

ARQULE INC
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Registration No. 333-213456

PROSPECTUS SUPPLEMENT

(TO PROSPECTUS DATED OCTOBER 5, 2016)

\$30,000,000

COMMON STOCK

We have entered into a Capital on Demand™ Sales Agreement, or sales agreement, with JonesTrading Institutional Services LLC (“JonesTrading”) relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$30 million from time to time through JonesTrading acting as sales agent, at our discretion.

Our common stock is listed for trading on The Nasdaq Global Market under the symbol “ARQL.” On October 24, 2016, the last reported sale price of our common stock on The Nasdaq Global Market was \$1.45 per share.

Sales of our common stock, if any, under this prospectus supplement may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through the Nasdaq Global Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

We will pay JonesTrading commissions for its services in acting as agent in the sale of our common stock. JonesTrading will be entitled to compensation at a commission rate equal to up to 3.0% of the aggregate gross sales price of the shares sold.

Investing in our common stock involves significant risks. Before buying shares of our common stock, you should carefully consider the risks described under the caption “Risk Factors” beginning on page S-3 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

The date of this prospectus supplement is October 25, 2016

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About this Prospectus Supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock and updates the information contained in the accompanying prospectus and the documents incorporated by reference herein and therein. The second part is the accompanying prospectus, which provides more general information, some of which does not apply to this offering. If information included or incorporated by reference in this prospectus supplement is inconsistent with the accompanying prospectus or the information incorporated by reference therein, then this prospectus supplement or the information incorporated by reference in this prospectus supplement will apply and will supersede the information in the accompanying prospectus and the documents incorporated by reference therein. For a more detailed understanding of our common stock, you should read both this prospectus supplement and the accompanying prospectus, together with additional information described under the heading “Where You Can Find More Information.”

This prospectus supplement is part of a shelf registration statement on Form S-3 (File No. 333-213456) that we filed with the U.S. Securities and Exchange Commission, or SEC, on September 2, 2016 and amended on September 23, 2016. Under the shelf registration process, we may from time to time offer and sell any combination of the securities described in the accompanying prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf. Neither we nor the sales agent have authorized anyone to provide you with different or additional information. If anyone provides you with different or additional information, you should not rely on it. Neither we nor the sales agent are making an offer to sell or soliciting an offer to buy our common stock under any circumstance in any jurisdiction where the offer or solicitation is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf is accurate only as of the date of the respective document in which the information appears, and that any information in documents that we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus supplement, the accompanying prospectus, and the information incorporated herein and therein by reference includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Unless the context indicates otherwise, in this prospectus supplement and the accompanying prospectus the terms “ArQule,” “we,” “us” and “our” refer to ArQule, Inc., a Delaware corporation, and its subsidiaries on a consolidated basis.

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Forward-Looking Statements

This prospectus supplement, the accompanying prospectus, and the information incorporated by reference in this prospectus supplement and the accompanying prospectus contain “forward-looking statements” within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act, which are subject to the safe harbor created by those sections for such statements. Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to our management. All statements other than statements of historical facts are forward-looking statements. Terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and variations thereof are intended to identify forward-looking statements, but these terms are not the exclusive means of identifying such statements. Those statements appear in this prospectus supplement, the accompanying prospectus and the documents incorporated herein and therein by reference, particularly in the sections entitled “Prospectus Summary” and “Risk Factors,” and include statements regarding the intent, belief or current expectations of us and our management that are subject to known and unknown risks, uncertainties and assumptions. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our common stock to decline, and you may lose all or part of your investment.

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 the progress of product development efforts including clinical trials and preclinical activities conducted by ourselves and third parties, 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 efficiency, if positive early results are not repeated in later studies or in humans, if the therapeutic value of our compounds is not realized, 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. Accordingly, you should not place undue reliance on these forward-looking statements, which represent our estimates and assumptions only as of the date they are made. You should read this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein with the understanding that our actual results in subsequent periods may materially differ from current expectations. Except as required by law, we assume no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events or otherwise.

Prospectus Summary

This summary highlights information contained elsewhere in this prospectus supplement and the accompanying prospectus. It does not contain all of the information you should consider before making an investment decision. Before you decide to invest in our securities, you should read the entire prospectus supplement and the accompanying prospectus carefully, including the risk factors and the financial statements and related notes included or incorporated by reference herein and therein.

Overview

We are a biopharmaceutical company engaged in the research and development of innovative therapeutics to treat cancers and rare diseases. Our mission is to discover, develop and commercialize novel small molecule drugs in areas of high unmet need that will dramatically extend and improve the lives of our patients. These drugs target biological pathways implicated in a wide range of cancers and certain non-oncology indications. Our discovery and development efforts are guided, when possible, by an understanding of the role of biomarkers, which are indicators of a particular biological condition or process and may predict the clinical benefit of our compounds in defined patient populations. Our prioritized clinical-stage pipeline consists of four drug candidates, all of which are in targeted patient populations making ArQule a leader among companies our size in precision medicine.

We have a long history of kinase drug discovery and development, having discovered and introduced eight kinase inhibitors into human clinical trials with a ninth about to enter the clinic. Our drug discovery efforts have been informed by our historical expertise in chemistry, our work in rational drug design and by our insight into kinase binding and regulation. We have applied this knowledge to produce significant chemical matter for a number of kinase targets and to build an extensive library of proprietary compounds with the potential to target multiple kinases in oncology and other therapeutic areas, such as rare diseases. We expect to bring further preclinical programs forward either directly or with collaborators and to interrogate our library against new targets beyond kinases.

