ARQULE INC
Form S-3/A
November 24, 2003

As Filed with the Securities and Exchange Commission on November 24, 2003

Registration No. 333-109564

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

Amendment No. 1
to
FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

ARQULE, INC.

(Exact name of registrant as specified in its charter)

DELAWARE	**58-1959440**
(State or other jurisdiction of incorporation or organization)	(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:

STEVE PARKER, ESQ.
Arnold & Porter
1600 Tysons Boulevard, Suite 900
McLean, Virginia 22102-4865
(703) 720-7000

J. DAVID JACOBS, ESQ.
Vice President, Legal,
General Counsel and Secretary
ArQule, Inc.
19 Presidential Way
Woburn, Massachusetts 01801
(781) 994-0300

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: x

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

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 November 24, 2003

ArQule, Inc.

UP TO 4,571,353 SHARES OF OUR COMMON STOCK
$0.01 PAR VALUE

The persons listed in this prospectus under Selling Stockholders may offer and sell up to 4,571,353 shares of our common stock. Information on the selling stockholders, and the times and manner in which they may offer and sell shares of our common stock under this prospectus, is provided under Selling Stockholders and Plan of Distribution. We will not receive any proceeds from the sale of these shares by the selling stockholders.

Our common stock is quoted on the Nasdaq National Market and traded under the symbol ARQL. On November 21, 2003, the last reported sale price for our common stock was $4.74 per share.

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

See Risk Factors beginning on page 3 for a discussion of 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 November ___, 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

You should rely only on the information provided in this prospectus, 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 this prospectus.

INFORMATION ABOUT ARQULE, INC.

We are a drug discovery company with expertise in small-molecule chemistry and intelligent drug design, and we also provide chemistry services to collaborators and customers. In our drug discovery program, we use our parallel, predictive chemistry technology platform to design new molecules aimed at two therapeutic focus areas: inflammation and oncology. In inflammation, we are developing compounds for activity against the p38 MAP Kinase target. We are currently optimizing lead compounds for rheumatoid arthritis and expect to select a GLP-toxicology candidate for preclinical (animal) testing before the end of 2003. In oncology, we are developing a novel approach to selectively killing cancer cells by restoring and activating cellular checkpoints. On September 30, 2003, we announced the commencement of Phase 1 clinical trials of our lead compound in this area, CO-501.

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. We provide our products and services under collaboration agreements with a number of pharmaceutical companies, including Pfizer, Inc, Bayer AG, Solvay Pharmaceuticals B.V. and Sankyo Company, Ltd.

ArQule recently acquired Cyclis Pharmaceuticals, Inc. in a merger. Cyclis was a privately-held cancer therapeutics company. 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 risks described below together with all of the other information included in this prospectus 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 below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. 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 might 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.

RISKS RELATING TO OUR BUSINESS AND STRATEGY

We may not be able to shift our primary focus successfully from that of a services-based business to that of a product-based business.

Historically we have derived most of our revenues from providing chemistry-based services on a fee-for-service basis. We have recently begun to use our expertise and technology to discover chemical compounds and develop them into drugs, on our own and in collaboration with partners while continuing to generate service revenue.

While we concentrate on shifting our business strategy, there is a risk that we will pay less attention to our original, ongoing business. Furthermore, customers, potential collaborators and others may be unable to recognize and accept our shift in strategy. Also, we may not implement the shift effectively, which may undermine our results even if the strategy, technology and management team work together effectively.

There are a variety of risks that our new business of developing drugs will add to our existing business, including:

success in developing drugs is highly uncertain;

revenues, if any, from product sales are years away; and

regulatory and other external risks can delay or block product development.

As the drug discovery process continuously evolves, it will be necessary for us to keep abreast, or ahead, of improvements in discovery technology. In all likelihood, we will gain access to some of these improvements from third parties. For example, we have begun and must continue to acquire and integrate considerable additional biological, clinical and regulatory expertise, which has not been a part of our historical chemistry-services business. We may be unsuccessful in accessing on a timely basis an adequate quantum of such improvements.

Development of our products is at an early stage and is uncertain and our approach and technology may never result in a commercial drug.

The discovery and development of drugs is inherently risky and involves a high rate of failure. Discovering and developing commercial drugs is new to us. Our management team has experience at other companies in drug discovery and development comparable to what we are undertaking, but it has not worked together to do this.

Our proposed products and research programs are in the early stages of development and require significant, time-consuming and costly research and development, testing and regulatory clearances. We do not expect that these product candidates will be commercially available for several years, if ever. In addition, we will pursue the discovery and development of products using our integrated technology platform in both our internal and collaborative programs to implement our strategy of reducing the cost and time incurred by the pharmaceutical industry for developing drug candidates. We have never identified a drug candidate that has been developed into a commercial drug using this platform. It is uncertain whether our technology platform will achieve these goals at all, or whether it will be competitive with platforms used by our competitors.

We must show the safety and efficacy of our product candidates through clinical trials, the results of which are uncertain.

