ARQULE INC Form S-3 December 15, 2003

QuickLinks -- Click here to rapidly navigate through this document

As Filed with the Securities and Exchange Commission on December 15, 2003

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

ARQULE, INC.

(Exact name of registrant as specified in its charter)

DELAWARE

(State or other jurisdiction of incorporation or organization)

58-1959440

(IRS Employer Identification No.)

19 Presidential Way Woburn, Massachusetts 01801 (781) 994-0300

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Dr. Stephen A. Hill President and Chief Executive Officer ArQule, Inc. 19 Presidential Way Woburn, Massachusetts 01801 (781) 994-0300

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

J. DAVID JACOBS Vice President, Legal, General Counsel and Secretary ArQule, Inc. 19 Presidential Way Woburn, Massachusetts 01801 (781) 994-0300 RICHARD E. BALTZ Arnold & Porter 555 Twelfth Street, N.W. Suite 1004 Washington, D.C. 20004 (202) 942-5000

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: ý

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: o

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: o

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box: o

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered ⁽¹⁾	Proposed Maximum Aggregate Offering Price ⁽²⁾⁽³⁾	Amount of registration fee
Common Stock, par value \$0.01 per share Warrants Preferred Stock, par value \$0.01 per share	\$50,000,000	\$4,045

(1)

Amount not specified as to each class of security to be registered pursuant to General Instruction II.D of Form S-3. An indeterminate number of shares of common stock, shares of preferred stock and warrants as may be issued from time to time at indeterminate prices are being registered hereby. Securities registered hereunder may be sold either separately or as units comprised of more than one type of security registered hereunder.

In no event will the aggregate initial public offering price of all securities issued from time to time pursuant to this Registration Statement exceed \$50,000,000.

(3)

(2)

Estimated solely for purposes of calculating the registration fee in accordance with Rule 457(c) of the Securities Act.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

PROSPECTUS

Subject to Completion

Preliminary Prospectus Dated December 15, 2003

ARQULE, INC.

UP TO \$50,000,000 OF OUR COMMON STOCK PREFERRED STOCK WARRANTS

We may offer from time to time up to \$50,000,000 in total of (a) shares of our common stock, (b) shares of our preferred stock, (c) warrants to purchase shares of common stock or preferred stock, or (d) any combination of our common stock, preferred stock or warrants. We may offer

the common stock, preferred stock and warrants (collectively, the "securities") separately or together, in separate series, in amounts, at prices and on terms to be set forth in one or more supplements to this prospectus (each, a "prospectus supplement"). 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 National Market and traded under the symbol "ARQL." On December 12, 2003, the last reported sale price for our common stock was \$4.61 per share.

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

An investment in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 4 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 , 2003

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the SEC is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

TABLE OF CONTENTS

	PAGE
About This Prospectus	2
Information About ArQule, Inc.	3
Risk Factors	3
Use of Proceeds	3
Plan of Distribution	4
Description of Common Stock	6
Description of Preferred Stock	7
Description of Warrants	8
Legal Matters	9
Experts	9
Incorporation of Certain Documents by Reference	9
Where You Can Find More Information	10

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains and incorporates by reference certain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements that are not descriptions of historical facts are forward-looking statements, based on management's estimates, assumptions and projections that are subject to risks and uncertainties. These statements can generally be identified by the use of forward-looking terminology such as "believes," "expects," "intends," "will," "should," or "anticipates" or similar terminology.