Company Information

We were incorporated in the State of Delaware in 1993. Our principal executive offices are located at One Wall Street, Burlington, MA 01803, and our telephone number is (781) 994-0300. Our website address is www.arqule.com. The information on, or that can be accessed through, our website is not part of this prospectus supplement or the accompanying prospectus.

The Offering

Common

stock offered Shares of our common stock having an aggregate offering price of up to \$30 million.
by us

Manner of offering

The sale of our common stock, if any, under this prospectus supplement may be made directly on or through the Nasdaq Global Market, the existing trading market for our common stock, to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. See “Plan of Distribution” on page S-8 of this prospectus supplement.

Sales agent

JonesTrading Institutional Services LLC.

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 drug candidates, and for general corporate purposes, including working capital. See “Use of Proceeds” on page S-7 of this prospectus supplement.

Risk factors

Investing in our common stock involves significant risks. See “Risk Factors” beginning on page S-5 of this prospectus supplement.

Nasdaq Global Market listing

Our common stock is listed on The Nasdaq Global Market under the symbol “ARQL.”

Risk Factors

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the section captioned “Risk Factors” in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2015, which is incorporated by reference in this prospectus supplement and the accompanying prospectus in its entirety, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC, together with other information in this prospectus supplement, the accompanying prospectus, and the information and documents incorporated by reference that we have authorized for use in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flows could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to Our Common Stock and This Offering

Our stock price has been and may continue to be volatile, and can be adversely affected by several factors.

The share prices of publicly traded biotechnology and emerging pharmaceutical companies, particularly companies without consistent product revenues and earnings, can be highly volatile and are likely to remain highly volatile in the future. The price which investors may realize in sales of their shares of our common stock may be materially different than the price at which our common stock is quoted, and will be influenced by a large number of factors, some specific to us and our operations, and some unrelated to our operations. Such factors may cause the price of our stock to fluctuate frequently and substantially. Such factors may include large purchases or sales of our common stock, shorting of our stock, positive or negative events, commentaries or publicity relating to our company, management or products, or other companies, management or products, including other immune therapies for cancer or immune therapies or cancer therapies generally, positive or negative events relating to healthcare and the overall pharmaceutical and biotech sector, the publication of research by securities analysts and changes in recommendations of securities analysts, legislative or regulatory changes, and/or general economic conditions. In the past, shareholder litigation, including class action litigation, has been brought against other companies that experienced volatility in the market price of their shares and/or unexpected or adverse developments in their business. Whether or not meritorious, litigation brought against a company following such developments can result in substantial costs, divert management’s attention and resources, and harm the company’s financial condition and results of operations.

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

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Since the price per share of our common stock being offered is expected to be substantially higher than the net tangible book value per share of our common stock, your interest will be diluted to the extent of the difference between the price per share you pay and the net tangible book value per share of our common stock. The future exercise of outstanding options and warrants will result in further dilution of your investment.

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We do not intend to pay any cash dividends in the foreseeable future and, therefore, any return on your investment in our common stock must come from increases in the market price of our common stock.

We have not paid any cash dividends on our common stock to date in our history, and we do not intend to pay cash dividends on our common stock in the foreseeable future. We intend to retain future earnings, if any, for reinvestment in the development and expansion of our business. Also, any credit agreements which we may enter into with institutional lenders may restrict our ability to pay dividends. Therefore, any return on your investment in our capital stock must come from increases in the fair market value and trading price of our common stock. Such increases in the trading price of our stock may not occur.

Our management will have broad discretion as to the use of proceeds from this offering, and we may not use the proceeds effectively.

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 improve our results of operations or enhance the value of our common stock. You will not have the opportunity, as part of your investment decision, to assess whether these proceeds are being used appropriately. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the further development of our product candidates and cause the price of our common stock to decline.

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.

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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.

We might not be able to maintain the listing of our common stock on The NASDAQ Global Market.

Our common stock is listed on The NASDAQ Global Market under the symbol “ARQL.” We might not be able to maintain the listing standards of that exchange. If we fail to maintain the listing requirements, our common stock might move to the Over the Counter Bulletin Board or in the “pink sheets” maintained by Pink OTC Markets, Inc. The OTC Bulletin Board and the “pink sheets” are generally considered to be markets that are less efficient and less broad than The NASDAQ Global Market. We have never declared or paid dividends on our capital stock, and we do not anticipate paying dividends in the foreseeable future.

Use of Proceeds

The net proceeds that we receive from sales of our common stock pursuant to this prospectus supplement will depend on the number of shares actually sold and the offering price for such shares. There can be no assurance that we will be able to sell any shares under, or fully utilize, the Sales Agreement as a source of financing. Based on the closing price of our common stock on October 24, 2016 of \$1.45, the maximum number of shares we could sell is 20,689,655. We estimate the offering expenses, other than the sales agent’s commissions, will be approximately \$85,000. If we were to sell 20,689,655 shares of common stock at the October 24, 2016 closing price, we would receive \$30.0 million in gross proceeds, which is approximately \$29.0 million in net proceeds. The actual proceeds, if any, to us will vary.

We intend to use the net proceeds from this offering to fund our research and development efforts, including clinical trials for our proprietary pipeline of drug candidates, and for general corporate purposes, including working capital.

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.

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Dilution

The net tangible book value of our common stock as of June 30, 2016 was approximately \$35.5 million, or \$0.50 per share. 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. Dilution in net tangible book value per share represents 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 afterwards.