Our product candidates are at the preclinical stages of development, with the exception of CO-501, which is now in Phase 1 clinical studies. Although several of our product candidates have demonstrated some success in preclinical studies, they may not prove to be similarly effective in humans. Before obtaining regulatory approvals for the commercial sale of our products, we must demonstrate, through preclinical studies (animal testing) and clinical trials (human testing), that our proposed products are safe and effective for use in each target indication. These types of testing are expensive and time-consuming, and failure can occur at any stage of testing. Acceptable results from initial preclinical studies and clinical trials of products under development are not necessarily indicative of results that will be obtained from subsequent or more extensive preclinical studies and clinical testing in humans. Clinical trials may not demonstrate sufficient safety and efficacy to obtain the required regulatory approvals or result in marketable products. The failure to adequately demonstrate the safety and efficacy of a product under development could delay or prevent regulatory approval of the potential product.

Clinical trials for the product candidates we are developing may be delayed by many factors, including that potential appropriate patients for testing are limited in number. The failure of any clinical trials to meet applicable regulatory standards could cause such trials to be delayed or terminated, which could further delay the commercialization of any of our product candidates. Any such delays will increase our product development costs. If such delays are significant they could negatively affect our financial results and the commercial prospects for our products.

We may face challenges in integrating ArQule and Cyclis and, as a result, may not realize the expected benefits of the merger.

We acquired Cyclis Pharmaceuticals, Inc. on September 8, 2003 by merging Cyclis with and into ArQule. Integrating the operations and personnel of ArQule and Cyclis will be a complex process. We must integrate the former Cyclis business, including the CO-501 program, and the Cyclis molecular biology expertise into our existing operations. We are uncertain that the integration will be completed rapidly or that it will achieve the anticipated benefits of the merger. The successful integration of ArQule and Cyclis will require, among other things, coordination of discovery and development efforts and integration of Cyclis operations and personnel into ArQule. The diversion of the attention of our management and any difficulties encountered in the process of combining the companies could cause the disruption of, or a loss of momentum in, the activities of the combined company s business. The inability to successfully integrate the operations and personnel of ArQule and Cyclis, or any significant delay in achieving integration, could have a material adverse effect on our business and operating results and the market price of our common stock.

We may not be able to continue collaborations, find new collaborators or successfully form collaborations.

We must maintain our collaborations and enter into new ones to earn revenue and obtain access to commercialization expertise. The availability of collaborators depends on the willingness of pharmaceutical and biotechnology companies to outsource drug discovery activities. There are only a limited number of large pharmaceutical companies, and these companies represent a significant portion of the market for our capabilities. The number could decline further through consolidation. If the number of our potential collaborators declines further, collaborators may be able to negotiate price discounts or other terms unfavorable to us.

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

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

Even if we are able to gain the interest of potential partners, the negotiation, documentation and implementation of collaborative arrangements are complex and time-consuming. Collaborative opportunities may not be available on commercially acceptable terms and, if formed, may not be commercially successful. If we are unable to form collaborations, given the consequent diminished revenue and expertise, we may be unable to develop drug products or successfully market any products we develop and, therefore, be unable to generate product revenue.

Our success depends on the efforts of our collaborators, whom we do not and cannot control.

We depend on our partners to develop and commercialize compounds and drug candidates after Phase 1, or possibly Phase 2, clinical trials, if not before. Each of our current collaborators has, and we expect that each future collaborator will have, significant discretion in determining the efforts and resources that it will apply to the development and commercialization of compounds and drug candidates covered by its collaboration with us.

We may not successfully enter into additional collaborations that allow us to participate in the future success of our proprietary drug candidates through milestone, royalty and/or license payments, and we may never receive any milestone, royalty and/or license payments under our current or any future collaborations.

One of our business strategies is to create our own proprietary drug candidates and to then enter into collaborations for the development of these drug candidates that will allow us to earn milestone, royalty and/or license payments. Our proprietary drug discovery program is in its early stage development and is unproven. Although we have expended, and continue to expend, time and money on internal research and development programs, we may be unsuccessful in creating valuable proprietary drug candidates that would enable us to form additional collaborations and receive milestone, royalty and/or license payments.

Our collaborations and internal programs may not result in the discovery of potential drug candidates that will be safe or effective. Although we have received license and milestone fees to date, we may never receive any royalty payments, or additional license and milestone fees, under our current or any future collaborations. Our receipt of any future milestone, royalty or license payments depends on many factors, including whether our collaborators want or are able to continue to pursue a potential drug candidate and the ultimate commercial success of the drug. Development and commercialization of potential drug candidates depend not only on the achievement of research objectives by us and our collaborators, but also on each collaborator s financial, competitive, marketing and strategic considerations and regulation in the United States and other countries. Pharmaceutical products our collaborators develop will require lengthy and costly testing in animals and humans and regulatory approval by governmental agencies prior to commercialization. These agencies may not approve the products for commercialization despite the substantial time and resources required to seek approvals and comply with appropriate statutes and regulations. If unforeseen complications arise in the development or commercialization of the potential drug candidates by our collaborators, we may not realize milestone, royalty or license payments.

