from those currently anticipated due to a number of factors, including risks relating to the early stage of products under development; uncertainties relating to clinical trials; dependence on third parties; future capital needs; and risks relating to the commercialization, if any, of our product candidates (such as marketing, safety, regulatory, patent, product liability, supply, competition and other risks). Additional important factors that could cause actual results to differ materially from our current expectations are identified in our other filings with the Securities and Exchange Commission. Our forward-looking statements are based on information available to us today, and we will not update these statements, except as may be required by law.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC" or the "Commission") using a "shelf" registration process. Under this shelf process, we may from time to time offer up to $100,000,000 in total of (a) shares of common stock, $0.01 par value per share, (b) shares of preferred stock, $0.01 par value per share, in one or more series, (c) warrants to purchase shares of common stock or preferred stock or (d) any combination of our common stock, preferred stock or warrants, either individually or as units consisting of one or more of the foregoing, each at prices and on terms to be determined at the time of sale. The common stock, preferred stock and warrants are collectively referred to in this prospectus as "securities." The securities offered pursuant to this prospectus may be one or more series of issuances and the total offering price of the securities will not exceed $100,000,000 (or its equivalent based on the applicable exchange rate at the time of the sale in one or more foreign currencies, currency units or composite currencies that we may designate).

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described below under the heading "Where You Can Find More Information."

You should rely only on the information provided in the registration statement, this prospectus and in any prospectus supplement, including the information incorporated by reference. We have not authorized anyone to provide you with different information. You should not assume that the information in this prospectus or any supplement to this prospectus is accurate at any date other than the date indicated on the cover page of these documents. Neither the delivery of this prospectus nor any sale made hereunder shall, under any circumstances, create an implication that there has not been any change of facts set forth in this prospectus or in our affairs since the date of this prospectus.

USE OF PROCEEDS

We will use the net proceeds received from the sale of the securities for development of our drug discovery approach and potential product candidates, clinical trials, working capital and general corporate purposes, at the discretion of management.

DILUTION

We will set forth in a prospectus supplement the following information regarding any material dilution of the equity interests of investors purchasing securities in an offering under this prospectus:

- the net tangible book value per share of our equity securities before and after the offering;
- the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers in the offering; and
- the amount of the immediate dilution from the public offering price which will be absorbed by such purchases.

PLAN OF DISTRIBUTION

We may sell the securities being offered by this prospectus separately or together through any of the following methods:

- directly to investors or purchasers;
- to investors through agents;
- directly to agents;
- to or through brokers or dealers;
- to the public through underwriting syndicates led by one or more managing underwriters;
- to one or more underwriters acting alone for resale to investors or to the public;

through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or

through a combination of any of these methods of sale.

Securities may also be issued upon exercise of warrants or as a dividend or distribution. We reserve the right to sell securities directly to investors on our own behalf in those jurisdictions where we are authorized to do so.

We may effect the distribution of the securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed from time to time;

at market prices prevailing at the times of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We will describe the method of distribution of the securities in the applicable prospectus supplement.

Direct Sales and Sales through Agents

We may directly solicit offers to purchase the securities offered by this prospectus. Agents designated by us from time to time may solicit offers to purchase the securities. We will name any agent involved in the offer or sale of the securities and set forth any commissions payable by us to an agent in the applicable prospectus supplement. Unless otherwise indicated in the applicable prospectus supplement, any agent will be acting on a best efforts basis for the period of his or her appointment. Any agent may be deemed to be an "underwriter" of the securities as that term is defined in the Securities Act.

Sales Through Underwriters or Dealers

If we use an underwriter or underwriters in the sale of securities, we will execute an underwriting agreement with the underwriter or underwriters at the time we reach an agreement for sale. We will set forth in the applicable prospectus supplement the names of the specific managing underwriter or underwriters, as well as any other underwriters, and the terms of the transactions, including compensation of the underwriters and dealers. This compensation may be in the form of discounts, concessions or commissions. Underwriters and others participating in any offering of the securities may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. We will describe any of these activities in the applicable prospectus supplement.

If a dealer is used in the sale of the securities, we or an underwriter will sell securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The applicable prospectus supplement will set forth the name of the dealer and the terms of the transactions.

We may directly solicit offers to purchase the securities, and we may sell directly to institutional investors or others. These persons may be deemed to be underwriters within the meaning of the Securities Act with respect to any resale of the securities. The applicable prospectus supplement will describe the terms of any direct sales, including the terms of any bidding or auction process.

Agreements we enter into with agents, underwriters and dealers may entitle them to indemnification by us against specified liabilities, including liabilities under the Securities Act, or to contribution by us to payments they may be required to make in respect of these liabilities. The applicable prospectus supplement will describe the terms and conditions of indemnification or contribution.