After giving effect to our sale of our common stock pursuant to this prospectus supplement and accompanying prospectus in the aggregate amount of \$30.0 million at an assumed offering price of \$1.45 per share, the last reported sale price of our common stock on the NASDAQ Global Market on October 24, 2016, and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of June 30, 2016 would have been \$64.5 million, or \$0.70 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.20 per share to our existing stockholders and an immediate dilution in net tangible book value of \$0.75 per share to new investors. The following table illustrates this per share dilution:

Offering price per share	\$1.45
Net tangible book value per share as of June 30, 2016	\$0.50
Increase in net tangible book value per share attributable to this offering	\$0.20
As adjusted net tangible book value per share on June 30, 2016 after this offering	0.70
Dilution per share to new investors purchasing our common stock in this offering	\$0.75

Information in the above table is based on 71,106,224 shares outstanding on June 30, 2016, and excludes:

9,189,198 shares of common stock issuable upon exercise of options outstanding as of June 30, 2016 at a weighted average exercise price of \$3.77 per share;

3,567,956 shares of common stock issuable upon the exercise of outstanding third party options as of June 30, 2016 at an exercise price of \$2.50 per share;

3,330,781 shares of common stock available for future issuance as of June 30, 2016 under our Equity Incentives Plan.

Plan of Distribution

We have entered into a Capital on DemandTM Sales Agreement (the “Sales Agreement”) with JonesTrading, under which we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$30,000,000 from time to time through JonesTrading acting as a sales agent. Sales of our common stock, if any, under this prospectus may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through the NASDAQ Global Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law.

Each time we wish to issue and sell common stock, we will notify JonesTrading of the number of shares to be issued, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed JonesTrading, unless JonesTrading declines to accept the terms of the notice, JonesTrading has agreed, subject to the terms and conditions of the Sales Agreement, to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. We may instruct JonesTrading not to sell shares of common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or JonesTrading may suspend the offering of shares of common stock being made through JonesTrading under the Sales Agreement upon proper notice to the other party.

We will pay JonesTrading commissions for its services in acting as agent in the sale of our common stock. JonesTrading will be entitled to compensation at a commission rate equal to up to 3.0% of the aggregate gross sales price of the shares sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse JonesTrading for certain specified expenses, including the fees and disbursements of its legal counsel in an amount not to exceed \$30,000, as provided in the Sales Agreement. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to JonesTrading under the terms of the Sales Agreement, will be approximately \$85,000.

Settlement for sales of common stock will occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and JonesTrading in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus will be settled through the facilities of American Stock Transfer & Trust Company or by such other means as we and JonesTrading may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, JonesTrading may be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of JonesTrading may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to JonesTrading against certain civil liabilities, including liabilities under the Securities Act.

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The offering of our common stock pursuant to the Sales Agreement will terminate upon the earlier of (i) the issuance and sale of all shares of our common stock subject to the Sales Agreement, or (ii) the termination of such Sales Agreement as permitted therein.

JonesTrading and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates for which services they may in the future receive customary fees.

Legal Matters

The validity of the common stock offered hereby and certain legal matters in connection with this offering will be passed upon by Arnold & Porter LLP. Duane Morris LLP is counsel to JonesTrading 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 by reference to the Annual Report on Form 10-K for the year ended December 31, 2015 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

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at 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 Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge by linking directly from our website at www.ArQule.com under the "Investor—Financial Information—SEC Filings" caption to the SEC's Edgar Database. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act relating to the common stock in this offering. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under “Incorporation by Reference” are also available on our Internet website, www.ArQule.com. We have not incorporated by reference into this prospectus supplement the information on, or that can be accessed through, our website, and you should not consider it to be a part of this prospectus supplement.

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Incorporation of Documents by Reference

The SEC allows us to “incorporate by reference” the information we file with it, which means that we can disclose important information to you by referring you to those documents. 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, 2015 filed with the Commission on February 29, 2016;
2. Our Current Reports on Form 8-K filed with the Commission on February 29, 2016, March 22, 2016, April 14, 2016, May 26, 2016, and on Form 8-K/A filed on March 4, 2016;
3. Our Quarterly Reports on Form 10-Q for the quarters ending March 31, 2016 and June 30, 2016 and filed with the Commission on May 4, 2016 and August 3, 2016, respectively;
4. Our definitive Proxy Statement on Schedule 14A, filed on April 14, 2016; and
5. 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

All reports and other documents that we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and the accompanying prospectus and deemed to be part of this prospectus supplement and the accompanying prospectus from the time of the filing of such reports and documents.

This prospectus supplement and the accompanying prospectus as further supplemented may contain information that updates, modifies or is contrary to information herein or in one or more of the documents incorporated by reference in this prospectus supplement or the accompanying prospectus. You should rely only on the information incorporated by reference or provided in this prospectus supplement and 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 of this prospectus supplement, the date of the accompanying prospectus or the date of the documents incorporated by reference in this

prospectus supplement and the accompanying prospectus, respectively.

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We will provide without charge to each person, including any beneficial owner, to whom this prospectus supplement and accompanying prospectus is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus supplement and accompanying prospectus, but not delivered with the prospectus supplement and accompanying prospectus, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus supplement or accompanying prospectus incorporates. You should direct written requests to:

Dawn Schottlandt

Senior Director, Investor Relations/Corporate Communications

ArQule, Inc.

One Wall Street

Burlington, MA 01803

(781) 994-0300

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PROSPECTUS

ARQULE, INC.