Any of our collaboration partners may fail to develop or commercialize a compound or product to which they have obtained rights from us for a variety of reasons, including that our partner:

- decides not to devote the necessary resources because of internal constraints or other priorities;
- decides to pursue a competitive potential drug or compound developed outside of our collaborations;
- cannot obtain necessary regulatory approvals; or
- exercises a right to terminate our collaboration.

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

To succeed, we must attract, retain and motivate highly skilled scientists and management. We compete intensely with pharmaceutical and biotechnology companies, including our collaborators, medicinal chemistry outsourcing companies, contract research companies, and academic and research institutions to recruit scientists and management. If we cannot hire additional qualified personnel, the workload may increase for both existing and new personnel. The shortage of experienced scientists could lead to increased recruiting, relocation and compensation costs, which may exceed our expectations and resources. These increased costs also may reduce our profit margins and make hiring new scientists impractical.

If we choose to acquire new and complementary businesses, products or technologies instead of developing them ourselves, we may be unable to complete these acquisitions or to successfully integrate an acquired business or technology in a cost-effective and non-disruptive manner.

From time to time, we may choose to acquire complementary businesses, products, or technologies instead of developing them ourselves. We do not know if we will be able to complete any acquisitions, or whether we will be able to successfully integrate any acquired businesses, operate them profitably or retain their key employees. Integrating any business, product or technology we acquire could be expensive and time-consuming, disrupt our ongoing business and distract company management. In addition, in order to finance any acquisition, we might need to raise additional funds through public or private equity or debt financings. In that event, we could be forced to obtain financing on less than favorable terms and, in the case of equity financing, that may result in dilution to our stockholders. If we are unable to integrate any acquired entities, products or technologies effectively, our business will suffer. In addition, under certain circumstances, amortization of assets or charges resulting from the costs of acquisitions could harm our business and operating results.

RISKS RELATED TO OUR FINANCIAL CONDITION

We may not achieve profitability.

From our inception in 1993 through June 30, 2003, we incurred cumulative losses of approximately $150 million. These losses have resulted principally from the costs of our research activities and enhancements to our technology. We have derived our revenue primarily from:

- license and technology transfer fees for access to our chemical synthesis and production platforms such as transfer of our AMAP technology to Pfizer;
- payments for product deliveries;
- research and development funding paid under our agreements with our collaboration partners; and
- to a limited extent, milestone payments.

To date, these revenues have generated profits only in 1997, 2000 and the first six months of 2003. We have not realized any revenue from royalties from the sale by any of our collaboration partners of a commercial product developed using our technology. We might never become profitable on a sustained basis.

Our revenue from collaborations is uncertain and not diversified.

To maintain our current relationships with collaborators and to meet the performance and delivery requirements in our contracts, we must provide drug discovery capabilities at appropriate levels, with acceptable quality and at acceptable cost. Our ability to deliver the drug discovery capabilities we want to offer to our collaborators is limited by many factors, including the difficulty of the chemistry, the lack of predictability in the scientific process and the shortage of qualified scientific personnel. In particular, a large portion of our revenue depends on producing collections of high-quality chemical compounds, which requires a high rate of production. Some of our collaborators can influence when we provide our drug discovery capabilities under their contracts, which could increase our current contractual commitments to provide chemical compounds even further. If we are unable to increase or maintain our current rate of compound synthesis to meet our existing or future contractual commitments, it may result in delayed or lost revenue, loss of collaborations and/or failure to expand our existing relationships.

Also, at present we depend largely on collaboration arrangements for our revenue and cannot be sure whether our collaborations will succeed or whether we will realize much of the potential revenue from our collaborations. In addition, a significant portion of our revenue is generated from our Pfizer collaboration. If this collaboration were to cease it would have a material adverse effect on our financial condition. Significant portions of the revenue from milestones and royalties that we may receive under these collaborations will depend upon our ability and/or our partners ability to successfully develop, license, introduce, market and sell new drugs developed using our chemical compounds and/or proprietary technology. We have little control over the efforts of our partners. We may not be able to achieve these milestones and may not be able to develop commercial drugs or other products on which royalties will be payable.

Our collaboration agreements require us to reach significant developmental stages in the drug discovery process in order to receive milestone payments. If we do not achieve these milestones as expected, our revenue will be delayed and/or reduced. For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other milestones, such as the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. These estimates are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control.

Products developed in collaborations will result in commercialized drugs generating royalties only after, among other things:

- significant preclinical and clinical development efforts;
- regulatory approvals;
- development of manufacturing capabilities; and
- successful marketing.

Our operating results likely will continue to fluctuate significantly.

Our ability to generate revenue from collaborations typically involves significant technical evaluation and/or commitment of capital by our collaborators and is subject to a number of significant risks, including collaborators budgetary constraints and internal acceptance reviews. In addition, some of our collaborators can influence when we deliver products and perform services under their contracts with us. This could cause our operating results to fluctuate significantly. In addition, we expect to continue to experience significant fluctuations in operating results due to factors such as general and industry specific economic conditions that may affect the research and development expenditures of pharmaceutical and biotechnology companies, as well as the timing of compound shipments to our collaborators.

