FORM S-1

General form of registration statement for all companies including face-amount certificate companies

Filing Date: **1999-03-26**
SEC Accession No. 0000927356-99-000448

FILER

RIBOZYME PHARMACEUTICALS INC

CIK:**892112**| IRS No.: **341697351** | State of Incorp.:**DE** | Fiscal Year End: **1231**
Type: **S-1** | Act: **33** | File No.: **333-75079** | Film No.: **99573664**
SIC: **2834** Pharmaceutical preparations

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BOULDER CO 80301

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BOULDER CO 80301
3034496500

As filed with the Securities and Exchange Commission on March 26, 1999.
Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Ribozyme Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	2834	34-1697351
(State or other jurisdiction of incorporation or organization)	(Primary Standard IndustrialClassification Code Number)	(I.R.S. Employer Identification Number)

2950 Wilderness Place
Boulder, Colorado 80301
(303) 449-6500
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

RALPH E. CHRISTOFFERSEN
Ribozyme Pharmaceuticals, Inc.
Chief Executive Officer and President
2950 Wilderness Place
Boulder, Colorado 80301
(303) 449-6500
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies:

HERBERT H. DAVIS III	JAMES R. TANENBAUM
ROTHGERBER JOHNSON & LYONS LLP	STROOCK & STROOCK & LAVAN LLP
1200 17th Street, Suite 3000	180 Maiden Lane
Denver, Colorado 80202	New York, New York 10038
(303) 623-9000	(212) 806-6048

Approximate date of commencement of proposed sale to the public: As soon as practicable after the Registration Statement becomes effective.

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, check the following box: [_]

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: [_]

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: [_]

If this Form is a post-effective amendment filed pursuant to Rule 462(d) 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: [_]

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

CALCULATION OF REGISTRATION FEE

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Title of Shares to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share(1)	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee

Common Stock, $0.01 par value per share..	1,800,000 Shares	$5.00	$9,000,000	$2,655.00

(1) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(c) under the Securities Act of 1933.

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 of 1933 or until the Registration Statement shall become effective on such date as the SEC, acting pursuant to said Section 8(a), may determine.

+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 Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.+

SUBJECT TO COMPLETION, DATED MARCH 26, 1999

PROSPECTUS

1,800,000 Shares

Ribozyme Pharmaceuticals, Inc.

Common Stock

Ribozyme Pharmaceuticals, Inc. is offering and selling 1,800,000 shares of common stock with this prospectus. Ribozyme Pharmaceuticals' common stock is quoted on the Nasdaq National Market under the symbol "RZYM." On March 24, 1999, the last reported sale price of the common stock on the Nasdaq National Market was $5.00 per share. See "Price Range of Common Stock."

	Per Share	Total
Public Offering Price	$	
Placement Agency Fees	$	
Proceeds to Ribozyme Pharmaceuticals	$	

Hambrecht & Quist LLC will act as the placement agent in connection with the offering and will use its best efforts to introduce Ribozyme Pharmaceuticals to investors. Ribozyme Pharmaceuticals is offering the shares on an all or none basis only to selected institutional and accredited investors. Hambrecht & Quist LLC has no commitment to buy any of the shares offered. All investor funds received prior to the closing of the offering will be deposited into escrow with an escrow agent until closing. If Ribozyme Pharmaceuticals does not receive investor funds for the full amount of the offering, the offering will be terminated and any funds received will be returned promptly.

Investing in the common stock involves a high degree of risk.
See "Risk Factors" beginning on page 5.

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

Prospectus dated March 26, 1999

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, including "Risk Factors" and the financial statements, before making an investment decision.

Ribozyme Pharmaceuticals, Inc.

Business

Ribozyme Pharmaceuticals is developing a new class of drugs based on Professor Thomas R. Cech's discovery of "ribozymes," for which he shared a Nobel Prize. Ribozymes, a form of ribonucleic acid ("RNA"), have the ability to selectively inhibit protein production. Because many human disease states result from abnormal protein production, we believe that ribozymes apply to a wide range of human diseases. We are currently conducting preclinical development and clinical trials for our two lead product candidates, ANGIOZYME and HEPTAZYME. We are collaborating with Chiron Corporation ("Chiron") in the development and commercialization of ANGIOZYME, a drug for the treatment of solid tumor cancers. We have completed Phase Ia clinical trials in healthy volunteers, will commence Phase Ib trials in cancer patients in the first quarter of 1999 and expect to begin Phase II trials by the end of the year. We are collaborating with Eli Lilly and Company ("Lilly") for the development and commercialization of HEPTAZYME, a drug for the treatment of Hepatitis C, a viral liver disease. HEPTAZYME is in preclinical testing, and we expect to file an investigational new drug application before the end of the year. We are also researching several other product candidates and expect to begin preclinical testing on one of these product candidates by the end of 1999.

Ribozymes also may be used for gene function identification and target validation, the process by which genes that cause or contribute to human disease are identified. We have target validation and discovery partnerships with Schering AG, Roche Biosciences, GlaxoWellcome, Chiron and Parke-Davis. In 1998, we transferred our gene function identification and target validation technology to a newly formed German company, Atugen Biotechnology GmbH ("Atugen"). Upon its formation, Atugen received over $20 million in multi-year funding from a combination of venture capital, an investment by us and German government grants and loans. Pursuant to this technology transfer, we acquired a substantial equity interest in Atugen while retaining our rights to develop ribozymes as therapeutics. As a result of this technology transfer, we will focus exclusively on the development of ribozymes as human therapeutics and will subcontract target validation and discovery services to Atugen.

The Market Opportunity

Our two lead product candidates, ANGIOZYME and HEPTAZYME, are therapeutics for large markets. ANGIOZYME is a drug which targets solid tumor cancers, such

as cancers of the lung, breast, prostate, colon and rectum. These cancers account for over 750,000 new cancer cases and 200,000 deaths per year in the United States alone. HEPTAZYME targets the Hepatitis C virus ("HCV"), the most common blood-borne infection in the United States. Each year in the United States, HCV infects approximately 50,000 people and causes 10,000 deaths. Existing therapies are ineffective in over 50% of Hepatitis C patients and have serious side effects.

The Ribozyme Advantage

We believe ribozymes offer significant advantages over other approaches to treating human disease. Ribozymes can selectively inhibit protein production by binding to and cutting apart its associated messenger RNA ("mRNA") sequence. Many common human diseases involve either abnormal protein production or RNA viruses. Ribozymes can be used to treat human disease in two ways. First, ribozymes can be designed

to inhibit abnormal protein production associated with a disease. Second, ribozymes can be designed to target RNA viruses or protein production in other infectious agents that cause disease. Ribozymes also are useful in identifying the function of specific genes (validating targets) and in diagnosing disease.

Strategy

Our primary business objective is to use our technology to identify and develop drugs containing ribozymes to treat or prevent human disease. Our strategy to achieve this objective includes the following:

- develop identified product candidates,
- identify new product candidates,
- partner with others to develop products,
- focus on human therapeutics and license other applications of our technology, and
- maintain and expand our patent portfolio and proprietary technology.

Patents

Our patents and proprietary technology provide a significant competitive advantage in the use of ribozymes in drug development. Our licenses to patents of Dr. Cech and others, together with patents issued to and filed by us, give us the exclusive rights to control the manufacture, use and sale of ribozymes. Our current patent portfolio includes 84 issued or allowed patents and over 100 applications.

Our corporate headquarters are located at 2950 Wilderness Place, Boulder, Colorado 80301, and our telephone number is (303) 449-6500. Our web site address is www.rpi.com. Information contained on our website does not constitute part of this prospectus.

The Offering

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Common stock offered.....	1,800,000 shares
Common stock to be outstanding after the offering..	10,982,135 shares
Use of proceeds.....	To fund preclinical and clinical trials of our products, continued research and development, and for general corporate purposes
Nasdaq National Market symbol.....	RZYM
</TABLE>

This information is based on the number of shares outstanding at March 15, 1999. It excludes:

- 1,478,493 shares reserved for issuance under our stock option plan, of

which 1,386,487 shares were outstanding at a weighted average exercise price of $4.18 per share.

. 487,458 shares issuable upon the exercise of outstanding warrants at a weighted average exercise price of $22.76 per share.

. 1,100,844 shares issuable to one of our collaborators upon conversion of outstanding debt, assuming a conversion price of $4.88 per share, which was the closing price of our common stock on March 15, 1999.

. 200,168 shares available for issuance under our Employee Stock Purchase Plan.

Summary Financial Data

The selected historical financial data presented below is derived from the financial statements of Ribozyme Pharmaceuticals. The financial statements for each of the five years ended December 31, 1994, 1995, 1996, 1997 and 1998 have been audited by Ernst & Young LLP, independent auditors. The as adjusted balance sheet data summarized below reflects the application of the net proceeds from the sale of the 1,800,000 shares of common stock offered by Ribozyme Pharmaceuticals at the assumed offering price of $5.00 after deducting estimated placement agency fees and offering expenses. You should read this information together with the more detailed information presented in "Selected Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our audited financial statements and related notes.

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	Year Ended December 31,				
	1994	1995	1996	1997	1998
	(in thousands except per share amounts)				
<S>	<C>	<C>	<C>	<C>	<C>
Statement of Operations Data:					
Total revenues	$ 1,587	$ 1,675	$ 1,709	$ 2,778	$ 9,622
Expenses:					
Research and development	9,212	12,204	14,189	15,170	16,941
General and administrative	1,291	1,397	1,943	1,886	1,813
Interest expense	334	554	845	844	704
Total expenses	10,837	14,155	16,977	17,900	19,458
Equity in loss of unconsolidated affiliate	--	--	--	--	1,082
Net loss	$ (9,250)	$ (12,480)	$ (15,268)	$ (15,122)	$ (10,918)
Net loss per share (basic and diluted)	(3.52)	(3.86)	(2.61)	(2.04)	(1.22)
Shares used in computing net loss per share (basic and diluted)	2,627	3,230	5,845	7,420	8,978

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	December 31, 1998	
	Actual	As Adjusted
<S>	<C>	<C>
Balance Sheet Data:		
Cash, cash equivalents and securities available-for-sale	$ 6,512	14,612
Working capital	4,467	12,567
Total assets	19,224	27,324
Capital lease obligations and long-term debt, net of current portion	4,545	4,545
Accumulated deficit	(73,422)	(73,422)
Total stockholders' equity	11,034	19,134

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RISK FACTORS

You should carefully consider the following risk factors and all other information contained in this prospectus before purchasing our common stock. Investing in our common stock involves a high degree of risk. Any of the following risks could materially adversely affect our business, operating results and financial condition and could result in a complete loss of your investment.