Actual results may differ materially from those projected in the forward-looking statements or from historical performance due to numerous risks and uncertainties that exist in our operations, development efforts and the business environment, including without limitation: the ability to transition successfully from chemistry services to drug discovery, to satisfy milestones, and to deliver compounds such as ARQ 501 to corporate collaborators; the ability to design small molecules that possess drug-like characteristics; the progress of product research and development activities and projected expenditures; the ability to advance compounds through preclinical and clinical trials; the ability to enter into future collaborations with pharmaceutical and biotechnology companies; and difficulties and costs associated with the integration of acquired businesses and the risks and uncertainties described this document and the applicable prospectus supplement. The forward-looking statements contained herein represent our judgment as of the date of this prospectus. We disclaim any intent or obligation to update any forward-looking statement except to the extent required by law.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC using a "shelf" registration process. Under this shelf process, we may from time to time offer up to \$50,000,000 in total of (a) shares of common stock, \$0.01 par value per share, (b) shares of preferred stock, \$0.01 par value per share, in one or more series, (c) warrants to purchase shares of common stock or preferred stock or (d) any combination of our common stock, preferred stock or warrants, either individually or as units consisting of one or more of the foregoing, each at prices and on terms to be determined at the time of sale. The common stock, preferred stock and warrants are collectively referred to in this prospectus as "securities." The securities offered pursuant to this prospectus may be one or more series of issuances and the total offering price of the securities will not exceed \$50,000,000 (or its equivalent based on the applicable exchange rate at the time of the sale in one or more foreign currencies, currency units or composite currencies that we may designate).

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

The registration statement that contains this prospectus, including the exhibits to the registration statement and the information incorporated by reference, provides additional information about the securities offered under this prospectus. That registration statement can be read at the SEC web site or at the SEC public reference room as discussed below under the heading "Where You Can Find More Information."

You should rely only on the information provided in 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.

2

INFORMATION ABOUT ARQULE, INC.

We are a biotechnology company engaged in the discovery and development of novel drugs for the treatment of cancer and inflammation.. We also provide chemistry services to collaborators and customers. In our drug discovery program, we use our technology platform to design new molecules focused on two therapeutic areas: oncology and inflammation.

In the field of oncology, we are striving to discover and develop small-molecule cancer drugs based on a novel proprietary technology, the Activated Checkpoint TherapySM or ACTSM platform, designed to selectively kill cancer cells and preserve normal cells by restoring and activating cellular checkpoints known to be defective in cancerous conditions. We hope to develop anti-cancer therapeutics which will be better tolerated by patients than traditional chemotherapies and have broad-spectrum activity against multiple types of cancer. Based on ACTSM principles, we will seek to discover and develop therapies that are effective as stand-alone therapies or as agents combined with traditional chemotherapies. Currently, we are applying the ACTSM technology to multiple discovery programs targeted at various checkpoint pathways. On September 30, 2003, we announced the commencement of Phase 1 clinical trials of our lead compound in this area, ARQ 501.

In inflammation, we are developing compounds for activity against the p38 MAP Kinase target. After optimizing lead compounds for inflammation, we advanced one compound, an Optimal Chemical Entity (OCE) molecule designated ARQ 101, through preliminary toxicity testing in animal models. Based these preliminary results, we have commenced definitive toxicity studies for the compound in accordance with the FDA's Good Laboratory Practices. ARQ 101 is our first GLP-toxicity candidate for which we have retained all rights.

We also apply our expertise in the design, production, and evaluation of chemical compounds in our chemistry services business. We assist our collaborators and customers with their development programs by, for example, generating potential drug candidates, assessing the suitability of drug candidates and selecting the most promising candidates, all using high throughput, automated chemistry.

ArQule now employs approximately 300 people, including 220 research scientists, and operates across three Massachusetts sites: Woburn (headquarters, discovery and development), Medford (lead generation), and Norwood (target identification and validation). Our principal executive offices are located at 19 Presidential Way, Woburn, MA 01801, where the phone number is 781-994-0300.

RISK FACTORS

You should carefully consider the specific risks set forth under the caption "Risk Factors" in the applicable prospectus supplement before making an investment decision. An investment in our common stock involves a high degree of risk. We operate in a dynamic and rapidly changing industry that involves numerous uncertainties. The risks and uncertainties described in the prospectus supplement are not the only ones we face. Other risks and uncertainties that we are unaware of or that we do not consider material at the time may impair our business, financial condition or results of operations. In any case, the value of our common stock, preferred stock or warrants could decline, and you may lose all or part of your investment. You should also refer to the other information contained in this prospectus or incorporated herein by reference, including our consolidated financial statements and the notes to those statements. See also "Special Note Regarding Forward-Looking Statements" in the table of contents.