We thus believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance. Our operating results in some periods may not meet the expectations of stock market analysts and investors, causing our stock price to decline.

We may not be able to fund our operations.

If our operations do not become profitable on a sustainable basis before we exhaust existing resources, we will need to obtain additional financing. Such financing could come from the proceeds of public or private debt or equity financings or corporate partnerships. We may not be able to obtain adequate funds for our operations from these sources when needed or on acceptable terms. If we raise additional capital through the sale of equity, or securities convertible into equity, each shareholder s proportionate ownership in ArQule may be diluted.

If we cannot obtain additional financing, we could be forced to delay or scale back our research and development programs. If adequate funds are not available, we may be required to curtail operations significantly or to obtain funds by entering into arrangements with collaboration partners or others that may require that we relinquish rights to certain technologies, product candidates, products or potential markets.

Moreover, our fixed expenses such as rent, license payments and other contractual commitments are substantial and will increase in the future. These fixed expenses will increase from:

construction or lease and maintenance expense for new facilities and capital equipment to the extent that our collaborators do not reimburse us for them;

obtaining additional licenses and collaborative agreements;

contracts for consulting, maintenance and administrative services; and

contracts for product manufacturing.

We believe that our cash, cash equivalents and short-term investment securities balances as of June 30, 2003 will be sufficient to meet our operating and capital requirements for the next several years. We have based this estimate on assumptions and estimates that may prove to be wrong. As a result, we may need or choose to obtain additional financing during that time. Such financing could come from the proceeds of public or private debt or equity financings or corporate partnerships.

Our indebtedness and debt service obligations may adversely affect our cash flow.

As of June 30, 2003, we had approximately $10.24 million of outstanding debt. During the next four years, we will be required to make principal and interest payments on our outstanding debt totaling approximately $10.6 million. If we are unable to generate sufficient cash to meet these obligations and have to use existing cash or investments, we may have to delay or curtail our research and development programs placing us at a possible competitive disadvantage to less leveraged competitors and competitors that have better access to capital resources.

RISKS RELATED TO INTELLECTUAL PROPERTY

Our patents and other proprietary rights may fail to protect our business.

To be successful and compete, we must obtain and protect patents on our technology and protect our trade secrets. Where appropriate, we seek patent protection for certain aspects of our technology, but patent protection may not be available for some of the compounds and technologies we are developing. The patent position of biotechnology firms is highly uncertain, involves complex legal and factual questions, and has recently been the subject of much litigation. No consistent policy has emerged from the U.S. Patent and Trademark Office or the courts regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology patents. In addition, there is a substantial backlog of biotechnology patent applications at the U.S. Patent and Trademark Office, and the approval or rejection of patent applications may take several years.

We do not know whether our patent applications will result in issued patents. For example, we may not have developed a method for treating a disease before others have developed similar methods. In addition, the receipt of a patent might not provide much practical protection. If we receive a patent with a narrow scope, then it will be easier for competitors to design products that do not infringe on our patent. We cannot be certain that we will receive any additional patents, that the claims of our patents will offer significant protection of our technology, or that our patents will not be challenged, narrowed, invalidated or circumvented.

Competitors may interfere with our patent protection in a variety of ways. Competitors may claim that they invented the claimed invention prior to us. Competitors may also claim that we are infringing on their patents and that therefore we cannot practice our technology as claimed under our patents. Competitors may also contest our patents by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our issued patents are not valid for a number of reasons. If a court agrees, we would lose that patent. As a company, we have no meaningful experience with competitors interfering with our patents or patent applications.

To protect or enforce our patent rights, we may initiate patent litigation against third parties, such as infringement lawsuits or interference proceedings. Such litigation can be expensive, take significant time and divert management s attention from other business concerns, which could increase our research and development expense and delay our product programs. Litigation that we initiate may provoke third parties to assert claims against us.

It is also unclear whether our trade secrets will prove to be adequately protected. To protect our trade secrets, we require our employees, consultants and advisors to execute confidentiality agreements. We cannot guarantee, however, that these agreements will provide us with adequate protection against improper use or disclosure of confidential information. Our employees, consultants or advisors may unintentionally or willfully disclose our information to competitors. In addition, in some situations, these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors had or have previous employment or consulting relationships. Like patent litigation, enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time-consuming, and

the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing than our federal and state courts to protect trade secrets. Furthermore, others may independently develop substantially equivalent knowledge, methods and know-how.

If we must spend significant additional time and money protecting our patents and trade secrets, we will have fewer resources to devote to the development of our technologies, and our business and financial prospects may be harmed.

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

There are many patents in our field of technology and we cannot guarantee that it does not infringe on those patents or that we will not infringe on patents granted in the future. If a patent holder believes our product infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology. Intellectual property litigation is costly and, even if we prevail, the cost of such litigation could adversely affect our business, financial condition and results of operations. In addition, litigation is time-consuming and could divert management attention and resources away from our business. If we do not prevail in litigation, we may have to pay substantial damages for past infringement.