We are in an early stage of development and have a limited operating history

We are a development stage biotechnology company. We have focused our research and development efforts on potential products and services based on ribozyme technology. We formed our company in 1992 and have only a limited operating history for you to review in evaluating our business. All of our products are in early stages of development, have never generated any sales and require extensive testing before commercialization. An investor in our common stock must consider the risks frequently encountered by early stage companies in the biotechnology industry. These risks include our ability to:

- obtain the financial resources necessary to develop, test, manufacture and market products,
- engage corporate partners to assist in developing, testing, manufacturing and marketing our products,
- satisfy the requirements of clinical trial protocols, including patient enrollment,
- establish and demonstrate the clinical efficacy of our products,
- obtain necessary regulatory approvals, and
- market our products to achieve acceptance and use by the medical community in general.

We have a history of losses and expect future losses

We have not yet generated any revenues from the commercial sale of our products and cannot assure you that we will ever generate revenues from product sales. To date, we have dedicated most of our financial resources to research and development and general and administrative expenses.

We have incurred significant losses and have had negative cash flows from operations since inception. We have funded our activities primarily from sales of stock, revenues under research and development agreements and lines of credit. As of December 31, 1998, our accumulated deficit was $73.4 million.

We expect to incur operating losses for at least the next several years because we plan to spend substantial amounts on research and development of products, including preclinical studies and clinical trials, and, if we obtain necessary regulatory approvals, on sales and marketing efforts. We cannot assure you that we will ever become profitable or that we will remain profitable, if and when we become profitable.

We depend upon our collaborative relationships and these third parties may not continue to work with us

Engaging corporate partners and other third parties to help us develop, test and manufacture our products is a key element of our strategy. As a result, many important aspects of our business depend upon the activities of these partners, including Chiron, Lilly and Schering AG, which may be outside of our control. These factors include:

- extension, renewal or termination of collaborative relationships by partners,
- payments based upon our company meeting performance milestones,
- development by partners of technologies that compete with those being developed with us, which would result in a potential loss of revenue for us,
- decision to develop or market any products with us,
- withdrawal of resources for our products,

- termination at will under existing agreements,
- loss of royalty payments and licensing rights to jointly developed products if we are unwilling or unable to fund our share of development costs.
- relinquish some or all of our rights to our products, and
- negotiation of additional collaborative agreements with partners.

Should our corporate partners, Chiron or Lilly, elect not to proceed with development of our two leading products, it may have a significant adverse affect on our operating results and the price of our common stock. Both Chiron and Lilly may unilaterally terminate their agreements with us. If other corporate partners with whom we have entered into collaborative agreements elect not to continue with our collaborations, it may have a significant adverse affect on our operating results and the price of our common stock.

We may not be successful in developing our products

All of our products are in an early stage of development and will require expensive and lengthy testing and regulatory clearances. None of our products has received necessary regulatory approvals. None of our products has entered clinical trials for efficacy and our most advanced product candidate, ANGIOZYME, has just completed Phase Ia trials. We may experience delays in clinical development if we cannot enroll a sufficient number of patients for our clinical trials. We do not expect any of our products to be commercially available for at least five years. The success of our business depends upon our ability to develop and market successfully our products, if and when they become commercially available. There are many reasons that we may fail in our efforts to develop our products, including the possibility that:

- our products will not be safe and/or effective, and therefore will not receive regulatory approval,
- our products will be too expensive to manufacture or market,
- our products will not receive broad market acceptance,
- other parties will hold proprietary rights that prevent us from marketing our products, and
- other parties will market similar or superior products with greater market acceptance.

The grant by us to our collaborators of exclusive rights to products against specified gene sequences could delay development of those products

We have granted exclusive rights to our collaborators to products targeting specific gene sequences. Many of these rights will revert to us if the product is not being actively developed by our collaborator, which could have the effect of slowing development of the product. However, some of our collaborators have the right to reserve exclusive rights to specified products for a period of time, even if they are not developing a product. Also, many of our collaboration agreements require us to offer our collaborators a right of first offer as to certain targets and products. Such requirements may slow our development process and may prevent us from entering into other collaborative agreements.

Under our product development collaboration with Chiron, Chiron has the exclusive right to develop products against up to five targets designated by it for the term of Chiron's collaboration with us, which could exceed 30 years. In addition, Chiron may at any time reserve for 18 months the exclusive rights to additional targets, not to exceed four. Under our gene function and target validation agreement, Chiron may reserve the exclusive right to products against additional targets for up to two and a half years.

Under our collaboration with Schering AG, Schering AG may reserve indefinitely the exclusive right to products against targets designated by it. Under our collaboration with Roche, Roche can reserve products against a specified number of diseases for up to three years. Under our collaborations, up to approximately 50 targets may be reserved at any time. Development of the products subject to these exclusivity provisions

is out of our control. Development may be delayed, and these products will not be available to us during the exclusivity term either to develop internally or in collaboration with third parties.

THERE IS UNCERTAINTY AS TO THE AVAILABILITY OF ADDITIONAL FINANCING

We anticipate that the net proceeds of this offering, together with our existing financial resources and expected revenues from our collaborations, should be sufficient to meet our capital and operating requirements into mid-2001. We will need to raise substantial additional capital to fund our operations. However, changes in research and development plans or changes in our collaborative relationships may require us to make additional, unexpected large future expenditures and may significantly reduce our expected revenues from our collaborations. Additional funding may be available in the public or private capital markets and through collaboration agreements with partners upon achievement of performance milestones. If we raise funds by selling more stock, your ownership share in us will be diluted. In addition, we may grant future investors rights superior to those of the common stock that you are purchasing. We do not know if additional funding will be available at all or on acceptable terms when needed. If the results of our clinical trials are not favorable, it will be much more difficult for us to raise additional funds. If we are unable to obtain funding, we may need to curtail some or all research and development programs, to obtain funds through arrangements that require us to relinquish rights to some or all of our products or to declare bankruptcy.

ATUGEN IS A NEWLY FORMED COMPANY AND WILL REQUIRE CONSIDERABLE TIME AND ATTENTION FROM OUR MANAGEMENT TEAM; WE MAY NOT EXERCISE CONTROL OVER ATUGEN'S MANAGEMENT

Atugen is a new company without a permanent CEO, a permanent CFO, or its own business development team. Pursuant to the terms of a service agreement between Atugen and us, Atugen has access to our management, including our business development team, for a limited time. There is no assurance that Atugen will be able to hire the management and business development professionals needed for its success. Therefore, our management may need to continue to dedicate time and resources to both the management and business development of Atugen which may detract from management's attention to our business. In addition, while we have the right to appoint two designees to Atugen's Board of Directors, we do not exercise control over Atugen's business and operations.

CLINICAL TRIAL RESULTS MAY RESULT IN DELAYS OR FAILURE TO OBTAIN FDA APPROVAL AND INABILITY TO SELL OUR PRODUCTS

Before approving a drug for commercial sale as a treatment for a disease, the FDA and other regulatory authorities require that the safety and effectiveness of the drug be demonstrated in humans. This is demonstrated by showing results from adequate and well-controlled clinical trials in which the drug is used to treat patients suffering from the disease. The clinical trial process is complex and uncertain. Positive results from preclinical testing and early clinical trials do not ensure positive results in later clinical trials. Our products may produce undesirable side effects in humans which could cause us, our collaborative partners or the FDA to delay or halt clinical trials of that product. We cannot predict when or whether our clinical trials will adequately demonstrate a product's safety and effectiveness or whether the FDA or other regulatory authority will agree with the sufficiency of the trial results. If our clinical trials do not demonstrate the safety or effectiveness of our products, or if we otherwise fail to obtain regulatory approval for our products, we will not be able to generate revenues from the commercial sale of our products.

THE FDA CAN IMPOSE OTHER RESTRICTIONS ON OUR OPERATIONS THAT INCREASE COSTS OR DELAY OR PROHIBIT SALES

The FDA and other regulatory authorities will continue to review our products and periodically inspect the facilities used to manufacture those products both before and after granting regulatory approvals. If the

FDA or other regulatory authorities identify problems with a product, the manufacturer or its facility, they may impose restrictions that may include:

- warning letters,
- operating restrictions,
- suspensions of regulatory approvals,
- delays in obtaining new product approvals,

. withdrawal of the product from the market,

. product recalls,

. seizure of products,

. fines,

. injunctions, and

. criminal prosecution.

These actions could significantly delay or prevent the marketing of our products.

Our products must obtain regulatory approval in other countries which could delay or prohibit sales in those countries

The Company and licensees of our products must obtain regulatory approvals in countries other than the United States before marketing products in those countries. The requirements governing the conduct of clinical trials, product licensing and pricing of drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after product licensing approval is granted. As a result, we or our licensees may obtain regulatory approval for a product in a particular country, but be subject to price regulation which may prevent the sale of the product at satisfactory prices.

Our products require materials that may not be readily available or cost effective, which may adversely affect our competitive position or profitability

All of the products we are developing are new chemical entities and are not yet available in commercial quantities. Raw materials necessary for the manufacture of our products may not be available in sufficient quantities or at a reasonable cost in the future. Therefore, our products may not be available at a reasonable cost in the future. Delays in obtaining raw materials or in product manufacturing could delay our submission of products for regulatory approval and our initiation of new development programs, which could, in turn, materially impair our competitive position and potential profitability.