USE OF PROCEEDS

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

3

PLAN OF DISTRIBUTION

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

directly to purchasers;

through agents;

to or through one or more underwriters or dealers;

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; and

through a combination of any of these methods of sale.

In addition, we may issue the securities being offered by this prospectus as a dividend or distribution.

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

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

at market prices prevailing at the times of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

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

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 prospectus supplement. Unless otherwise indicated in the 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 (the "Securities Act").

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 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 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 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 prospectus supplement will describe the terms of any direct sales, including the terms of any bidding or auction process.

4

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 prospectus supplement will describe the terms and conditions of indemnification or contribution.

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 prospectus supplement. The 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.

To the extent permitted by and in accordance with Regulation M under the Securities Exchange Act of 1934 (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 National Market may engage in passive market making transactions in the securities on the Nasdaq National Market during the business day prior to the pricing of an offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the

passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

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

DESCRIPTION OF COMMON STOCK

Authorized and Outstanding Capital Stock

As of December 5, 2003, we had 50,000,000 shares of common stock authorized, of which 28,079,609 shares were outstanding.

Listing

Our common stock is quoted on the Nasdaq National Market and traded under the symbol "ARQL."

5

Dividends

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

Fully Paid and Non-Assessable

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

Voting Rights

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

Preemptive and Other Rights

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

Meetings; Stockholder Action by Written Consent

Our By-Laws 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 Certificate of Incorporation provides that stockholders may not take action by written consent without a meeting.

Staggered Board of Directors

Our Board of Directors is divided into three classes, the members of each of which serve for staggered three-year terms. Our stockholders may elect only one-third of the directors each year; therefore, it is more difficult for a third party to gain control of our Board of Directors than if our Board was not staggered.

Transfer Agent and Registrar

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

DESCRIPTION OF PREFERRED STOCK

Our Amended and Restated Certificate of Incorporation authorizes our Board of Directors, without further stockholder action, to provide for the issuance of up to 1,000,000 shares of preferred stock, in one or more classes or series and to fix the rights, preferences, privileges, and restrictions thereof, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences and the number of shares constituting any series of the designation of such series, without further vote or action by the stockholders. We may amend from

6

time to time our Certificate of Incorporation to increase the number of authorized shares of preferred stock. Any such amendment would require the approval of the holders of a majority of the voting power of the shares entitled to vote thereon. As of the date of this prospectus, we have 1,000,000 shares of preferred shares authorized, but no shares of preferred stock outstanding.

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

the title and liquidation preference per share of the preferred stock and the number of shares offered;

the purchase price of the preferred stock;

the dividend rate (or method of calculation), the dates on which dividends will be paid and the date from which dividends will begin to accumulate;

any redemption or sinking fund provisions of the preferred stock;

any conversion provisions of the preferred stock;

the voting rights, if any, of the preferred stock; and

any additional dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions of the preferred stock.

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

DESCRIPTION OF WARRANTS

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

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

the title of such warrants;

the aggregate number of such warrants;

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

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

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

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

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

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

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

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

a discussion of certain federal income tax consequences; and

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

LEGAL MATTERS

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

EXPERTS

The financial statements incorporated in this prospectus by reference to our Annual Report on Form 10-K for the year ended December 31, 2002 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on authority of said firm as experts in accounting and auditing. (SEC 2300.95)

Any audited financial statements and schedules that are incorporated or that are deemed to be incorporated by reference into this prospectus that are the subject of a report by independent accountants will be so incorporated by reference in reliance upon such reports and upon the authority of such firm as experts in accounting and auditing to the extent covered by consents of these accountants filed with the SEC.

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.