Also, if we lose, the court may prohibit us from selling or licensing the product that infringes the patent unless the patent holder licenses the patent to us. The patent holder is not required to grant us a license. If a license is available, it may not be available on acceptable terms. For example, we might have to pay substantial royalties or grant cross-licenses to its patents. In addition, some licenses may be nonexclusive and, accordingly, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license, we could encounter delays in product development while we attempt to design around other patents or we could even be prohibited from developing, manufacturing or selling products requiring these licenses. If we are unable to cost-effectively redesign our products so they do not infringe a patent, we may be unable to sell some of our products. Any of these occurrences will result in lost revenues and profits for us.

Our collaborators may restrict our use of scientific information.

We may not be able to acquire any exclusive rights to technology or products derived from our collaborations. There is also a risk that disputes may arise as to the rights to technology or products developed in collaboration with other parties.

The success of our strategy depends, in part, on our ability to apply a growing base of knowledge, technology and data across all of our internal projects and our collaborations. Some of this data has been and will continue to be generated from our work with collaborators. Although we believe that certain of this information is not proprietary to our collaborators, our collaborators may disagree and may succeed in preventing us from using some or all of this information and/or technology ourselves or with others. Without the ability to use this information freely, we may be limited in our ability to improve the efficiency of our drug discovery and development process.

RISKS RELATED TO REGULATION

We may not obtain regulatory approval for the sale and manufacture of drug products.

The development and commercialization of drug candidates in the United States, including those drug candidates we develop alone or in collaboration with our partners, such as CO-501, are subject to regulation by U.S. regulatory authorities. Pharmaceutical products require lengthy and costly testing in animals and humans and regulatory approval by the appropriate governmental agencies prior to commercialization. Approval of a drug candidate as safe and effective for use in humans is never certain and these agencies may delay or deny approval of the products for commercialization. Changes in regulatory policy during the period of regulatory review may result in unforeseen delays or denial of approval. Similar delays and denials may be encountered in foreign countries.

As a company, ArQule has never obtained regulatory approval to manufacture and sell a drug. If we and/or our collaborators develop a drug candidate and cannot obtain this approval, we may not realize milestone or royalty payments based on commercialization goals for such drug candidate. Even if regulatory approval is obtained, regulatory authorities may require additional clinical studies after sales of a drug have begun. In addition, the identification of certain side effects after a drug is on the market may result in the subsequent withdrawal of approval, reformulation of the drug, additional pre-clinical and clinical trials, changes in labeling, recalls, warnings to physicians or the public, and negative publicity.

Any of these events could delay or prevent us from generating revenue from the commercialization of any drug candidates it develops or helps to develop.

We have only limited experience in regulatory affairs, and some of our products may be based on new technologies; these factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals. Moreover, certain of the products that are likely to result from our research and development programs may be based on new technologies and new therapeutic approaches that have not been extensively tested in humans. The regulatory requirements governing these types of products may be more rigorous than for conventional products. As a result, we may experience a longer regulatory process in connection with any products that we develop based on these new technologies or new therapeutic approaches.

We have limited capabilities in clinical development of drug candidates.

If ArQule proceeds with preclinical and clinical development of products, ArQule will be dependent on third-party providers of preclinical and clinical development services, including GLP synthesis and testing, or will be required to incur significant costs and devote significant efforts to establish its own development facilities and capabilities. If ArQule is unable to reach agreement with such third-party service providers on acceptable terms, or to establish its own development facilities, ArQule s preclinical and clinical development of products will be delayed and its financial results will be adversely affected.

We must show the safety and efficacy of our product candidates through clinical trials, the results of which are uncertain.

Before obtaining regulatory approvals for the commercial sale of our products, including CO-501, we must demonstrate, through preclinical studies (animal testing) and clinical trials (human testing), that our proposed products are safe and effective for use in each target indication. Further testing of any product candidates will be required, and failure can occur at any stage of testing. Acceptable results from initial preclinical studies and clinical trials of products under development are not necessarily indicative of results that will be obtained from subsequent or more extensive preclinical studies and clinical testing in humans. Clinical trials may not demonstrate sufficient safety and efficacy to obtain the required regulatory approvals or result in marketable products. Our failure to adequately demonstrate the safety and efficacy of a product under development could delay or prevent regulatory approval of the potential product.

Clinical trials for the product candidates we develop may be delayed by many factors, including that potential patients for testing are limited in number. The failure of any clinical trials to meet applicable regulatory standards could cause such trials to be delayed or terminated, which could further delay the commercialization of any of our product candidates. Any such delays will increase our product development costs. If such delays are significant, they could negatively affect our financial results and the commercial prospects for our products.

RISKS RELATING TO PRODUCT MANUFACTURING

Our development, testing and manufacture of potential drug candidates may expose us to potential liability.

We develop, test and manufacture the precursors to drugs generally intended for use in humans. If our drug discovery activities result in the manufacture and sale of drugs, we could be liable if persons are injured or die while using these drugs. We may have to pay substantial damages and/or incur legal costs to defend claims resulting from injury or death, and we may not receive expected royalty or milestone payments if commercialization of a drug is limited or ended as a result of such claims. We have product liability insurance that contains customary exclusions and provides coverage per occurrence at levels, in the aggregate, which we believe are customary and commercially reasonable in our industry. However, our product liability insurance does not cover every type of product liability claim that we may face or loss we may incur and may not adequately compensate us for the entire amount of covered claims or losses or for the harm to our business reputation. Also, we may be unable to maintain our current insurance policies or obtain and maintain necessary additional coverage at acceptable costs or at all.