UP TO \$100,000,000 OF OUR

COMMON STOCK

PREFERRED STOCK

WARRANTS

DEBT SECURITIES

UNITS

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,

debt securities; or

units consisting of any combination of our common stock, preferred stock, warrants or debt securities.

We may offer the common stock, preferred stock, warrants, debt securities, and units (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 One Wall Street, Burlington, Massachusetts 01803 and our telephone number is (781) 994-0300.

An investment in our securities involves a high degree of risk. See “Risk Factors” on page 2 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 October 5, 2016

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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 biopharmaceutical company engaged in the research and development of innovative therapeutics to treat cancers and rare diseases. Our mission is to discover, develop and commercialize novel small molecule drugs in areas of high unmet need that will dramatically extend and improve the lives of our patients. These drugs target biological pathways implicated in a wide range of cancers and certain non-oncology indications. Our discovery and development efforts are guided, when possible, by an understanding of the role of biomarkers, which are indicators of a particular biological condition or process and may predict the clinical benefit of our compounds in defined patient populations. Our clinical-stage pipeline consists of five drug candidates, all of which are in targeted patient populations making ArQule a leader among companies our size in precision medicine.

Our lead product candidate is tivantinib (ARQ 197), an orally administered, small molecule inhibitor of the c-Met receptor tyrosine kinase (“MET”) and its biological pathway. MET is a promising target for cancer therapy, based on its multiple roles in cancerous cell proliferation, tumor spread, new blood vessel formation and resistance to certain drug therapies. We and our partners, Daiichi Sankyo Co., Ltd. (“Daiichi Sankyo”) and Kyowa Hakko Kirin Co., Ltd. (“Kyowa Hakko Kirin”), are implementing a worldwide clinical development program with tivantinib. Our strategy is to focus on the most promising indications within our clinical programs based upon continually generated and updated clinical and pre-clinical data. Our lead indication is liver cancer (“hepatocellular carcinoma” or “HCC”), and we are currently conducting two Phase 3 trials with our partners. We have also completed earlier-stage single agent and combination therapy trials and pre-clinical experiments with tivantinib and other anti-cancer agents that may provide data to support trials in additional indications.

Our executive offices are located at One Wall Street, Burlington, MA 01803.

The Securities We May Offer

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;
- debt securities; or
- units consisting of any combination of our common stock, preferred stock, warrants, or debt securities.

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

RATIO OF EARNINGS TO FIXED CHARGES AND PREFERRED DIVIDENDS

If we offer debt securities and/or preference equity securities under this prospectus, then we will, if required at that time, provide a ratio of earnings to fixed charges and/or a ratio of combined fixed charges and preference dividends to earnings, respectively, in the applicable prospectus supplement for such offering.

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 securities 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 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, 2015. See also the information contained under the heading “Special Note Regarding Forward Looking Statements” immediately below.

SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

In addition to historical information, this report contains forward-looking statements. You can identify these forward-looking statements by their use of words such as “anticipate,” “assume,” “believe,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “project,” “target,” “will” and other words and terms of similar meaning. You also can identify them by the fact that they do not relate strictly to historical or current facts. All statements which address operating performance, events or developments that we expect or anticipate will occur in the future, such as projections about our future results of operations, our financial condition, research, development and commercialization of our product candidates and anticipated trends in our business are forward-looking statements.

In this prospectus and the reports that we incorporate by reference herein, we make forward-looking statements regarding our drug development pipeline and our clinical trials involving tivantinib. Additional forward-looking statements relate to our agreements with Kyowa Hakko Kirin and Daiichi Sankyo, including potential future milestones and royalty payments that could result from the future development of tivantinib.

Drug development involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. Although we believe that the expectations reflected in our forward looking statements are reasonable as of the date thereof, such expectations are based on certain assumptions regarding the progress of product development efforts including clinical trials and preclinical activities conducted by us and third parties, 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, 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 efficiency, if positive early results are not repeated in later studies or in humans, if the therapeutic value of our compounds is not realized, 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.

We also make forward-looking statements regarding the adequacy of our financial resources. Our capital resources may not be adequate because our cash requirements may vary materially from those now planned depending upon the results of our drug discovery and development strategies, the outcomes of our clinical trials, our ability to enter into additional corporate collaborations in the future and the terms of such collaborations, results of research and development, the need for currently unanticipated capital expenditures, competitive and technological advances, acquisitions, financial market conditions, and other factors. Additionally, our corporate collaborators may terminate their agreements with us, thereby eliminating that source of funding, because we may fail to satisfy the prescribed terms of the collaborations or for other reasons.

We cannot guarantee that we will be able to develop any of our drug candidates into a commercial product generating revenues. If we experience increased losses, we may have to seek additional financing from public and private sales of our securities, including equity securities. There can be no assurance that additional funding will be available when needed or on acceptable terms.

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 million 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, (d) debt securities, or (e) units consisting of any combination of our common stock, preferred stock, warrants, or debt securities, 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, warrants, debt securities, and units 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 million (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

Unless otherwise specified in a prospectus supplement accompanying this prospectus, we currently intend to use the net proceeds received from the sale of the securities for research and development of our product candidates including the conduct of clinical trials and related activities, 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 distribute 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 of 1933, as amended (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 Securities Exchange Act of 1934, as amended (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 THE SECURITIES

This prospectus contains a summary of the common stock, the preferred stock, the warrants, the senior debt securities, the subordinated debt securities and the units that we may offer from time to time. The following summaries are not meant to be a complete description of each security. However, this prospectus, the accompanying prospectus supplement and the accompanying pricing supplement, if applicable, contain the material terms and conditions for each security. You should read these documents as well as the documents filed as exhibits to or incorporated by reference to this registration statement.