We experience a substantial degree of uncertainty relating to patents that could result in the loss of patent protection or in claims against us

Our success will depend to a large extent on our ability and our licensors' abilities to:

. obtain and maintain United States and foreign patent protection for products and processes,

. preserve trade secrets, and

. operate without infringing the proprietary rights of third parties.

Legal standards relating to the validity of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these patents are still developing. As a result, our ability to obtain and enforce patents that protect our products is uncertain and involves complex legal and factual questions. Our basic patents expire in 2008 in the United States and in 2007 in Europe and Japan; however, although our license to these patents extends through 2007 or 2008, our licensor preserves the right to

terminate our license before such time under certain circumstances. We have received approval of some patent applications for improvements and modifications to these patents and we have filed patent applications for other improvements and modifications which have not yet been approved.

We cannot be certain that the inventors of subject matter covered by our patents and patent applications were the first to invent or the first to file patent applications for these inventions. Furthermore, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Existing or future patents may be successfully challenged, invalidated, found to be unenforceable, infringed upon, or circumvented by others so that our patent rights would not create an effective competitive barrier. We also cannot assure you that the scope of our issued patents will be sufficiently broad to offer meaningful protection against competitive products. We have filed documents in opposition of two patents granted to a competitor in

Europe. Competitors have filed documents in opposition of our patents in Europe and Japan. The patent opposition in Japan has been resolved in our favor. We may not have identified all United States and foreign patents that pose a risk of infringement.

We may incur substantial costs and delays as a result of proceedings and litigation regarding patents and other proprietary rights

Litigation regarding patents and other intellectual property rights is extensive in the biotechnology industry. Patents have been applied for and, in some cases, issued to others claiming technologies closely related to ours. As a result, and in part due to the ambiguities and evolving nature of intellectual property law, we periodically receive notices of potential infringement of patents held by others. Although we have successfully resolved these types of claims to date, we may not be able to do so in the future.

We may be forced to litigate if an intellectual property dispute arises. Such litigation could involve proceedings declared by the United States Patent and Trademark Office or the International Trade Commission, as well as affected third parties. Intellectual property litigation can be extremely expensive, and such expense, as well as the consequences should we not prevail, could seriously harm our business.

Proceedings and litigation involving our patents or patent applications could result in adverse findings about:

. the patentability of our inventions and products, and/or

. the enforceability, validity or scope of protection offered by our patents.

The manufacture, use or sale of our products may infringe on the patent rights of others. If we are unable to avoid infringing another party's patent rights, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, do not successfully defend an infringement action or are unable to have infringing patents declared invalid, we may:

. incur substantial monetary damages,

. encounter significant delays in marketing our products, and

. be unable to participate in the manufacture, use or sale of products or methods of treatment requiring licenses.

In addition, we regularly enter into agreements to in-license technologies and patent rights. Should we fail to comply with the terms of those agreements, including payment of any required maintenance fees or royalties, we would lose the rights to those technologies and patents.

Disclosure of our trade secrets could aid competitors

Because trade secrets and other unpatented proprietary information are critical to our business, we attempt to protect our trade secrets by entering into confidentiality agreements with third parties, employees

and consultants. However, these agreements can be breached and, if they are, there may not be an adequate remedy available to us. In addition, third parties may independently discover trade secrets and proprietary information. If our trade secrets become known, our competitive position may suffer. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights.

Our executive officers, key personnel and advisors are critical to our business and they may not remain with us in the future

Our future success depends to a significant extent on the skills, experience and efforts of our management and scientific team. In addition, we rely on consultants and advisors, including the members of our scientific advisory board, to formulate research and development strategy. The loss of any or all of these individuals could damage our business.

We may not be able to recruit and retain the personnel that we need to succeed

Our products and services are highly technical in nature. In general, only highly qualified and trained scientists have the necessary skills to develop

and market our products and provide our services. We face intense competition in recruiting these professionals from pharmaceutical and biotechnology companies, universities and other research institutions. Any failure on our part to hire, train and retain a sufficient number of qualified professionals would seriously damage our business. We do not generally enter into employment agreements requiring scientific employees to continue in our employment for any period of time.

We may not be able to keep up with the rapid technological change in the biotechnology and pharmaceutical industries, which could obsolete our products

Biotechnology and related pharmaceutical technologies have undergone and continue to undergo rapid and significant change. We expect that the technologies associated with biotechnology research and development will continue to develop rapidly. Our future will depend in large part on our ability to maintain a competitive position with respect to these technologies. Any compounds, products or processes that we develop may become obsolete before we recover expenses incurred in developing those products.

Competition in the biotechnology and pharmaceutical markets may result in competing products and reduce our revenues

The markets for our products will be very competitive. Our competitors include multinational pharmaceutical and chemical companies, specialized biotechnology firms, and universities and other research institutions. Our competitors may be more successful because of:

. greater financial resources,

. greater experience in research and development,

. greater success in obtaining regulatory approval,

. stronger sales and marketing efforts, and

. earlier receipt of approval for competing products.

Competitors may have developed or could develop new technologies that compete with our products or even render our products obsolete.

We believe that customers in our markets display a significant amount of loyalty to their initial supplier of a particular product. Therefore, it may be difficult to generate sales to customers who have purchased products from competitors. To the extent we are unable to be the first to develop and supply new products, our competitive position will suffer.

We lack sales and marketing experience and will rely upon third parties to market our products

We will have to develop a sales force or rely on arrangements with third parties to market, distribute and sell any products we develop. We intend to rely on third parties with established direct sales forces to market the products we develop. These third parties may have significant control over important aspects of the commercialization of our products, including market identification, marketing methods, pricing, sales force recruitment and management and promotional activities. We may be unable to control the actions of these third parties. We may be unable to make arrangements with third parties to perform these activities on favorable terms. Further, any internal capabilities or third-party arrangements may not be successful.

Our success may depend on third-party reimbursement of patients' costs for our products

Our ability to market products successfully will depend in part on the extent to which various third parties are willing to reimburse patients for the costs of our products and related treatments. These third parties include government authorities, private health insurers and other organizations, such as health maintenance organizations. Third-party payors are increasingly challenging the prices charged for medical products and services. Accordingly, if less costly drugs are available, third-party payors may not authorize or may limit reimbursement for our products, even if our products are safer or more effective than the alternatives. In addition, the trend toward managed healthcare and government insurance programs could result in lower prices and reduced demand for our products. Cost containment measures instituted by healthcare providers and any general healthcare reform could affect our ability to sell products and may have a material adverse effect on us. We cannot predict the effect of future legislation or regulation concerning the

healthcare industry and third-party coverage and reimbursement on our business.

Accidents related to hazardous materials could adversely affect our business

Our operations require the controlled use of hazardous and radioactive materials. Although we believe our safety procedures comply with the standards prescribed by federal, state and local regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be liable for any damages that result, which could seriously damage our business. Additionally, an accident could damage our research and manufacturing facilities and operations.

Potential product liability claims could affect our earnings and financial condition

We face a potential risk of product liability claims based on the testing, manufacturing and marketing of our products. We carry product liability insurance relating to potential claims arising from our clinical trials which is limited in scope and amount but which we believe to be adequate. However, we may be unable to maintain this insurance at a reasonable cost or in sufficient amounts to protect us against potential losses. A successful product liability claim or series of claims brought against us could have an adverse effect on our business.

You will experience immediate and substantial dilution

Purchasers in this offering will pay more for their shares than existing stockholders or individuals who acquire shares by exercising options granted before this offering. At an assumed public offering price of $5.00 per share, you will experience immediate dilution of $3.52 per share in pro forma net tangible book value. You will also experience additional dilution upon (1) the exercise by holders of outstanding options and warrants, (2) the conversion by Schering AG of outstanding debt into shares of our common stock or (3) upon Lilly's equity investment.

Absence of dividends could reduce our attractiveness to investors

Some investors favor companies that pay dividends. We have never declared or paid any cash dividends on our common stock. We intend to retain any future earnings for funding growth and, therefore, we do not

anticipate paying cash dividends on our common stock in the foreseeable future. Because we may not pay dividends, your return on this investment likely depends on your ability to sell our stock at a profit.

We have never declared or paid cash dividends on our common stock. We currently intend to retain future earnings, if any, to support the development of our business and for general corporate purposes, and do not anticipate paying any cash dividends in the foreseeable future. We are also party to agreements restricting our payment of dividends.

Our common stock has limited trading volume and a history of volatility which could impair your investment

The historical trading volume of our common stock has been limited. An active public market for the common stock may not develop or be sustained. As a result, you may be unable to sell shares purchased in this offering at the time or price desired. The trading price of our common stock may fluctuate substantially due to:

- quarterly variations in our operating results,
- our ability to raise additional funds,
- changes in the status of our corporate collaborative agreements,
- changes in earnings estimates by market research analysts,
- clinical trials of products,
- research activities, technological innovations or new products by us or our competitors,
- developments or disputes concerning patents or proprietary rights,
- sales of our stock by existing holders,
- timing or denial by the FDA of clinical trial protocols or marketing

applications,

- securities class actions or other litigation,

- changes in government regulations, and

- general economic conditions.

The market price of the common stock, and the market prices for securities of biotechnology companies generally, have fluctuated dramatically in recent years. These fluctuations have sometimes been unrelated to the operating performance of the affected companies. As a result, the value of your shares could vary significantly from time to time.

Both our corporate documents and Delaware law have anti-takeover provisions that may discourage transactions for control at premium prices

Our corporate documents:

- require procedures to be followed and time periods to be met for any stockholder to propose matters to be considered at annual meetings of stockholders, including nominating directors for election at those meetings, and

- authorize our Board of Directors to issue up to 5,000,000 shares of preferred stock without stockholder approval and to set the rights, preferences and other designations, including voting rights, of those shares as the Board of Directors may determine.