Delayed Delivery Contracts

We may authorize underwriters, dealers and agents to solicit offers by certain institutional investors to purchase offered securities under contracts providing for payment and delivery on a future date specified in the applicable prospectus supplement. The applicable prospectus supplement will also describe the public offering price for the securities and the commission payable for solicitation of these delayed delivery contracts. Delayed delivery contracts will contain definite fixed price and quantity terms. The obligations of a purchaser under these delayed delivery contracts will be subject to only two conditions:

- that the institution's purchase of the securities at the time of delivery of the securities is not prohibited under the law of any jurisdiction to which the institution is subject; and

- that we shall have sold to the underwriters the total principal amount of the offered securities, less the principal amount covered by the delayed delivery contracts.

"At the Market" Offerings

We may from time to time engage a firm to act as our agent for one or more offerings of our securities. We sometimes refer to this agent as our "offering agent." If we reach agreement with an offering agent with respect to a specific offering, including the number of securities and any minimum price below which sales may not be made, then the offering agent will try to sell such securities on the agreed terms. The offering agent could make sales in privately negotiated transactions or using any other method permitted by law, including sales deemed to be an "at the market" offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on the NASDAQ Global Market, or sales made to or through a market maker other than on an exchange. The offering agent will be deemed to be an "underwriter" within the meaning of the Securities Act with respect to any sales effected through an "at the market" offering.

Market Making, Stabilization and Other Transactions

To the extent permitted by and in accordance with Regulation M under the Exchange Act, in connection with an offering an underwriter may engage in over-allotments, stabilizing transactions, short covering transactions and penalty bids. Over-allotments involve sales in excess of the offering size, which creates a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would be otherwise. If commenced, the underwriters may discontinue any of these activities at any time.

To the extent permitted by and in accordance with Regulation M under the Exchange Act, any underwriters who are qualified market makers on the NASDAQ Global Market may engage in passive market making transactions in the securities on the NASDAQ Global Market during the business day prior to the pricing of an offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

No securities may be sold under this prospectus without delivery, in paper format, in electronic format on the Internet, or both, of the applicable prospectus supplement describing the method and terms of the offering.

DESCRIPTION OF COMMON STOCK

Authorized and Outstanding Capital Stock

As of April 28, 2010, we had 100,000,000 shares of common stock authorized, of which 44,786,656 shares were outstanding.

Listing

Our common stock is quoted on the NASDAQ Global Market and traded under the symbol "ARQL."

Dividends

Our Board of Directors may authorize, and we may make, distributions to our common stockholders, subject to any restriction in our Amended and Restated Certificate of Incorporation and to those limitations prescribed by law. However, we have never paid cash dividends on our common stock or any other securities, and we do not anticipate paying any cash dividends in the foreseeable future. We currently intend to retain future earnings, if any, for use in our business.

Fully Paid and Non-Assessable

All shares of our outstanding common stock are fully paid and non-assessable. Any additional shares of common stock that we issue will be fully paid and non-assessable.

Voting Rights

Each share of our common stock is entitled to one vote in each matter submitted to a vote at a meeting of stockholders including in all elections for directors; stockholders are not entitled to cumulative voting in the election for directors. Our stockholders may vote either in person or by proxy.

Preemptive and Other Rights

Holders of our common stock have no preemptive rights and have no other rights to subscribe for additional securities of our company under Delaware law. Nor does the common stock have any conversion rights or rights of redemption. Upon liquidation, all holders of our common stock are entitled to participate pro rata in our assets available for distribution, subject to the rights of any class of preferred stock then outstanding.

Meetings; Stockholder Action by Written Consent

Our Bylaws provide that we must hold an annual meeting of stockholders. Special meetings of our stockholders may be called at any time only by a majority of our Board of Directors or by our President.

All actions must be taken at an annual or special meeting. Our Amended and Restated Certificate of Incorporation provides that stockholders may not take action by written consent without a meeting.

Staggered Board of Directors

Our Board of Directors is divided into three classes, the members of each of which serve for staggered three-year terms. Our stockholders may elect only one-third of the directors each year; therefore, it is more difficult for a third

party to gain control of our Board of Directors than if our Board was not staggered.

Transfer Agent and Registrar

American Stock Transfer & Trust Company is our transfer agent and registrar.

DESCRIPTION OF PREFERRED STOCK

Our Amended and Restated Certificate of Incorporation authorizes our Board of Directors, without further stockholder action, to provide for the issuance of up to 1,000,000 shares of preferred stock, in one or more classes or series and to fix the rights, preferences, privileges, and restrictions thereof, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences and the number of shares constituting any series of the designation of such series, without further vote or action by the stockholders. We may amend from time to time our Certificate of Incorporation to increase the number of authorized shares of preferred stock. Any such amendment would require the approval of the holders of a majority of the voting power of the shares entitled to vote thereon. As of the date of this prospectus, we have 1,000,000 shares of preferred shares authorized, but no shares of preferred stock outstanding.