DESCRIPTION OF COMMON STOCK

Authorized and Outstanding Common Stock

As of August 25, 2016, we had 100,000,000 shares of common stock authorized, of which 71,115,109 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 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 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 were not staggered.

Transfer Agent and Registrar

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

DESCRIPTION OF PREFERRED STOCK

Our 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.

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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. As of the date of this prospectus, we have no warrants outstanding.

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 DEBT SECURITIES

We may issue senior debt securities or subordinated debt securities. Senior debt securities will be issued under an indenture, the “senior indenture,” between us and the trustee named in the applicable prospectus supplement, as trustee. Subordinated debt securities will be issued under a separate indenture, the “subordinated indenture,” between us and the trustee named in the applicable prospectus supplement, as trustee. The senior indenture and the subordinated indenture are sometimes collectively referred to in this prospectus as the “indentures.” The indentures will be subject to and governed by the Trust Indenture Act of 1939. A copy of the form of each of these indentures is filed as an exhibit to the registration statement of which this prospectus is a part. This prospectus describes the general terms and provisions of the debt securities. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus. The prospectus supplement will also indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities.

The following briefly describes the general terms and provisions of the debt securities and the indentures governing them which may be offered. The particular terms of the debt securities offered, and the extent, if any, to which these general provisions may apply to the debt securities so offered, will be described in a prospectus supplement relating to those securities. The following descriptions of the indentures are not complete and are subject to, and are qualified in their entirety by reference to, all the provisions of the respective indentures.

General

The indentures permit us to issue the debt securities from time to time, without limitation as to aggregate principal amount, and in one or more series. The indentures also do not limit or otherwise restrict the amount of other indebtedness which we may incur or other securities which we or our subsidiaries may issue, including indebtedness which may rank senior to the debt securities. Nothing in the subordinated indenture prohibits the issuance of securities representing subordinated indebtedness that is senior or junior to the subordinated debt securities.

Unless we give you different information in the prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “Description of Debt Securities—Subordination” and in the applicable prospectus supplement.

We may issue debt securities if the conditions contained in the applicable indenture are satisfied. These conditions include the adoption of resolutions by our board of directors that establish the terms of the debt securities being issued. Any resolution approving the issuance of any issue of debt securities will include the terms of that issue of debt securities, which may include:

the title and series designation;

the aggregate principal amount and the limit, if any, on the aggregate principal amount or initial issue price of the debt securities which may be issued under the applicable indenture;

the principal amount payable, whether at maturity or upon earlier acceleration;

whether the principal amount payable will be determined with reference to an index, formula or other method which may be based on one or more currencies, currency units, composite currencies, commodities, equity indices or other

indices;

- whether the debt securities will be issued as original issue discount securities (as defined below);
- the date or dates on which the principal of the debt securities is payable;
- any fixed or variable interest rate or rates per annum or the method or formula for determining an interest rate;
- the date from which any interest will accrue;
- any interest payment dates;
- whether the debt securities are senior or subordinated, and if subordinated, the terms of the subordination;
- the price or prices at which the debt securities will be issued, which may be expressed as a percentage of the aggregate principal amount of those debt securities;
- the stated maturity date;

whether the debt securities are to be issued in global form;

any sinking fund requirements;

any provisions for redemption, the redemption price and any remarketing arrangements;

the denominations of the securities or series of securities;

whether the debt securities are denominated or payable in United States dollars or a foreign currency or units of two or more foreign currencies;

any restrictions on the offer, sale and delivery of the debt securities;

the place or places where payments or deliveries on the debt securities will be made and may be presented for registration of transfer or exchange;

whether any of the debt securities will be subject to defeasance in advance of the date for redemption or the stated maturity date;

the terms, if any, upon which the debt securities are convertible into other securities of ours or another issuer and the terms and conditions upon which any conversion will be effected, including the initial conversion price or rate, the conversion period and any other provisions in addition to or instead of those described in this prospectus;

any other terms of the debt securities which are not inconsistent with the provisions of the applicable indenture;

a description of any documents or certificates that must be received prior to the issuance of any definitive securities;

whether and under what circumstances additional amounts will be paid to non-U.S. citizens in connection with any tax, assessment or governmental charge and whether securities may be redeemed in lieu of paying such additional fees;

the identity of each security registrar or paying agent (if other than trustee);

any provisions granting special rights to securities holders upon the occurrence of specified events;

any deletions from, modifications of, or additions to any default events or covenants set forth in the form of indenture;

·the portion of the principal amount payable upon the declaration of acceleration of the maturity of any securities; and

the date any bearer securities of or within the series and any temporary global security representing outstanding securities shall be dated, if other than date of original issuance.

The debt securities may be issued as “original issue discount securities” which bear no interest or interest at a rate which at the time of issuance is below market rates and which will be sold at a substantial discount below their principal amount. If the maturity of any original issue discount security is accelerated, the amount payable to the holder of the security will be determined by the applicable prospectus supplement, the terms of the security and the relevant indenture, but may be an amount less than the amount payable at the maturity of the principal of that original issue discount security. Special federal income tax and other considerations relating to original issue discount securities will be described in the applicable prospectus supplement.

Please see the prospectus supplement or pricing supplement you have received or will receive for the terms of the specific debt securities we are offering.

You should be aware that special U.S. Federal income tax, accounting and other considerations may apply to the debt securities. The prospectus supplement relating to an issue of debt securities will describe these considerations.