These provisions, alone or in combination with each other, may discourage transactions involving actual or potential changes of control, including transactions that otherwise could involve payment of a premium over prevailing market prices to holders of common stock.

In addition, we are subject to provisions of the Delaware General Corporation Law that may make some business combinations more difficult. Accordingly, transactions that otherwise could involve payment of a premium over prevailing market prices to holders of common stock may be discouraged or more difficult for our company than for other companies organized in other jurisdictions.

Year 2000 issues may result in unanticipated costs or adverse effects on operations

Many currently installed systems and software products are coded to accept only two digit entries in the date code field. Beginning in the year 2000, these date code fields will need to accept four digit entries to distinguish 21st century dates from 20th century dates. As a result, in less than one year, computer systems and/or software used by many companies may need to be upgraded to comply with these "Year 2000" requirements. We are in the process of working with our software vendors to ensure that the software that we have licensed from third parties will operate properly in the year 2000 and beyond. In addition, we are working with our external suppliers, service providers and corporate partners to ensure that they and their systems will be able to support our needs and, where necessary, interoperate with our server and networking hardware and software infrastructure in preparation for the year 2000.

We anticipate that we will incur less than $60,000 to complete our review and remediation efforts. However, significant uncertainty exists concerning the potential costs and effects associated with any year 2000 compliance. Any year 2000 compliance problems of ours, our customers or vendors could have a material adverse effect on our business, results of operations and financial condition.

FORWARD-LOOKING STATEMENTS

Certain statements under the captions "Prospectus Summary," "Risk Factors," "Use of Proceeds," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Business," and elsewhere in this prospectus are "forward-looking statements." These forward-looking statements include, but are not limited to, statements about our plans, objectives, expectations and intentions and other statements contained in this prospectus that are not historical facts. When used in this prospectus, the words "expect," "anticipate," "intend," "plan," "believe," "seek," "estimate" and similar expressions are generally intended to identify forward-looking statements. Because these forward-looking statements involve risks and uncertainties, there are important factors that could cause actual results to differ materially from

those expressed or implied by these forward-looking statements, including our plans, objectives, expectations and intentions and other factors discussed under "Risk Factors."

USE OF PROCEEDS

Ribozyme Pharmaceuticals will receive an estimated $7,300,000 in net proceeds from the sale of the 1,800,000 shares of common stock offered by us, assuming a public offering price of $5.00 per share and after deducting the estimated placement agency fee and offering expenses. We intend to use these proceeds to fund our preclinical studies and clinical trials of our products, research and development and for working capital and other general corporate purposes. The amounts we actually expend will vary significantly depending on a number of factors, including:

- results of preclinical studies and clinical trials of products,
- progress of our research and development programs,
- cost and timing of regulatory approvals,
- terms of any collaborative arrangements into which we enter,
- commercial potential of our products,
- status of competitive products,
- technological advances, and
- hiring of additional personnel.

As a result, we will retain significant discretion in the application of these funds.

We anticipate that the net proceeds of this offering, together with our existing financial resources and expected revenues from our collaborations, should be sufficient to meet our capital and operating requirements into mid-2001. This estimate is based on assumptions that could be negatively impacted by the matters discussed in "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations--Liquidity and Capital Resources."

Until we use the net proceeds as described above, we will invest them in short-term, interest-bearing, investment grade securities.

PRICE RANGE OF COMMON STOCK

Our common stock is traded on the Nasdaq National Market under the symbol "RZYM." The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock as reported on the Nasdaq National Market.

<TABLE>
<CAPTION>

	HIGH	LOW
<S>	<C>	<C>
YEAR ENDED DECEMBER 31, 1997		
First Quarter	$16.50	$9.88
Second Quarter	$12.38	$8.63
Third Quarter	$12.00	$7.38
Fourth Quarter	$11.38	$7.00
YEAR ENDED DECEMBER 31, 1998		
First Quarter	$ 9.34	$5.13
Second Quarter	$10.50	$4.88
Third Quarter	$ 6.25	$2.00
Fourth Quarter	$ 7.63	$3.31
YEAR ENDED DECEMBER 31, 1999		
First Quarter (through March 24, 1999)	$ 5.75	$4.06

</TABLE>

The sale price of the common stock as reported on the Nasdaq National Market on March 24, 1999, was $5.00 per share. At March 24, 1999, there were approximately 148 holders of record of our common stock.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock during any of the periods presented above. We currently intend to retain future earnings, if any, to support the development of our business and for general corporate purposes, and do not anticipate paying any cash dividends in the foreseeable future. We are also party to agreements restricting our ability to pay dividends.

CAPITALIZATION

The following table describes our capitalization as of December 31, 1998, on an actual basis and as adjusted to give effect to our receipt of the estimated net proceeds from the sale of 1,800,000 shares of common stock offered by us at the public offering price of $5.00 per share, after deducting the estimated placement agency fee and offering expenses. When you read this table, it is important that you also read "Use of Proceeds," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes.

<TABLE>
<CAPTION>

	December 31, 1998	
	Actual	As Adjusted
	(in thousands)	
<S>	<C>	<C>
Long-term debt and capital lease obligations, net of current	$ 4,545	$ 4,545
Stockholders' equity:		
Voting convertible preferred stock, $0.01 par value per share; 5,000,000 shares authorized; no shares outstanding	0	0
Common stock, $0.01 par value per share; 20,000,000 shares authorized; 9,181,455 shares issued and outstanding, actual; 10,981,455 shares issued and outstanding, as adjusted*	92	110
Additional paid-in capital	84,434	92,516
Deferred compensation	(69)	(69)
Accumulated deficit	(73,423)	(73,423)
Total stockholders' equity	11,034	19,134
Total capitalization	$ 15,579	$ 23,679

</TABLE>

* As of March 15, 1999, as adjusted amount excludes the following:

- 1,478,493 shares reserved for issuance under our stock option plan, of which 1,386,487 shares were outstanding, at a weighted average exercise price of $4.18 per share;
- 487,458 shares issuable upon exercise of outstanding warrants at a weighted average exercise price of $22.76 per share;
- 1,100,844 shares issuable to one of our collaborators upon conversion of outstanding debt, assuming a conversion price of $4.88 per share (our common stock price on March 15, 1999); and
- 200,168 shares available for issuance under our Employee Stock Purchase Plan. See "Description of Capital Stock--Warrants" and "Management--Stock Option Plan."

DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by dividing the net tangible book value (total assets less intangible assets and total liabilities) by the number of outstanding shares of common stock.

Our net tangible book value as of December 31, 1998, was $8.1 million in the aggregate or $0.89 per share. After giving effect to the sale of the 1,800,000 shares of common stock we are offering at an assumed public offering price of $5.00 per share, and the deduction of the estimated placement agency fee and offering expenses payable by us, our net tangible book value as of December 31, 1998, as adjusted, would have been $16.2 million in the aggregate, or $1.48 per share. This represents an immediate increase in the net tangible book value of $0.59 per share to existing stockholders and an immediate dilution in net tangible book value of $3.52 per share to new investors purchasing shares in this offering.

The following table illustrates this per share dilution:

Public offering price per share		$5.00
Net tangible book value per share as of December 31, 1998	$0.89	
Increase per share attributable to new investors	$0.59	
As adjusted net tangible book value per share after this offering		$1.48
Dilution per share to new investors		$3.52

At December 31, 1998, we had outstanding the following options and warrants to purchase shares of common stock:

	NUMBER	WEIGHTED AVERAGE EXERCISE PRICE
Stock option plan	1,347,572	$ 4.21
Warrants	487,458	$22.76
Total	1,835,030	

Additionally, on March 15, 1999, there were:

- 92,006 options available for future grant under our stock option plan,
- 200,168 shares available for issuance under our Employee Stock Purchase Plan, and
- 1,100,844 shares issuable to one of our collaborators upon conversion of outstanding debt, assuming a conversion price of $4.88 per share (our common stock price on March 15, 1999).

To the extent we issue these additional shares, there will be further dilution to new investors.

SELECTED FINANCIAL DATA

The following selected financial data are derived from our audited financial statements. Our financial statements for 1994, 1995, 1996, 1997 and 1998 have been audited by Ernst & Young LLP, independent auditors. These historical results do not necessarily indicate future results. When you read this data, it is important that you also read our financial statements and related notes, as well as the section "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year Ended December 31,				
	1994	1995	1996	1997	1998
	(amounts in thousands, except per share data)				
Statement of Operations Data:					
Revenues:					
Collaborative agreements	$ 1,145	$ 1,178	$ 759	$ 1,976	$ 8,963
Grant and other					

income.....	172	102	14	7	25
Interest income.....	270	395	936	795	634
Total revenues.....	1,587	1,675	1,709	2,778	9,622
Expenses:					
Research and development.....	9,212	12,204	14,189	15,170	16,941
General and administrative.....	1,291	1,397	1,943	1,886	1,813
Interest expense.....	334	554	845	844	704
Total expenses.....	10,837	14,155	16,977	17,900	19,458
Equity in loss of unconsolidated affiliate.....	--	--	--	--	1,082
Net loss.....	$ (9,250)	$ (12,480)	$ (15,268)	$ (15,122)	$ (10,918)
Net loss per share (basic and diluted)....	$ (3.52)	$ (3.86)	$ (2.61)	$ (2.04)	$ (1.22)
Shares used in computing net loss per share (basic and diluted)....	2,627	3,230	5,845	7,420	8,978
Balance Sheet Data:					
Cash, cash equivalents and securities available-for-sale.....	$ 7,734	$ 6,420	$ 17,594	$ 16,102	$ 6,512
Working capital.....	5,640	4,648	15,788	13,238	4,467
Total assets.....	12,392	14,223	25,292	24,850	19,224
Capital lease obligations and long-term debt, net of current portion.....	1,853	3,179	2,430	2,752	4,545
Accumulated deficit.....	(19,635)	(32,115)	(47,383)	(62,505)	(73,422)
Total stockholders' equity.....	8,247	8,478	20,362	18,870	11,034

</TABLE>

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following Management's Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the Financial Statements of Ribozyme Pharmaceuticals and the notes therein included elsewhere in this prospectus. Our discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties, such as our plans, objectives, expectations and intentions. Our actual results and the timing of certain events could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including those set forth under "Risk Factors," "Business" and elsewhere in this prospectus.