The particular terms of any series of preferred stock being offered by us under this shelf registration statement will be described in the prospectus supplement relating to that series of preferred stock. Those terms may include:

- the title and liquidation preference per share of the preferred stock and the number of shares offered;
- the purchase price of the preferred stock;
- the dividend rate (or method of calculation), the dates on which dividends will be paid and the date from which dividends will begin to accumulate;
- any redemption or sinking fund provisions of the preferred stock;
- any conversion provisions of the preferred stock;
- the voting rights, if any, of the preferred stock; and
- any additional dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions of the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock. Warrants may be issued independently or together with the shares of common stock or preferred stock offered by any prospectus supplement to this prospectus and may be attached to or separate from such shares. Further terms of the warrants will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of the warrants in respect of which this prospectus is being delivered, including, where applicable, the following:

- the title of such warrants;

the aggregate number of such warrants;

the price or prices at which such warrants will be issued;

the designation, terms and number of shares of common stock or preferred stock purchasable upon exercise of such warrants;

the designation and terms of the shares of common stock or preferred stock with which such warrants are issued and the number of such warrants issued with such shares;

the date on and after which such warrants and the related common stock or preferred stock will be separately transferable, including any limitations on ownership and transfer of such warrants;

the price at which each share of common stock or preferred stock purchasable upon exercise of such warrants may be purchased;

the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;

the minimum or maximum amount of such warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

a discussion of certain federal income tax consequences; and

any other terms of such warrants, including terms, procedures and limitations relating to the exchange and exercise of such warrants.

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus and any related unit agreements and unit certificates. While the terms summarized below will apply generally to any units that we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any units offered under that prospectus supplement may differ from the terms described below.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the Commission, any form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of such unit agreements and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus and the complete unit agreement and any supplemental agreements that contain the terms of the units.

We may issue, in one more series, units comprised of shares of our common stock or preferred stock and warrants to purchase common stock or preferred or any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We may evidence units by unit certificates that we issue under a separate agreement. We may issue the units under a unit agreement between us and one or more unit agents. If we elect to enter into a unit agreement with a unit agent, the unit agent will act solely as our agent in connection with the units and will not assume any obligation or relationship of agency or trust for or with any registered holders of units or beneficial owners of units. We will

indicate the name and address and other information regarding the unit agent in the applicable prospectus supplement relating to a particular series of units if we elect to use a unit agent.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The other provisions regarding our common stock, preferred stock and warrants as described in this section will apply to each unit to the extent such unit consists of shares of our common stock and preferred stock and warrants to purchase our common stock.

LEGAL MATTERS

Arnold & Porter LLP has rendered an opinion that the securities offered hereby, when sold, will be legally issued, fully paid and non-assessable.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2009 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information that we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. These documents may include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as Proxy Statements. Any documents that we subsequently file with the SEC will automatically update and replace the information previously filed with the SEC. Thus, for example, in the case of a conflict or inconsistency between information set forth in this prospectus and information incorporated by reference into this prospectus, you should rely on the information contained in the document that was filed later. Any documents that we file with the SEC after the date of this Registration Statement and prior to the effectiveness of this Registration Statement shall be deemed to be incorporated by reference into this prospectus.

This prospectus incorporates by reference the documents listed below that we previously have filed with the SEC and any additional documents that we may file with the SEC (File No.000-21429) under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (excluding portions thereof deemed to be "furnished" to the SEC pursuant to Item 2.02, Item 7.01 or Item 9.01 of a Current Report on Form 8-K) between the date of this prospectus and the termination of the offering of the securities:

1. Our Annual Report on Form 10-K for the year ended December 31, 2009 filed with the Commission on March 2, 2010;

2. Our Current Report on Form 8-K filed with the Commission on March 31, 2010 (excluding any information furnished in such reports under Items 2.02, 7.01 or 9.01);

3. Our definitive Proxy Statement on Schedule 14A, filed on April 12, 2010; and

4. The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on September 25, 1996, including any amendment or report filed for the purpose of updating such description.

You can obtain a copy of any or all of the documents, at no cost, by requesting them in writing, by email or by telephone at the following address:

William B. Boni, Vice President,
Investor Relations and Corporate Communications
ArQule, Inc.
19 Presidential Way
Woburn, MA 01801
(781) 994-0300
wboni@arqule.com

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement under the Securities Act that registers the distribution of the securities offered under this prospectus. The registration statement, including the attached exhibits and schedules and the information incorporated by reference, contains additional relevant information about us and the securities. The rules and regulations of the SEC allow us to omit from this prospectus certain information included in the registration statement.

In addition, we file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy this information and the registration statement at the SEC public reference room located at 107 F Street, N.E., Washington D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room.

In addition, any information we file with the SEC, including the documents incorporated by reference into this prospectus, is also available on the SEC's website at http://www.sec.gov. We also maintain a web site at http://www.arqule.com, which provides additional information about our company and through which you can also access our SEC filings. The information set forth on our web site is not part of this prospectus.

7,150,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

April 11, 2012

Citigroup Leerink Swann

Lazard Capital Markets RBC Capital Markets Oppenheimer & Co.