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

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

Because we have limited manufacturing capabilities, if we decide to manufacture products we will be dependent on third-party manufacturers or will be required to incur significant costs and devote significant efforts to establish our own manufacturing facilities and capabilities.

We have limited experience with the FDA s good manufacturing practices and no commercial scale manufacturing capabilities. In order to continue to develop products and services, apply for regulatory approvals and commercialize products and services, we will need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities.

There are a limited number of manufacturers that operate under the FDA s good manufacturing practices regulations capable of manufacturing our products. As a result, we may experience difficulty finding manufacturers for our products with adequate capacity for future needs. If we are unable to arrange for third-party manufacturing of our products, or to do so on commercially reasonable terms, we may not be able to complete development of our products or market them.

Reliance on a third-party manufacturer entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control and the possibility of termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

We may in the future elect to manufacture certain of our products in our own manufacturing facilities. We need to invest substantial additional funds and need to recruit qualified personnel in order to build or lease and operate any manufacturing facilities.

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, may, 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 CO-501 to corporate collaborators; the ability to predict consistently and successfully absorption, distribution, metabolic, elimination and toxicological (ADMET) properties and 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. 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.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of our common stock by the selling stockholders.

SELLING STOCKHOLDERS

The selling stockholders were the former stockholders of Cyclis Pharmaceuticals, Inc. We issued the shares covered by this prospectus to them in connection with the acquisition of Cyclis. Pursuant to the merger agreements, we agreed to register for resale the shares issued to the selling stockholders.

The following table sets forth the names of the selling stockholders, the number of shares of common stock owned beneficially by each selling stockholder as of September 19, 2003 and the number of shares that may be offered pursuant to this prospectus. In the last three years, none of the selling stockholders has held any position or office with, been employed by, or otherwise had a material relationship with, us or any of our predecessors or affiliates other than as stockholders, except as noted below. The table has been prepared based upon information furnished to us by or on behalf of the selling stockholders.

The selling stockholders may decide to sell all, some, or none of the shares of common stock listed below. We cannot provide you with an estimate of the number of shares of common stock that the selling stockholders will hold in the future.

For purposes of this table, beneficial ownership is determined in accordance with SEC rules, and includes voting power and investment power with respect to shares and shares owned pursuant to options, warrants or other rights exercisable within 60 days of September 19, 2003.

As explained below under Plan of Distribution, we have agreed with the selling stockholders to bear certain expenses (other than broker discounts and commissions, if any) in connection with the registration statement, which includes this prospectus.

In some instances, the shares of common stock offered pursuant to this prospectus may be sold by the pledgees, donees, transferees, assignees or other successors-in-interest that receive their shares from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer after the date of this prospectus, and the term selling stockholders as used herein shall include such pledgees, donees, transferees, assignees or other successors-in-interest.

Selling Stockholder	Number of Shares Beneficially Owned Prior to Offering (1)		Number of Shares Offered (2)	Number of Shares Beneficially Owned After Offering (3)	
	Number	Percent		Number	Percent
Ackerman, Samuel K. (5), (7)	727,773	2.59%	727,773	0	0
Alves, Barbara	11	*	11	0	0
Ampersand 1995 Companion Fund Limited Partnership (8)	12,287	*	12,287	0	0
Ampersand 1995 Limited Partnership (8)	779,545	2.78%	779,545	0	0
Ampersand 1999 Companion Fund Limited Partnership (9)	40,950	*	40,950	0	0
Ampersand 1999 Limited Partnership (9)	2,006,750	7.16%	2,006,750	0	0
Billings, Alisa L. (4)	63,344	*	63,344	0	0
Bochner, Steven, Charles Schwab & Co. custodian	846	*	846	0	0
Brown, Fred	166	*	166	0	0
Budowsky, Edward I.	78,607	*	78,607	0	0
Campbell, Jennifer	69	*	69	0	0
Celebi, John K. (4), (5)	65,791 (13)	*	63,291	2,500	*
Chen, Chang-Rung (4), (5)	494	*	494	0	0
D Andrea, Alan D. (6)	3,955	*	3,955	0	0
Dahlberg, William K. (4), (5)	2,928 (13)	*	2,678	250	*
Davie, Joseph M. (6)	33,761	*	33,761	0	0
Driscoll, Tracy A. (4), (5)	685 (13)	*	560	125	*
Evan, Gerard (6)	988	*	988	0	0
General Electric Capital Corporation (10)	1,830	*	1,830	0	0