Overview of our Business

Ribozyme Pharmaceuticals was founded to develop commercial products and services based upon the significant potential of "ribozymes," a discovery of Professor Thomas R. Cech for which he shared a Nobel Prize. Our primary business focus is to use our technology to develop a new class of drugs consisting of ribozymes to treat or prevent human disease. We are in various stages of preclinical development and clinical trials for two lead product candidates: ANGIOZYME for the treatment of solid tumor cancers and HEPTAZYME for the treatment of Hepatitis C. Chiron is our collaborator for the development and commercialization of ANGIOZYME. Lilly is our collaborator for the development and commercialization of HEPTAZYME. We have gene function identification and target validation agreements with Schering AG, Roche Biosciences and GlaxoWellcome. In addition, we have existing gene function identification and target validation agreements with Chiron and Parke-Davis which are substantially complete, but we may be obligated to perform additional work.

We recently completed Phase Ia clinical trials for our most advanced product candidate, ANGIOZYME. We expect to commence Phase Ib trials in the first quarter of 1999 and Phase II trials by the end of the year. We expect to file an IND for our second product candidate, HEPTAZYME, by the end of the year and commence clinical trials in 2000. To date, we have committed substantially all our resources to our research and product development programs. We have not

generated any revenues from product sales, nor do we anticipate any in the foreseeable future. Our revenues consist primarily of research payments and milestones from our collaborators. We depend upon funding from external financing and corporate collaborations for our research and product development programs and expect to do so for the foreseeable future.

We expect to commit significant additional resources conducting clinical trials for ANGIOZYME and HEPTAZYME, as well as for clinical trials for other potential product candidates. In addition, although we believe our existing manufacturing facilities and those available from contract manufacturers will be satisfactory for the manufacture of our current product candidates through clinical trials, we will need to commit significant resources in order to support manufacture on a commercial scale. We have not been profitable since inception and have an accumulated deficit of $73.4 million as of December 31, 1998. Losses have resulted primarily from our research and development programs. We anticipate incurring additional losses as ANGIOZYME, HEPTAZYME and other product candidates advance through development. In addition, some payments under our collaborations are contingent upon our meeting particular research or development goals. Therefore, we are subject to significant variation in the timing and amount of our revenues and results of operations from period to period.

In 1998, we transferred our gene function identification and target validation technology to Atugen in exchange for a substantial equity interest. We will continue our existing gene function identification and target validation agreements with our collaborators by subcontracting services to be performed to Atugen. Atugen will enter into gene function identification and target validation agreements directly with collaborators, but we will retain rights to (1) use the technology internally, and (2) develop ribozymes as therapeutic agents against targets validated by Atugen. In 1998, we received a one-time license fee from Atugen for a portion of our gene function identification and target validation technology. We will receive

payments for: (1) management and administrative services we provide, (2) oligonucleotides and (3) prosecution of relevant patents. In addition, we will retain exclusive manufacturing rights to ribozyme therapeutic agents resulting from validation services. Atugen will be reimbursed for any subcontracting services it provides to us on a full time equivalent basis.

Our revenues are denominated in U.S. dollars, therefore, we have not been exposed to foreign currency translation risks and have not engaged in any hedging instruments.

Results of Operations for Years Ended December 31, 1998, 1997 and 1996

Revenues. Revenues from collaborative agreements increased from $2.0 million for the year ended December 31, 1997, to $9.0 million in 1998. The increase was primarily due to $6.0 million recorded for Chiron partnership payments related to the product development of ANGIOZYME. In addition, we received approximately $650,000 in collaborative revenue in 1998 due to new target validation agreements with Roche, Parke-Davis and GlaxoWellcome.

Revenues from collaborative agreements increased from $759,000 in 1996 to $2.0 million in 1997. The increase was primarily due to $1.5 million in research payments made by Schering AG in 1997. The 1997 payments from Schering AG were the first payments in the collaboration which includes $2.0 million in annual research funding over the five-year term of the collaboration, provided the agreement is extended for each of those years.

Interest income was $936,000, $795,000 and $635,000 for the years ended 1996, 1997, and 1998, respectively. The higher interest income in 1996 resulted from increased cash balances due to our initial public offering in April 1996. Interest income has decreased in the last three years due to declining cash balances. Interest income generally fluctuates as a result of cash available for investment and prevailing interest rates.

Expenses. Research and development expenses increased from $14.2 million in 1996 to $15.2 million in 1997, and increased to $16.9 million for the year ended December 31, 1998. These increases were primarily due to the hiring of additional personnel and the overall scale-up of research and product development. Research and development expenses consist primarily of:

- clinical and preclinical supplies and related costs,
- salaries and benefits for scientific, regulatory, quality control and pilot manufacturing personnel,
- consultants,

. supplies,

. occupancy costs, and

. depreciation for laboratory equipment and facilities.

In 1998, expenses were primarily related to ANGIOZYME development and target validation service costs. We expect research and development expenses to continue to increase as ANGIOZYME and HEPTAZYME proceed through clinical trials and manufacturing.

General and administrative expense decreased slightly from $1.9 million in 1996 to $1.89 million in 1997, and decreased slightly again to $1.81 million for the year ended December 31, 1998. The slight decrease in general and administrative expense in 1997 was primarily due to higher expenses in 1996 which included one-time cash and stock bonus payments made to our executive officers in connection with our initial public offering in April 1996. The decrease in 1998 was due to reimbursements of $480,000 made to us from Atugen related to management's time during closing and start-up of operations. We expect general and administrative expenses to increase as a result of hiring additional management and administrative personnel and the incurring of legal and other professional fees in connection with the overall expansion of our operations and business development efforts.

Interest expense has remained stable at $845,000 in 1996, $844,000 in 1997 and $704,000 in 1998. We expect interest expense to increase as we continue to borrow under existing or new lines of credit to finance equipment purchases.

In 1998, in connection with our initial cash investment of $2.0 million and the transfer of our gene identification and target validation technology to the newly formed affiliate, Atugen, we retained a 49.5% equity interest in the voting stock of this company. However, at December 31, 1998, our interest represents 83.2% of the outstanding common stock of Atugen. We do not meet the criteria for consolidation of this affiliate because (1) we control less than 50% of Atugen's voting stock, and (2) the preferred shareholders retain significant participating rights. Accordingly, we have accounted for our investment in Atugen under the equity method. As a result, we have recorded our share of the unconsolidated affiliate's 1998 net loss, or $1.1 million as equity in loss of unconsolidated affiliate in our 1998 Statement of Operations. At December 31, 1998, our remaining net investment in Atugen is $860,000, which we expect to be eliminated entirely during 1999 as we share further in Atugen's losses.

Liquidity and Capital Resources

We have financed our operations since inception through public offerings in April 1996 and October 1997, private placements of preferred stock and funds received under our collaborative agreements. From inception through December 31, 1998, we have received approximately:

. $29.0 million in net proceeds from private placements,

. $31.1 million in net proceeds from public offerings,

. $39.2 million from our collaborations, and

. $9.8 million from equipment financing.

We had cash, cash equivalents and securities available-for-sale of $6.5 million at December 31, 1998, compared with $16.1 million at December 31, 1997, and $17.6 million at December 31, 1996. The $9.6 million decrease from 1997 to 1998 and the $1.5 million decrease from 1996 to 1997 were primarily the result of cash used for research and development, investment in equipment, payments under loan facilities and expenses incurred for general corporate purposes, offset by net proceeds from the sale of common stock and preferred stock, loan proceeds and research payments from collaborations.

We invest our cash, cash equivalents and securities available-for-sale in interest-bearing investment grade securities.

Total additions for property, plant and equipment during 1998 were $936,000, most of which were financed through our existing equipment loan facility with Schering AG.

Schering AG made a $2.5 million equity investment in us in May 1997 in exchange for 212,766 shares of common stock and made an additional equity investment of $2.5 million for 465,117 shares in April 1998. Separately,

Schering AG provided loans of $2.0 million in each of 1997 and 1998. We received an additional $1.0 million advanced on this loan facility in January 1999. Schering AG will continue to provide loans of up to $2.0 million annually for each of the next three years, provided that the collaboration is continued, at Schering AG's option, in each of those years. If Schering AG does not continue the collaboration, we will need to seek alternative sources of financing. Amounts not used in any calendar year may be carried forward to future years. According to the terms of our agreement with Schering AG, 50% of any borrowings on the line of credit must be collateralized by equipment purchases. The loans, which carry an interest rate of 8.0% per annum, are immediately convertible into equity at the option of Schering AG. At December 31, 1998, the outstanding borrowings of $4.3 million were convertible into approximately 992,000 shares of our common stock. Principal and interest payments are deferred until maturity of the loans which is April 2004. In addition, Schering AG made research payments of $2.0 million and $1.5 million in 1998 and 1997, respectively. If the collaboration is continued, Schering AG will make research payments of $2.0 million a year for each year through April 2001, but Schering AG may terminate its collaboration at any time. We may

earn success fees upon product development milestones and will manufacture synthetic ribozyme products and receive royalties on sales of products resulting from the collaboration. Schering AG may terminate the research collaboration at any time by paying us termination fees.

We anticipate that net proceeds of this offering, together with our existing financial resources and expected revenues from our collaborations should be sufficient to meet our anticipated operating and capital requirements through mid-2001. We expect to incur substantial additional costs, including:

- costs related to our research, drug discovery and development programs,
- preclinical and clinical trials of our products, if developed,
- prosecuting and enforcing patent claims,
- general administrative and legal items, and
- manufacturing and marketing of products, if any.