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. 0-21429) under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus and the termination of the offering of the securities. These documents contain important information about us.

1. Our Annual Report on Form 10-K for the year ended December 31, 2002 filed with the Commission on March 31, 2003;

2. Our Quarterly Reports on Form 10-Q for the periods ended March 31, 2003, June 30, 2003 and September 30, 2003, filed with the Commission on May 15, 2003, August 8, 2003 and November 12, 2003, respectively;

3. Our Current Reports on Form 8-K filed with the Commission on May 2, 2003, July 21, 2003, August 19, 2003 and September 17, 2003; and

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

8

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:

Jean Devine Director of Investor Relations ArQule, Inc. 19 Presidential Way Woburn, MA 01801 (781) 994-0300 <u>jdevine@arqule.com</u>

See also "Where You Can Find More Information."

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 450 Fifth Street, N.W., 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 <u>http://www.sec.gov</u>. We also maintain a web site at <u>http://www.arqule.com</u>, 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.

9

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. Other Expenses of Issuance and Distribution.

The following table sets forth the estimated costs and expenses in connection with the sale and distribution of the securities being registered, all of which will be paid by ArQule.

SEC Registration	\$ 4,045
Accounting fees and expenses	\$ 15,000*
Printing fees and expenses	\$ 9,000*
Legal fees and expenses	\$ 25,000*
Miscellaneous expenses	\$ 3,000*
Total	\$ 56,045*

Estimated

ITEM 15. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law ("DGCL"), permits, under certain circumstances, the indemnification of any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative other than an action by or in the right of the corporation) by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving in a similar capacity for another enterprise at the request of the corporation. To the extent that a present or former director or officer of the corporation has been successful in defending any such proceeding, the DGCL provides that he shall be indemnified against expenses (including attorneys' fees), actually and reasonably incurred by him in connection therewith. With respect to a proceeding by or in the right of the corporation, such person may be indemnified against expenses (including attorneys' fees), actually and reasonably incurred, if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation. The DGCL provides, however, that indemnification shall not be permitted in such a proceeding if such person is adjudged liable to the corporation unless, and only to the extent that, the court, upon application, determines that he is entitled to indemnification under the circumstances. With respect to proceedings other than those brought by or in the right of the corporation, notwithstanding the outcome of such a proceeding, such person may be indemnified against judgments, fines and amounts paid in settlement, as well as expenses, if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action, had no reason to believe his conduct was unlawful. Except with respect to mandatory indemnification of expenses to successful defendants as described in the preceding paragraph or pursuant to a court order, the indemnification described in this paragraph may be made only upon a determination in each specific case (1) by majority vote of the directors that are not parties to the proceeding, even though less that a quorum, or (2) by a committee of the directors that are not a party to the proceeding who have been appointed by a majority vote of directors who are not party to the proceeding, even though less than a quorum, or (3) if there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion, or (4) by the stockholders.

The DGCL permits a corporation to advance expenses incurred by a proposed indemnitee in advance of final disposition of the proceeding, provided that the indemnitee undertakes to repay such advanced expenses if it is ultimately determined that he is not entitled to indemnification. Also, a corporation may purchase insurance on behalf of an indemnitee against any liability asserted against

him in his designated capacity, whether or not the corporation itself would be empowered to indemnify him against such liability. ArQule has adopted provisions in its bylaws that provide for indemnification of its officers and directors to the maximum extent permitted under the DGCL. As authorized by the DGCL, ArQule's Amended and Restated Certificate of Incorporation limits the liability of directors of ArQule for monetary damages. The effect of this provision is to eliminate the rights of ArQule and its stockholders to recover monetary damages against a director for breach of the fiduciary duty of care as a director except in certain limited situations. This provision does not limit or eliminate the rights of ArQule or any stockholder to seek non-monetary relief such as an injunction or rescission in the event of a breach of a director's duty of care. This provision will not alter the liability of directors under federal securities laws. ArQule has purchased an insurance policy that purports to insure the officers and directors of ArQule against certain liabilities incurred by them in the discharge of their functions as such officers and directors. The foregoing descriptions are only general summaries. For additional information we refer you to the full text of our Amended and Restated Certification of Incorporation and amendment number 1 thereto, filed as exhibit 3.1 to our Form S-1 (file no. 333-22945) and 3.1 to our Form 10-Q for the quarter ended June 30, 2002, and our bylaws, filed as Exhibit 3.1 to our Form 10-Q for the period ending June 30, 1999.