Registration and Transfer

Holders may present debt securities in registered form for transfer or exchange for other debt securities of the same series at the offices of the applicable indenture trustee according to the terms of the applicable indenture and the debt securities.

Unless otherwise indicated in the applicable prospectus supplement, the debt securities will be issued in fully registered form, and in denominations of \$1,000 and any integral multiple thereof and the bearer securities of such series other than bearer securities issued in global form shall be issuable in denominations of \$5,000.

No service charge will be required for any transfer or exchange of the debt securities but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with any transfer or exchange.

Payment and Place of Payment

We will pay or deliver principal and any premium and interest in the manner, at the places and subject to the restrictions set forth in the applicable indenture, the debt securities and the applicable prospectus supplement. However, at our option, we may pay any interest by check mailed to the holders of registered debt securities at their registered addresses.

Global Securities

Each indenture provides that we may issue debt securities in global form. If any series of debt securities is issued in global form, the prospectus supplement will describe any circumstances under which beneficial owners of interests in any of those global debt securities may exchange their interests for debt securities of that series and of like tenor and principal amount in any authorized form and denomination.

Events of Default

Unless otherwise indicated in the applicable prospectus supplement, the following are events of default under the senior indenture with respect to the senior debt securities and under the subordinated indenture with respect to the subordinated debt securities:

· default in the payment of any principal or premium or make-whole amount, if any, on the debt securities when due;

· default in the payment of any interest on the debt securities, or of any coupon pertaining thereto, when due, which continues for 30 days;

· default in the performance or breach of any other obligation contained in the applicable indenture for the benefit of that series of debt securities (other than defaults or breaches otherwise specifically addressed), which continues for 90 days after written notice of the default or breach;

- specified events in bankruptcy, insolvency or reorganization of us or any of our significant subsidiaries; and
- any other event of default provided with respect to the debt securities of any series.

If an event of default (other than an event of default arising from specified events in bankruptcy of us or any of our significant subsidiaries) occurs and is continuing for any series of debt securities, the indenture trustee or the holders of not less than 25% in aggregate principal amount or, under certain circumstances, issue price of the outstanding debt securities of that series may declare all amounts, or any lesser amount provided for in the debt securities of that series, to be immediately due and payable.

At any time after the applicable indenture trustee or the holders have accelerated a series of debt securities, but before the applicable indenture trustee has obtained a judgment or decree for payment of money due, the holders of a majority in aggregate principal amount of outstanding debt securities of that series may rescind and annul that acceleration and its consequences, provided that all payments and/or deliveries due, other than those due as a result of acceleration, have been made and all events of default have been remedied or waived.

The holders of a majority in principal amount or aggregate issue price of the outstanding debt securities of any series may waive any default with respect to that series, except a default:

- in the payment of any amounts due and payable or deliverable under the debt securities of that series; or

in an obligation contained in, or a provision of, an indenture which cannot be modified under the terms of that indenture without the consent of each holder of each series of debt securities affected.

The holders of a majority in principal amount or, under certain circumstances, issue price of the outstanding debt securities of a series may direct the time, method and place of conducting any proceeding for any remedy available to the applicable indenture trustee or exercising any trust or power conferred on the indenture trustee with respect to debt securities of that series, provided that any direction is not in conflict with any rule of law or the applicable indenture and the trustee may take other actions, other than those that might lead to personal liability, not inconsistent with the direction. Subject to the provisions of the applicable indenture relating to the duties of the indenture trustee, before proceeding to exercise any right or power under the indenture at the direction of the holders, the indenture trustee is entitled to receive from those holders reasonable security or indemnity against the costs, expenses and liabilities which it might incur in complying with any direction.

A holder of any debt security of any series will have the right to institute a proceeding with respect to the applicable indenture or for any remedy under the indenture, if:

that holder previously gives to the indenture trustee written notice of a continuing event of default with respect to debt securities of that series;

the holders of not less than 25% in principal amount of the outstanding securities of that series have made written request and offered the indenture trustee indemnity satisfactory to the indenture trustee to institute that proceeding as indenture trustee;

the indenture trustee will not have received from the holders of a majority in principal amount or, under certain circumstances, issue price of the outstanding debt securities of that series a direction inconsistent with the request; and

the indenture trustee fails to institute the proceeding within 60 days.

However, the holder of any debt security or coupon has the right to receive payment of the principal of (and premium or make-whole amount, if any) and interest on, and any additional amounts in respect of, such debt security or payment of such coupon on the respective due dates (or, in the case of redemption, on the redemption date) and to institute suit for the enforcement of any such payment.

We are required to furnish to the indenture trustees annually a statement as to the performance of our obligations under the indentures and as to any default in that performance.

Modification and Waiver

Unless otherwise indicated in the applicable indenture supplement, we and the applicable indenture trustee may amend and modify each indenture or debt securities under that indenture with the consent of holders of at least a majority in principal amount or, under certain circumstances, issue price of each series of all outstanding debt securities then outstanding under the indenture affected. However, without the consent of each holder of any debt security issued under the applicable indenture, we may not amend or modify that indenture to:

- change the stated maturity date of the principal of (or premium or make-whole amount, if any, on), or any installment of principal or interest on, any debt security issued under that indenture;
- reduce the principal amount of or any make-whole amount, the rate of interest on or any additional amounts payable in respect thereof, or any premium payable upon the redemption of any debt security issued under that indenture;
- reduce the amount of principal of an original issue discount security or make-whole amount, if any, issued under that indenture payable upon acceleration of its maturity; or provable in bankruptcy or adversely affect any right of repayment of a debt security;
- change the place or currency of payment of principal or any premium or any make-whole amount or interest on, any debt security issued under that indenture;
- impair the right to institute suit for the enforcement of any payment or delivery on or with respect to any debt security issued under that indenture;
- reduce the percentage in principal amount of debt securities of any series issued under that indenture, the consent of whose holders is required to modify or amend the indenture or to waive compliance with certain provisions of the

indenture; or

match any change that adversely affects the right to convert or exchange any security or decrease the conversion/exchange rate or increase the conversion/exchange price.