We do not have any currently available credit facilities from which we may borrow. In the future we may raise additional capital through public or private financing, as well as from new collaborative relationships, new credit facilities and other sources. We cannot assure you that funds will be available on favorable terms, if at all. If we raise additional funds by issuing equity securities, the holdings of existing stockholders will be further diluted. In addition, future collaborative relationships may not successfully reduce our funding requirements which may require us to relinquish or reduce rights to our technologies or products. See "Risk Factors."

At December 31, 1998, we had available net operating loss carryforwards, research and development credit carryforwards and state investment credit carryforwards of $73.4 million, $1.5 million and $31,000, respectively, for income tax purposes. Our ability to utilize our net operating loss carryforwards is subject to an annual limitation in future periods pursuant to the "change in ownership" rules under Section 382 of the Internal Revenue Code.

Year 2000 Affect on Computer Systems

Year 2000 issues result from the inability of some computer programs or computerized equipment to accurately calculate, store or use a date subsequent to December 31, 1999. The erroneous date can be interpreted in a number of different ways; typically the year 2000 is represented as the year 1900. This could result in a system failure or miscalculations causing disruptions of operations, including, among other things, a temporary inability to process transactions, send invoices or engage in similar normal business.

Based on our evaluations and remediation efforts, we do not anticipate that we will incur any significant costs relating to the assessment and remediation of year 2000 issues. To date, we estimate that we have spent approximately $20,000 in reviewing and remediating year 2000 issues and that total expenditures incurred in completing our review and remediation efforts will not exceed $60,000. These expenditures are budgeted as part of our operating expenses. However, expenditures for year 2000 remediation efforts may exceed this amount if unforeseen complications arise. Also, we or our vendors, suppliers and corporate partners may not be able to successfully identify and remedy all potential year 2000 problems.

We have developed and are implementing a contingency plan including the

following:

- maintaining all data in hard copy that is generated or collected by our vendors, suppliers and collaborators so any loss of data due to year 2000 problems could be re-entered manually,

- maintaining all of our accounting records in hard copy so that we can continue to manually pay vendors, employees, consultants and collaborators in the event that our accounting software or other computer programs or systems malfunction,

- maintaining hard copies of all scientific and business related electronic data,

- archiving critical business paperwork,

- scheduling manufacturing campaigns not to extend or overlap the year 2000 time change, and

- upgrading security systems.

We continue to review these requirements to complete our contingency plan for noncritical business functions.

We do not believe that we will have to modify or replace any significant portions of our computer applications in order for our computer systems to continue to function properly in the year 2000. However, a "worst case" scenario may include the temporary interruption of research, development and business if we need to upgrade or replace computer systems.

BUSINESS

An overview of our company

Ribozyme Pharmaceuticals is developing a new class of drugs based on Professor Thomas R. Cech's discovery of "ribozymes," for which he shared a Nobel Prize. Ribozymes, a form of ribonucleic acid ("RNA"), have the ability to selectively inhibit protein production. Because many human disease states result from abnormal protein production, we believe that ribozymes are applicable to a wide range of human diseases. We are currently conducting preclinical development and clinical trials for our two lead product candidates, ANGIOZYME and HEPTAZYME. We are collaborating with Chiron for the development and commercialization of ANGIOZYME, a drug for the treatment of solid tumor cancers. We are collaborating with Lilly for the development and commercialization of HEPTAZYME, a drug for the treatment of Hepatitis C, a viral liver disease. Ribozymes also are useful in identifying the function of specific genes (target validation) and in diagnosing disease. Our primary business focus is to use our patented technology to develop a new class of drugs containing ribozymes to treat or prevent human disease. In 1998, we transferred our target validation and discovery technology to Atugen in return for a substantial equity interest.

The traditional process of drug discovery and development

Traditional drug discovery and development is difficult, time consuming and extremely costly. Historically, diseases have been treated using drugs developed based on clinical observation of symptoms which were correlated with abnormal physiological processes and, where possible, biochemical changes. Most drugs are chemicals designed to inhibit the function of a targeted molecule with as few unwanted side effects as possible. Drug discovery is a complex process, which includes:

- selecting a target (usually a protein),

- developing a screening assay,

- chemically synthesizing large numbers of different molecules tested in cell cultures and in animal models for their effect on the target,

- using those test results to narrow down the number of molecules, and

- refining the molecules through additional chemical synthesis and testing.

Unfortunately, drugs produced from this traditional process may have

undesirable side effects due to interactions with non-targeted molecules. These side effects can limit the effective use of a drug.

Pharmaceutical companies are under intense competitive pressure to identify and commercialize novel drugs having fewer side effects more quickly and cost effectively. Pricing pressures from managed care organizations, governmental agencies and other third-party payors, coupled with the proliferation of new technologies that offer revolutionary approaches to drug design and development, are causing major changes in the drug development process.

Genetic function and human disease

The abnormal production of proteins, which are products of genes, directly causes many human diseases. The abnormality may be due to a defective gene or to the over- or under-production of a protein by a "normal" gene. The abnormal production of proteins may have direct effects on cells within the body or may initiate a series of events involving other proteins within the body, thereby producing disease. The gene functions of infectious agents, such as viruses, allow replication and growth of infectious agents in the human body.

Production of proteins from genes, called protein "expression," generally involves two steps. First, the information from the DNA sequence of the gene is "transcribed" to mRNA. The second step involves

"translation" of the mRNA and its information into a protein. The process by which genetic information is "expressed" in the form of a protein is highly selective; production of a particular protein generally requires its own specific DNA sequence which leads to a corresponding specific mRNA sequence. Blocking a gene's function, and hence the production of its associated proteins, is an increasingly vital tool in treating and diagnosing human disease.

Our ribozyme technology

Our approach to drug discovery and development begins by either identifying a gene in humans causing or contributing to disease or identifying an essential gene in a disease-causing infectious agent. We analyze the nucleotide sequence of the target gene and create a complementary ribozyme nucleotide sequence.

A ribozyme is a sequence of nucleotides that has a catalytic core capable of cleaving a specific mRNA molecule. Ribozymes act as "molecular scissors" by cutting mRNA molecules into two ineffective strands, thereby preventing protein production. Each ribozyme destroys only a specifically targeted mRNA sequence, thereby minimizing the risk of unwanted side effects. In addition, ribozymes can be used to identify gene function and validating the disease contributing function of a specific gene. In this way, ribozymes assist in the identification of new drug candidates. Our ribozyme technology is an important bridge between the growing body of knowledge regarding gene function and its contribution to the treatment or prevention of human diseases.

We initially test the effectiveness of the ribozyme in cell cultures or in animal models. If the ribozyme reduces or stops production of the protein associated with the disease, or slows the associated growth or spread of the disease, not only has the disease contributing function of the gene been validated, but also a drug candidate has been identified.

Once we identify a target gene and related ribozyme, we optimize the ribozyme's effectiveness by (1) varying the length of the portion of the ribozyme which binds to the mRNA to maximize the ribozyme's selectivity and (2) modifying the chemical structure to increase the ribozyme's stability in the human body. To successfully commercialize ribozyme products to treat or prevent human disease, we must successfully deal with technical issues such as:

- ribozyme design,
- stability,
- selectivity,
- drug delivery and cellular absorption,
- safety,
- effectiveness, and
- manufacturing synthesis and scale up.

To date, we have achieved a number of significant milestones important to the

development of ribozymes and related technical issues, including the following:

Design. We have developed a proprietary computer program to design ribozymes against sites in a target mRNA sequence. This program allows us to accelerate the identification of potential ribozyme product candidates and design multiple back-up candidates.

Stability. To be useful as a treatment, a ribozyme must remain stable in human serum and cells long enough to destroy the targeted mRNA and ideally long enough for each ribozyme molecule to destroy several mRNA molecules. Unmodified ribozymes are stable and fully active in human serum for only a few seconds. We have successfully produced chemically-modified ribozymes that are stable and fully active in

human serum and cells for more than 10 days. We believe this level of stability will be sufficient for ribozymes to be effective drugs.

Selectivity. Based on third-party studies and our internal work, we believe that a ribozyme with a binding region of approximately 15 nucleotides is optimal. A binding region of this length is expected to match, on a statistical basis, only one specific mRNA sequence in the entire human genome. Since the ribozyme should interact only with the target mRNA, it should not affect other gene function and, therefore, should not have side effects when used as a drug. The high degree of selectivity of ribozymes has been demonstrated both by us and by third parties.

Drug Delivery and Cellular Absorption. Successful development of any drug requires that the drug be delivered to the desired site in the body. We are exploring local and systemic delivery of chemically synthesized ribozymes, as well as vector delivery. For example, we have demonstrated systemic delivery of chemically synthesized ribozymes without any delivery vehicle using either intravenous or subcutaneous delivery in several animal models and in humans. Additionally, we have identified several proprietary carriers which, when combined with chemically synthesized ribozymes, have shown significant increases in the effective delivery of ribozymes to a variety of different cell types relative to ribozymes without a carrier.

Safety. We have completed single and multiple dose animal safety studies with several ribozymes which have confirmed the ribozymes' lack of toxicity. For example, ANGIOZYME has shown a lack of toxicity in rodents and monkeys. As a result, the FDA has allowed initial human clinical trials to be carried out in healthy volunteers. A Phase Ia trial in healthy volunteers has now been completed and has shown an excellent safety and tolerability profile.

Effectiveness. We have demonstrated through internal research and in conjunction with our collaborators that our ribozymes reduce the amount of target mRNA and the level of corresponding protein produced as well as inhibit the spread of disease. Studies showing the effectiveness of ribozymes have been conducted in multiple animal models for cancer in both models of solid tumor growth and metastasis, and in cell cultures for viral replication.