ITEM 16. Exhibits

The exhibits listed on the Index to Exhibits of this Registration Statement are filed herewith or are incorporated herein by reference to other filings.

Exhibit No.	Description
Exhibit 5.1	Opinion of Arnold & Porter
Exhibit 23.1	Independent Auditors' Consent
Exhibit 23.2	Consent of Arnold & Porter (contained in opinion of Arnold & Porter filed as Exhibit 5.1)
Exhibit 24.1	Powers of Attorney of certain directors of the Company

ITEM 17. Undertakings

A. The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i)

To include any Prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii)

To reflect in the Prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of Prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement;

(iii)

To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;

provided, however, that paragraphs (A) (1) (i) and (A) (1) (ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this Registration Statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

B. The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

C. Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers, and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer, or controlling person of the Registrant in the successful defense of any action, suit, or proceeding) is asserted by such director, officer, or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

II-3

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Woburn, Commonwealth of Massachusetts, on December 11, 2003.

ARQULE, INC.

By: /s/ STEPHEN A. HILL

Stephen A. Hill

President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

SIGNATURE:	TITLE:	DATE:	
/s/ STEPHEN A. HILL	President and Chief Executive Officer (Principal		
Stephen A. Hill	Executive Officer)	December 11, 2003	
/s/ THOMAS J. PHAIR, JR.	Corporate Controller (Acting Principal	December 12, 2002	
Thomas J. Phair, Jr.	Accounting and Financial Officer)	December 12, 2003	
/s/ LAURA AVAKIAN	— Director	December 11, 2003	
Laura Avakian		December 11, 2005	

SIGNATURE:	TITLE:	DATE:
/s/ TIMOTHY C. BARABE	Director	December 12, 2003
Timothy C. Barabe		
/s/ WERNER CAUTREELS	- Director	December 15, 2003
Werner Cautreels		December 15, 2005
/s/ ARIEL ELIA	 Chairman of the Board 	December 12, 2003
Ariel Elia		December 12, 2005
/s/ TUAN HA-NGOC	— Director	December 11, 2003
Tuan Ha-Ngoc		December 11, 2005
/s/ PATRICK J. ZENNER	— Director	December 12, 2003
Patrick J. Zenner	II-4	December 12, 2005

INDEX TO EXHIBITS

The following documents are filed herewith (unless otherwise indicated) and made a part of this registration statement.

Exhibit No.	Description
Exhibit 5.1	Opinion of Arnold & Porter
Exhibit 23.1	Independent Auditors' Consent
Exhibit 23.2	Consent of Arnold & Porter (contained in opinion of Arnold & Porter filed as Exhibit 5.1)
Exhibit 24.1	Powers of Attorney of certain directors of the Company

QuickLinks

TABLE OF CONTENTS SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS ABOUT THIS PROSPECTUS INFORMATION ABOUT ARQULE, INC. RISK FACTORS USE OF PROCEEDS PLAN OF DISTRIBUTION DESCRIPTION OF COMMON STOCK DESCRIPTION OF PREFERRED STOCK DESCRIPTION OF WARRANTS LEGAL MATTERS EXPERTS INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE WHERE YOU CAN FIND MORE INFORMATION PART II INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. Other Expenses of Issuance and Distribution. ITEM 15. Indemnification of Directors and Officers. ITEM 16. Exhibits ITEM 17. Undertakings SIGNATURES INDEX TO EXHIBITS