The holders of at least a majority in principal amount of the outstanding debt securities of any series issued under that indenture may, with respect to that series, waive past defaults under the indenture, except as described under “—Events of Default.”

Unless otherwise indicated in the applicable prospectus supplement, we and the applicable indenture trustee may also amend and modify each indenture without the consent of any holder for any of the following purposes:

- to evidence the succession of another person to our company;
- to add to our covenants for the benefit of the holders of all or any series of debt securities;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add or change any provisions of the indentures to facilitate the issuance of bearer securities;

to change or eliminate any of the provisions of the applicable indenture in respect of any series of debt securities, so long as any such change or elimination will become effective only in respect of any series of securities when there is no outstanding security of that series which is entitled to the benefit of that provision;

to establish the form or terms of debt securities of any series;

to evidence and provide for the acceptance of appointment by a successor indenture trustee;

to cure any ambiguity, to correct or supplement any provision in the applicable indenture, or to make any other provisions with respect to matters or questions arising under that indenture, so long as the interests of holders of debt securities of any series are not adversely affected in any material respect by the actions taken to cure, correct or supplement a provision in an indenture;

to secure securities;

to provide for conversion rights of the holders of the debt securities of any series to enable those holders to convert those securities into other securities;

to close the indenture with respect to the authentication and delivery of additional series of securities or to qualify or maintain qualifications of the applicable indenture under the Trust Indenture Act; or

to supplement any of the provisions of an indenture as is necessary to permit or facilitate the defeasance or discharge of any series of securities under specified provisions of the indenture, provided that any such action shall not adversely affect the interests of the holders of securities of such series or any other series of securities under the indenture in any material respect.

Consolidation, Merger and Sale of Assets

Unless otherwise indicated in the applicable prospectus supplement, we may consolidate or merge with or into any other corporation, and we may sell, lease or convey all or substantially all of our assets to any corporation, provided that the resulting corporation, if other than our company, is a corporation organized and existing under the laws of the United States of America or any U.S. state and assumes all of our obligations to:

pay or deliver the principal and any premium or make-whole amount, if any, and any interest on, the debt securities;

- perform and observe all of our other obligations under the indentures and supplemental indentures; and

we are not, or any successor corporation, as the case may be, is not, immediately after any consolidation or merger, in default under the indentures.

The indentures do not provide for any right of acceleration in the event of a consolidation, merger, sale of all or substantially all of the assets, recapitalization or change in our stock ownership. In addition, the indentures do not contain any provision which would protect the holders of debt securities against a sudden and dramatic decline in credit quality resulting from takeovers, recapitalizations or similar restructurings.

Regarding the Indenture Trustee

The indenture trustee provides trust services to us and our affiliates in connection with certain trust preferred securities and related junior subordinated debentures that we currently have outstanding.

The occurrence of any default under either the senior indenture, the subordinated indenture or the indenture between us and the indenture trustee relating to our junior subordinated debentures could create a conflicting interest for the indenture trustee under the Trust Indenture Act. If that default has not been cured or waived within 90 days after the indenture trustee has or acquired a conflicting interest, the indenture trustee would generally be required by the Trust Indenture Act to eliminate that conflicting interest or resign as indenture trustee with respect to the debt securities issued under the senior indenture or the subordinated indenture, or with respect to the junior subordinated debentures issued to certain Delaware statutory trusts of ours under a separate indenture. If the indenture trustee resigns, we are required to promptly appoint a successor trustee with respect to the affected securities.

The Trust Indenture Act also imposes certain limitations on the right of the indenture trustee, as a creditor of ours, to obtain payment of claims in certain cases, or to realize on certain property received in respect to any cash claim or otherwise. The indenture trustee will be permitted to engage in other transactions with us, provided that, if it acquires a conflicting interest within the meaning of Section 310 of the Trust Indenture Act, it must generally either eliminate that conflict or resign.

International Offering

If specified in the applicable prospectus supplement, we may issue debt securities outside the United States. Those debt securities will be described in the applicable prospectus supplement. In connection with any offering outside the United States, we will designate paying agents, registrars or other agents with respect to the debt securities, as specified in the applicable prospectus supplement.

We will describe in the applicable prospectus supplement whether our debt securities issued outside the United States: (1) may be subject to certain selling restrictions; (2) may be listed on one or more foreign stock exchanges; and (3) may have special United States tax and other considerations applicable to an offering outside the United States.

Defeasance

We may terminate or “defease” our obligations under the senior indenture with respect to the senior debt securities of any series by taking the following steps:

(1) depositing irrevocably with the senior indenture trustee an amount, which through the payment of interest, principal or premium, if any, will provide an amount sufficient to pay the entire amount of the senior debt securities:

- in the case of senior debt securities denominated in U.S. dollars, U.S. dollars or U.S. government obligations;

in the case of senior debt securities denominated in a foreign currency, of money in that foreign currency or foreign government obligations of the foreign government or governments issuing that foreign currency; or

- a combination of money and U.S. government obligations or foreign government obligations, as applicable;

(2) delivering:

an opinion of independent counsel that the holders of the senior debt securities of that series will have no federal income tax consequences as a result of that deposit and termination;

- an opinion of independent counsel that registration is not required under Investment Company Act of 1940;

· an opinion of counsel as to certain other matters;

officers' certificates certifying as to compliance with the senior indenture and other matters; and

(3) paying all amounts due under the senior indenture.