Manufacturing Capabilities and Scale Up. To meet our needs for preclinical studies, clinical trials and the eventual commercialization of ribozymes, we must have the ability to manufacture a sufficient amount of ribozymes. We and our collaborators have developed proprietary technology allowing us to synthesize several thousand stabilized ribozymes in milligram quantities per month. These quantities are sufficient to permit us to perform direct cell-based screening of multiple potential target sites in short periods of time. We have also developed the capability to manufacture kilogram quantities under the FDA's current good manufacturing practices ("cGMP"). In addition, when we combine our manufacturing capabilities with available contract manufacturing, we expect to be able to produce those drugs currently under development in sufficient quantities, and of the quality required by the FDA, for our anticipated clinical trials.

The potential advantages of ribozymes in treating a disease

We believe that ribozymes offer the following advantages over traditional approaches to treating diseases:

Potential Broad Applicability. Once a gene has been identified, a ribozyme can be designed to target and destroy the associated mRNA to inhibit the related gene function. Therefore, all diseases for which a gene can be identified as a cause or an essential contributing factor of diseases are potentially treatable with a ribozyme drug. In addition, identifying the essential genes of viruses and other infectious agents that cause human disease creates the potential to develop ribozyme products to inhibit these genes from functioning and, consequently, prevent the targeted infectious agent from

surviving or reproducing.

High Selectivity. The mechanism by which traditional drugs act on a target gene or protein often is not well understood. Consequently, the side effects of such drugs are difficult to predict and characterize. Side effects may be reduced or avoided by using ribozymes designed to attach to and cut only a specific targeted mRNA, a significant advantage over traditional drug therapies. We have observed the selectivity of ribozymes in both animal studies and human clinical trials. Because of this selectivity, only the function of the targeted genetic sequence is affected; other molecules and gene functions are not altered.

Destruction of Target. Instead of temporarily preventing gene function like traditional drugs, ribozymes destroy the target mRNA and stop the associated protein production. By contrast, most drugs do not destroy their target. This inherent feature of ribozymes may offer significant advantage in the treatment of diseases caused by infectious agents such as viruses. For example, cleavage of target viral mRNA by ribozymes will inhibit the virus's ability to propagate, which may cause significant reduction in viral load in the patient.

Our business strategy

Our primary business objective is to use our technology to identify and develop drugs containing ribozymes to prevent or treat human disease. Our secondary objective is to license our technology to others on terms which could provide us an economic benefit. Our strategy for achieving these objectives includes the following goals:

Develop Identified Product Candidates. We are developing two products, ANGIOZYME and HEPTAZYME. In collaboration with Chiron, we are developing ANGIOZYME for the treatment of solid tumor cancers and metastasis, and possibly for other diseases that require extensive new blood vessel formation. We have completed a Phase Ia clinical trial for ANGIOZYME in healthy volunteers. We will soon commence Phase Ib clinical trials in cancer patients. Internally, we identified a second product, HEPTAZYME, for the treatment of Hepatitis C. In collaboration with Lilly, we are conducting preclinical testing for HEPTAZYME and we plan to file an IND before year-end.

Identify New Product Candidates. We have developed a variety of sources to identify additional product candidates. Internally, we are researching several product candidates and intend to begin preclinical testing and development of one of these product candidates by year-end. We believe that our relationship with Atugen could provide an important source of new product candidates for us. Atugen will seek additional partners in the pharmaceutical and biotechnology industries using Atugen's gene function identification and validation technology. We have retained rights to develop ribozymes against any targets validated by Atugen on its own or for its partners. We are engaged in several collaborations to validate selected genetic sequences as candidates for drugs development. Under these collaborations, we have the right to develop ribozyme products against validated targets not developed by our collaborators.

Partner with Others to Develop Products. We intend to develop our products in collaboration with larger corporate partners. In the past, we have entered into collaborations prior to identifying product candidates and performing the research and preclinical testing necessary to bring such products to development. In the future, we intend to demonstrate a product candidate's commercial potential through preclinical testing and, perhaps, early clinical trials using internally funded research. We believe entering into a development collaboration after a product's potential has been demonstrated will improve our negotiating position. Our development process with HEPTAZYME prior to entering into the Lilly collaboration is an example of this new partnering strategy.

Focus on Human Therapeutics and License Other Applications of Our Technology. We will look for opportunities to license our technology on terms which provide a reasonable opportunity for significant business benefit. In late 1998, we transferred our gene function identification and validation technology to Atugen in exchange for an equity interest in Atugen. We expect Atugen to continue to build the target validation and discovery business by actively pursuing collaborations with new corporate partners. We will benefit from Atugen's activities through our ownership interest in Atugen, as well as through the rights we retained to develop ribozymes against targets validated by Atugen.

Maintain and Expand Patent Portfolio and Proprietary Technology. To maximize the value of our technology, we dedicate substantial resources to the discovery of new inventions. We aggressively pursue patent protection. We currently own, or have exclusive licenses to, 84 issued or allowed patents worldwide and have over 100 patent applications pending worldwide.

OUR PRODUCT PROGRAMS

The development process for our products starts with research and preclinical development. Research includes identification of a target protein, synthesis of an appropriate ribozyme to block expression of the target protein, and testing the activity of the ribozyme in a specific cell population. Preclinical testing includes pharmacology and toxicology testing in cell cultures and animal models, product formulation, dosage studies and manufacturing scale-up for submission of the necessary data to comply with regulatory requirements of the FDA and similar agencies in other countries prior to commencement of human trials. Regulatory requirements concerning the conduct of clinical trials are described below in the section "--Government regulation of our drug development activities."

We are currently in various stages of development and clinical trials for two products. ANGIOZYME is being developed to treat solid tumor cancers, but it may also be applicable to other diseases such as diabetic retinopathy and macular degeneration. HEPTAZYME is being developed to treat Hepatitis C.

Angiozyme

For a cancerous tumor to grow, the body must generate new blood vessels surrounding the tumor to supply the blood necessary for tumor growth, a process known as angiogenesis. In many cases, the Vascular Endothelial Growth Factor ("VEGF") molecule and its receptor are essential to angiogenesis. ANGIOZYME was developed to inhibit the production of the VEGF receptor, thereby slowing or stopping angiogenesis and related tumor growth. Animal studies conducted by us and by independent third parties showed dramatic reduction in tumor growth and metastasis. Animal studies using ribozymes alone and in conjunction with existing cytotoxic cancer therapies demonstrated the elimination of metastasis of the cancer. As a result of our research and preclinical studies, the FDA approved an IND allowing us to begin clinical trials. We completed Phase Ia clinical trials in healthy volunteers in January 1999. These trials, conducted on 14 healthy volunteers, demonstrated safety and tolerability and showed no drug related side effects. We will soon commence Phase Ib clinical trials testing safety and tolerability in at least 16 cancer patients with a broad spectrum of solid tumors and metastasis. We expect to initiate Phase II clinical trials prior to the end of 1999.

If the results of clinical trials are positive, ANGIOZYME could be developed as a treatment of some solid tumor cancers such as cancers of the lung, breast, prostate, colon and rectum. These cancers account for over 750,000 new cancer cases and over 200,000 deaths per year in the United States alone. In addition, ANGIOZYME could also be used in products for the treatment of other diseases in which angiogenesis is a contributor such as the eye diseases, macular degeneration and diabetic retinopathy.

ANGIOZYME is being developed in collaboration with Chiron. We have control of all development activities and decision. The material terms of the agreement with Chiron are discussed below.

Heptazyme

We are developing a potential product to treat Hepatitis C, a viral disease of the liver ("HCV"). There are over four million chronically infected persons in the United States and over 175 million worldwide. HCV infects approximately 50,000 people with over 10,000 deaths associated with HCV each year in the United States. It is the most common blood borne infection in the United States and has been identified as a "silent epidemic" and "a daunting challenge to public health" by the United States Congress.

Current therapies for HCV are effective in less than 50% of existing patients and they have serious side effects. Our research and preclinical testing has indicated that HEPTAZYME selectively cuts HCV RNA in a manner that significantly inhibits viral replication in cell culture. These results were presented at a meeting of the American Association for the Study of Liver Diseases in November 1998. It is also expected to be effective against all known HCV sub-types, which now number over 90. We intend to conduct toxicology and other preclinical studies commencing in the second quarter of 1999 and file an IND with the FDA by the end of 1999.

HEPTAZYME is being developed in collaboration with Lilly. The material terms of the agreement are described below.

Other Programs. In collaboration with Chiron, the City of Hope and Children's Hospital (Los Angeles), we have successfully completed a gene therapy HIV Phase I/IIa clinical trial. The treatment phase of this trial was completed in December 1997. Five patients were treated, and no drug-related toxicities were observed. In 1998, a proof-of-principle Phase II clinical trial in AIDS Lymphoma patients was initiated. The pilot trial is intended to assess the viability of the gene therapy approach for delivering anti-HIV ribozymes. The commercial viability of current gene therapy technologies and thus the future of this program will be decided during 1999.

Internally, we are researching several product candidates and intend to begin preclinical testing and development of one of these product candidates by year-end.

Chiron Collaboration. In July 1994, we entered into an agreement with Chiron to collaborate exclusively on up to five specific targets selected by Chiron. Four targets are currently subject to the exclusivity provision, including ANGIOZYME and the target of our HIV product, thus Chiron has the right to select an additional exclusive target. From time to time during the term of the collaboration, Chiron also has the right to reserve four potential targets. In addition, Chiron may replace exclusive targets with other targets including reserved targets. No target may be selected as an exclusive or reserved target if the rights to such target have been granted to a third party or such target is the subject of an active internal development program.

Unless otherwise mutually agreed, no target may be reserved for more than 18 months after its designation. During the 18-month period, we cannot develop, or grant rights to third parties to develop, products against a reserved target. Following such period, Chiron will not have any rights to a reserved target unless during the 18-month period the reserved target replaces another target as an exclusive target.