Selling Stockholder	Number of Shares Beneficially Owned Prior to Offering (1)		Number of Shares Offered (2)	Number of Shares Beneficially Owned After Offering (3)	
	Number	Percent		Number	Percent
Goldberg, Alfred L. (6)	5,274	*	5,274	0	0
Goldstein, Martin	5,549	*	5,549	0	0
Henkel, Candice F. (4)	14,516	*	14,516	0	0
Jiang, Zhiwei (4), (5)	14,652 (13)	*	12,402	2,250	*
Kaelin, William G., Jr. (6)	3,955	*	3,955	0	0
Lacasse, Christine M.	92	*	92	0	0
Li, Chiang J. (4), (5)	503,832 (13)	1.79%	475,082	28,750	*
Li, Xiaotong (4), (5)	988	*	988	0	0
Li, Youzhi (4), (5)	3,428 (13)	*	2,678	750	*
Mang, William A. (4), (5)	454 (13)	*	329	125	*
Mielnicki, Michael	1,201	*	1,201	0	0
Monath, Andrea M.	11,098	*	11,098	0	0
Monath, Nicolas B.	11,098	*	11,098	0	0
Monath, Thomas P.	15,534	*	15,534	0	0
Mousa, Magdi (4), (5)	2,810 (13)	*	2,060	750	*
Mushi, Neru (4), (5)	2,068 (13)	*	1,318	750	*
Pardee, Arthur B. (6)	9,889	*	9,889	0	0
Reddy, Dasharatha G. (4), (5)	10,864 (13)	*	8,364	2,500	*
Rock, Lisa June	64	*	64	0	0
Ryan, John L. (6)	16,785	*	16,785	0	0
Saks, Samuel R. (6)	16,811	*	16,811	0	0
Salvesen, June R. (4), (5)	118,770	*	118,770	0	0
Tobias, Andrea and Jeffrey	1,775	*	1,775	0	0
Vaze, Moreshwar B. (4), (5)	823	*	823	0	0
Walker, Douglas	2,523	*	2,523	0	0
Wang, Aijin (4), (5)	988	*	988	0	0
Weinberg, Robert A. (6)	988	*	988	0	0
Weller Noko, Ltd. (11)	8,974	*	8,974	0	0
WS Investment Company 94A (12)	761	*	761	0	0
Xiangao, Sun (4), (5)	3,428 (13)	*	2,678	750	*
Zhang, Qingxiu	55	*	55	0	0

* Less than one percent.

(1) Based upon 28,014,163 shares of common stock outstanding on October 6 , 2003.

(2) The amounts in this column represent the maximum amount of shares that each shareholder may offer under this prospectus. Approximately a pro rata portion of the maximum amount of shares that each selling shareholder may offer under this prospectus has been deposited into escrow under the terms of an Indemnity and Escrow Agreement entered into in connection with the closing of the merger of ArQule and Cyclis Pharmaceuticals, Inc. The escrow agreement provides that these shares may be utilized to satisfy certain indemnification rights of ArQule, and its respective Affiliates, successors and assigns, and the respective officers and directors of each of the foregoing that are properly noticed under the terms of the escrow agreement prior to September 8, 2004. On September 8, 2004, all escrowed shares remaining in the escrow fund and not otherwise set aside to satisfy previously noticed but unsettled indemnification claims will be distributed to the selling stockholders on approximately a pro rata basis.

(3) Assumes the sale of all shares offered hereby and no other transactions in the common stock by the selling stockholders.

(4) Former Cyclis Pharmaceuticals, Inc. employee.

(5) Current ArQule, Inc. employee.

16

(6) Former member of Cyclis Pharmaceuticals, Inc. Scientific Advisory Board.

(7) Former President, Chief Executive Officer, and director of Cyclis Pharmaceuticals, Inc.

(8) Richard A. Charpie is the Managing Partner of AMP-95 MCLP LLP, which is the General Partner of AMP-95 Management Company Limited Partnership, which is the General Partner of Ampersand 1995 Limited Partnership and Ampersand 1995 Companion Fund Limited Partnership. Dr. Charpie is a former director of Cyclis Pharmaceuticals, Inc.

(9) Richard A. Charpie is the Principal Managing Member of AMP-99 Management Company Limited Liability Company, which is the General Partner of Ampersand 1999 Limited Partnership and Ampersand 1999 Companion Fund Limited Partnership. Dr. Charpie is a former director of Cyclis Pharmaceuticals, Inc.

(10) Chris Jacobs, Senior Vice President and Chief Financial Officer of General Electric Capital Corporation, has voting and investment power over the ArQule shares owned by General Electric Capital Corporation.

(11) Richard N. Weller, president of Noko, Inc., the general partner of Weller Noko, Ltd., has voting and investment power over the ArQule shares owned by Weller Noko, Ltd.

(12) The general partners of Wilson Sonsini Goodrich & Rosati of Palo Alto, California and James A. Terranova as the manager of WS Investments have voting and investment power over the ArQule shares owned by WS Investment Company 94A.

(13) This number includes options exercisable within 60 days of September 19, 2003. The exact number of options exercisable within 60 days for each selling shareholder is listed in the column entitled Number of Shares Beneficially Owned After Offering .