Further, the defeasance cannot cause an event of default under the senior indenture or any other agreement or instrument and no default under the senior indenture or any such other agreement or instrument can exist at the time the defeasance occurs.

Subordination

The subordinated debt securities will be subordinated in right of payment to all "senior debt," as defined in the subordinated indenture. In certain circumstances relating to our liquidation, dissolution, receivership, reorganization, insolvency or similar proceedings, the holders of all senior debt will first be entitled to receive payment in full before the holders of the subordinated debt securities will be entitled to receive any payment on the subordinated debt securities.

If the maturity of any subordinated debt securities is accelerated, we will have to repay all senior debt before we can make any payment on the subordinated debt securities.

In addition, we may make no payment on the subordinated debt securities in the event:

there is an event of default with respect to any senior indebtedness which permits the holders of that senior indebtedness to accelerate the maturity of the senior indebtedness; and

the default is the subject of judicial proceedings or we receive notice of the default from an authorized person under the subordinated indenture.

By reason of this subordination in favor of the holders of senior indebtedness, in the event of an insolvency our creditors who are not holders of senior indebtedness or the subordinated debt securities may recover less, proportionately, than holders of senior indebtedness and may recover more, proportionately, than holders of the subordinated debt securities. Unless otherwise specified in the prospectus supplement relating to the particular series of subordinated debt securities, "senior debt" is defined in the subordinated indenture as:

the principal, premium, if any, unpaid interest (including interest accruing on or after the filing of any petition in bankruptcy or for reorganization relating to us whether or not a claim for post-filing interest is allowed in such proceeding), fees, charges, expenses, reimbursement and indemnification obligations, and all other amounts payable under or in respect of the following indebtedness of us for money borrowed, whether any such indebtedness exists as of the date of the indenture or is created, incurred, assumed or guaranteed after such date:

(i) any debt (a) for money borrowed by us, or (b) evidenced by a bond, note, debenture, or similar instrument (including purchase money obligations) given in connection with the acquisition of any business, property or assets, whether by purchase, merger, consolidation or otherwise, but shall not include any account payable or other obligation created or assumed in the ordinary course of business in connection with the obtaining of materials or services, or (c) which is a direct or indirect obligation which arises as a result of banker's acceptances or bank letters of credit issued to secure obligations of us, or to secure the payment of revenue bonds issued for the benefit of us whether contingent or otherwise;

(ii) any debt of others described in the preceding clause (i) which we have guaranteed or for which it is otherwise liable;

(iii) the obligation of us as lessee under any lease of property which is reflected on our balance sheet as a capitalized lease; and

(iv) any deferral, amendment, renewal, extension, supplement or refunding of any liability of the kind described in any of the preceding clauses (i), (ii) and (iii).

“Senior debt” does not include:

(1) any such indebtedness, obligation or liability referred to in clauses (i) through (iv) above as to which, in the instrument creating or evidencing the same or pursuant to which the same is outstanding, it is provided that such indebtedness, obligation or liability is not superior in right of payment to the subordinated debt securities, or ranks pari passu with the subordinated debt securities, (2) any such indebtedness, obligation or liability which is subordinated to indebtedness of us to substantially the same extent as or to a greater extent than the subordinated debt securities are subordinated, (3) any indebtedness to one of our subsidiaries and (4) the subordinated debt securities.

The subordinated indenture does not limit or prohibit the incurrence of additional senior indebtedness, which may include indebtedness that is senior to the subordinated debt securities, but subordinate to our other obligations. Any prospectus supplement relating to a particular series of subordinated debt securities will set forth the aggregate amount of our indebtedness senior to the subordinated debt securities as of a recent practicable date.

The prospectus supplement may further describe the provisions, if any, which may apply to the subordination of the subordinated debt securities of a particular series.

Restrictive Covenants

The subordinated indenture does not contain any significant restrictive covenants. The prospectus supplement relating to a series of subordinated debt securities may describe certain restrictive covenants, if any, to which we may be bound under the subordinated indenture.

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, warrants to purchase common stock or preferred stock, debt securities or any combination of those securities. 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, warrants and debt securities as described in this section will apply to each unit to the extent such unit consists of shares of our common stock, preferred stock, warrants and debt securities.

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. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

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, 2015 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, 2015 filed with the Commission on February 29, 2016;
2. Our Current Reports on Form 8-K filed with the Commission on February 29, 2016, March 4, 2016, March 22, 2016, April 14, 2016 and May 26, 2016;
3. Our Quarterly Reports on Form 10-Q for the quarters ending March 31, 2016 and June 30, 2016 and filed with the Commission on May 4, 2016 and August 3, 2016, respectively;

4. Our definitive Proxy Statement on Schedule 14A, filed with the Commission on April 14, 2016; and
5. 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:

Dawn Schottlandt

Senior Director, Investor Relations/Corporate Communications
ArQule, Inc.
One Wall Street

Burlington, MA 01803
(781) 994-0300

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 100 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.

\$30,000,000

Common Stock

PROSPECTUS SUPPLEMENT

October 25, 2016