PLAN OF DISTRIBUTION

The selling stockholders, including their pledgees, transferees, assignees, donees or other successors-in-interest, may, from time to time, sell any or all of their shares of common stock on the Nasdaq National Market, or on any other stock exchange, market or trading facility on which the stock may from time to time be trading or in privately negotiated transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

by pledge to secure debts and other obligations;

through the writing of options on the shares;

short sales;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act of 1933, as amended, if available, rather than under this prospectus.

The selling stockholders may also engage in short sales against the box, puts and calls and other transactions in our securities or derivatives of ArQule securities and may sell or deliver shares in connection with these trades. The selling stockholders may pledge their shares to their brokers under the margin provisions of customer agreements. If a selling stockholder defaults on a margin loan, the broker may, from time to time, offer and sell the pledged shares.

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

ArQule is bearing its own fees and expenses incident to the registration of the shares. To the extent required, we will amend or supplement this prospectus to disclose material

arrangements regarding the plan of distribution. In addition, upon our being notified by a selling stockholder that a donee, pledgee, assignee, transferee or other successor-in-interest intends to sell more than 500 shares, we will file a supplement to this prospectus pursuant to such proposed sale.

To comply with the securities laws of certain jurisdictions, registered or licensed brokers or dealers may need to offer or sell the shares offered by this prospectus. The applicable rules and regulations under the Exchange Act may limit any person engaged in a distribution of the shares of common stock covered by this prospectus in its ability to engage in market activities with respect to such shares. A selling stockholder, for example, will be subject to applicable provisions of the Exchange Act and the rules and regulations under it, which provisions may limit the timing of purchases and sales of any shares of common stock by that selling stockholder.

LEGAL MATTERS

The validity of the shares of common stock offered hereby has been passed upon for us by Arnold & Porter, Washington, D.C.

EXPERTS

PricewaterhouseCoopers LLP, independent auditors, have audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2002, as set forth in their report, which is incorporated by reference in this prospectus. Our financial statements are incorporated by reference in reliance on PricewaterhouseCoopers LLP s report, given on their authority as experts in accounting and auditing.

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 from a periodic report filed after the date of 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;

2. Our Quarterly Reports on Form 10-Q for the periods ended March 31, 2003, June 30, 2003 and September 30, 2003;

3. Our Current Reports on Form 8-K filed with the SEC 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.

You can obtain a copy of any or all of the documents incorporated by reference in this prospectus (other than an exhibit to a documents unless that exhibit is specifically incorporated by reference into that document) from the SEC on its web site at http://www.sec.gov. You also can obtain these documents from us without charge by visiting our Internet web site at http://www.arqule.com or 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
jdevine@arqule.com

WHERE YOU CAN FIND MORE INFORMATION

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

In addition, we file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy this information and the registration statement at the SEC public reference room located at 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, the SEC maintains a web site that contains reports, proxy statements and other information about issuers of securities, like us, who file such material electronically with the SEC. The address of that web site is http://www.sec.gov. We also maintain a web site at http://www.arqule.com, which provides additional information about our company. The information set forth on our web site is not part of this prospectus.

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 Fee	$ 1,722
Accounting fees and expenses	5,000
Printing fees and expenses	5,000
Legal fees and expenses	30,000
Nasdaq Additional Listing Fee	22,500
Total	$ 64,222

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
4.1	Specimen Common Stock Certificate (filed as Exhibit 4.1 to our Registration Statement on Form S-1 (File No. 333-11105) and incorporated herein by reference)
5.1	Opinion of Arnold & Porter*
23.1	Consent of Arnold & Porter (contained in opinion of Arnold & Porter filed as Exhibit 5.1)
23.2	Consent of PricewaterhouseCoopers LLP*
24.1	Power of Attorney*

* Previously filed on October 8, 2003.

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;

(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 Securities and Exchange 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 the Registration Statement.

(2) That, for the purpose of determining any liability under the Securities Act, 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, 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 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.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Company 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 November 21, 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, as amended, 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 Stephen A. Hill	President, Chief Executive Officer and Director (Principal Executive Officer)	November 21, 2003
/s/ Thomas J. Phair, Jr. Thomas J. Phair, Jr.	Controller (Acting Principal Accounting and Financial Officer)	November 24, 2003
* Ariel Elia	Chairman of the Board	November 21, 2003
* Laura Avakian	Director	November 21, 2003
* Timothy C. Barabe	Director	November 21, 2003
* Werner Cautreels	Director	November 21, 2003
* Tuan Ha-Ngoc	Director	November 21, 2003
* Michael Rosenblatt	Director	November 21, 2003
* Patrick J. Zenner	Director	November 21, 2003

By: /s/ Stephen A. Hill — Director

Stephen A. Hill, attorney-in-fact
pursuant to power of attorney

INDEX TO EXHIBITS

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

Exhibit No.	Description
4.1	Specimen Common Stock Certificate (filed as Exhibit 4.1 to our Registration Statement on Form S-1 (File No. 333-11105) and incorporated herein by reference)
5.1	Opinion of Arnold & Porter*
23.1	Consent of Arnold & Porter (contained in opinion of Arnold & Porter filed as Exhibit 5.1)
23.2	Consent of PricewaterhouseCoopers LLP*
24.1	Power of Attorney*

* Previously filed.