Pursuant to the collaboration, we commenced a five-year joint research program which expires in July 1999. During the five-year program, each party pays for its own research and preclinical development of products. Additional collaborative research may be done on a product against targets by mutual agreement and either party may research and conduct preclinical testing on its own, at its own cost.

Either party may propose that an IND be submitted and Phase I clinical trials be commenced for a product against exclusive targets. If the other party does not agree to share equally in the development costs through Phase I clinical trials, the party not sharing in the Phase I development cost forfeits any rights to the proposed product.

If, after jointly funded Phase I clinical trials have been completed, one party discontinues funding its share of the costs of clinical development that party would not share equally in the profits from product sales but would receive a royalty based on net sales of that product. However, the non-participating party may regain its interest in the profits of the product by repaying the other party one-half of the development costs incurred solely by the other party, plus a predetermined risk premium, at either the commencement of Phase III testing or the filing of a New Drug Application ("NDA") or Product License Application ("PLA").

In some instances we may pay up to 50% of such payment in shares of common stock. If development of a product is funded equally by the parties, we will share equally the profits from product sales.

We have retained the right to manufacture chemically synthesized ribozyme products resulting from the collaboration whether developed jointly or individually by each party.

Chiron holds exclusive worldwide marketing rights for all jointly developed products, subject to a co-promotion agreement for sales in North America and Europe. In Asia, Chiron has exclusive marketing rights with the right to sublicense, although we have retained the right to share in 50% of the profits.

The collaboration terminates on the later of (1) 30 years after the first commercial sale of the last jointly developed product arising out of the collaboration or (2) upon the expiration of patents or 15 years after the first commercial sale for a solely developed product.

As part of the collaboration, in 1994 Chiron made an equity investment of

$4.36 million in our stock. In addition, Chiron purchased 377,202 shares of our common stock for $3.64 million in 1996. Also in 1996, Chiron purchased warrants for 444,444 shares of our common stock for $2.0 million, exercisable at a price of $22.50 per share with an expiration date of December 30, 2004.

We and Chiron could not reach agreement on a development plan for ANGIOZYME. In consideration for the payment by Chiron of $5.0 million of our research costs related to ANGIOZYME prior to the filing of the IND for ANGIOZYME, we amended the collaboration agreement in the following manner. If the parties do not agree as to the plans, timing or budget for any development activities, our proposed plans, timing and budget will be adopted but we must then fund 55% of the costs for such development activities. If the total costs do not exceed our proposed budget, Chiron must pay us 5% of the total costs incurred for such development activities.

Lilly Collaboration. In March 1999, we entered into a collaboration with Eli Lilly and Company ("Lilly") pursuant to which Lilly was granted the exclusive worldwide right to develop and commercialize HEPTAZYME and any other ribozyme drug for the treatment of HCV infection. If Lilly abandons or does not diligently pursue the development of HEPTAZYME or another ribozyme drug for the treatment of HCV infection, all rights to HEPTAZYME and such other ribozymes revert to us, subject to the right of Lilly to receive royalty payments, if applicable, on the sale of products developed by us or our third-party collaborators.

Lilly will pay us $9.2 million in 1999, which includes: funding for research, clinical trial materials and a $7.5 million equity investment. Including development milestones, which we will be entitled to receive if a commercial product is offered for sale in the United States, Europe and Japan, we would receive as much as $38 million, including the $9.2 million. In addition we will be entitled to royalties on the sale of products developed pursuant to the collaborations. We would also realize increased revenues from product manufacturing and research.

We have the right to manufacture all ribozymes for clinical trials. In addition, we have the manufacturing rights for any commercial product developed from the collaboration subject to Lilly's right to manufacture a portion of the commercial product, in which event Lilly must pay us an increased royalty on product sales.

Gene Validation

We developed a gene function identification and target validation business internally to generate revenues and accelerate the discovery of potential drugs using ribozymes. We entered into gene function identification and target validation agreements with Schering AG, Chiron, Parke-Davis, Roche and GlaxoWellcome and developed with our collaborators additional technologies helpful in target validation and discovery. These technologies use ribozymes and other oligonucleotides to block the function of genetic sequences selected by our partners. The effect of the ribozyme or other oligonucleotides in cell cultures or animal models is then analyzed to determine whether the protein associated with the disease or the disease itself is reduced or eliminated. Alternatively, a genetic sequence, the function of which is unknown, can be analyzed using ribozyme inhibition in a collection of cell culture assays or animal models that represent a broad range of biological functions.

Gene Validation Collaborations. We entered into gene function identification and target validation agreements with various collaborators and granted licenses to these collaborators to use our technology to develop products identified or validated under these collaborations.

. Schering AG. In April 1997, we entered into a research collaboration with Schering AG focusing on the use of ribozymes and related technologies for gene function validation. We provide our expertise in ribozyme design, synthesis and delivery, and Berlex Laboratories, Inc., a United States subsidiary of Schering AG, provides candidate gene or expressed sequence tag targets, screening in cell culture and animal models as well as development and commercialization expertise to the collaboration. We anticipate that hundreds of potential targets may be examined over a five-year period.

Schering AG may reserve exclusive rights to a specified number of targets at any time. Rights to a Schering AG target will revert to us, however, if Schering AG is not developing or selling a product against such target. Schering AG may not reserve exclusive rights to a target if we have granted a third party license for products against that target or we are conducting an active internal program for the development of a product against that target. Schering AG has a license to commercialize both ribozyme and non-ribozyme

products from any validated targets subject to paying us certain milestone success fees and royalties on product sales. We have the right to manufacture ribozyme products developed by Schering AG and to develop independently any ribozyme product not developed by Schering AG, unless Schering AG is developing a non-ribozyme product against the same target and agrees to pay specified milestone success payments to us in exchange for our relinquishing our right to make ribozyme products against such target.

In May 1997, Schering AG purchased 212,766 shares of our common stock for $2.5 million and in 1998 Schering AG purchased 465,117 shares of common stock for $2.5 million. Separately, Schering AG provided loans of $2.0 million in both 1997 and 1998. We received an additional $1.0 million on this loan facility in January 1999. Schering AG will continue to provide loans of up to $2.0 million annually through 2001, provided that the collaboration continues in each of those years. If Schering AG does not continue the collaboration, we will need to seek alternative sources of financing. The loans, which carry an interest rate of 8% per annum, are immediately convertible into equity at Schering AG's option. At December 31, 1998, our outstanding borrowings of $4.3 million were convertible into approximately 992,000 shares of our common stock. Principal and interest payments are deferred until maturity of the loans which is in April 2004. In addition, Schering AG made research payments of $1.5 million in 1997 and $2.0 million in 1998 and, provided that the collaboration is continued, will make research payments of $2.0 million a year through 2001, but Schering AG may terminate its collaboration at any time. Upon payment of termination fees to us, the research collaboration may be terminated at Schering AG's option at any time.

. Roche. In May 1998, we entered into a gene function identification and target validation collaboration with Roche. Roche may obtain the exclusive right to up to a specified number of targets over approximately five years if it requests and pays for validation research for such targets. Roche may reserve the rights to all targets related to a particular disease for up to three years. It may not obtain the rights to products for a target or disease which we have granted to third parties or to targets which we have patented

or for which we have pending patent applications. We do not receive periodic fees from Roche but rather Roche pays us a set amount for the specific research activities conducted on its behalf and for materials used in the research program.

Roche also is obligated to make payments for successful target validations. Roche has the right to develop ribozyme or non-ribozyme products against targets discovered or validated under the collaboration subject to the payment to us of milestone success fees and royalties on product sales. We have the right to manufacture ribozyme products developed by Roche and to develop independently any ribozyme product not developed by Roche.

. GlaxoWellcome. In July 1998, we entered into an agreement with GlaxoWellcome to evaluate our gene function identification and validation technology on a limited number of genes. GlaxoWellcome paid research fees to us in connection with the evaluation program for reagents plus the cost of any services or additional reagents requested by them. We will not be entitled to any royalties or other payments in connection with products developed by GlaxoWellcome against the initial targets covered by the evaluation agreement.

. Chiron. In May 1996, we entered into a gene function identification and target validation collaboration with Chiron for the use of ribozymes to validate gene function. We and Chiron each pay a portion of the research and development expenses of the collaboration. We paid Chiron $1.8 million for research funding related to the collaboration. We do not receive periodic fees but rather Chiron pays a predetermined amount for materials actually used in the collaboration. The collaboration with Chiron is substantially complete, but we may be obligated to perform additional work.

Chiron has the option to reserve exclusive rights to a specified number of targets for up to two and a half years as well as the exclusive right to any products developed against the targets subject to the collaboration. We are entitled to: (1) receive success payments related to the development of any products arising under the agreement; (2) receive milestone success payments for the development of ribozyme products and royalties on sales of any commercial products containing ribozymes; (3) manufacture synthetic ribozymes; and (4) develop any ribozyme product not developed by Chiron subject to the payment of royalties on product sales to Chiron. Chiron also has the right to manufacture endogenously delivered ribozyme products developed by us.

. Parke-Davis. In March 1998, we entered into a gene function identification and target validation collaboration with Parke-Davis to use our technology to validate genes as therapeutic targets. We do not receive periodic fees but

rather Parke-Davis pays for our research and for materials provided by us. Parke-Davis will have the exclusive right to develop oligonucleotide products against targets validated under the collaboration pursuant to a mutually satisfactory license which we anticipate would provide for the payment of milestone success fees and royalties on product sales. The collaboration with Parke-Davis is substantially complete, but we may be obligated to perform additional work.

We expect to subcontract these agreements to Atugen in the future, subject to the consent of our collaborators. If an agreement is subcontracted to Atugen, we will retain any rights we have now under the collaboration to (1) milestone success payments under the collaboration agreement; (2) royalties on products developed by our collaborators; and (3) develop ribozyme products which our collaborators choose not to develop under the terms of the agreements subject to royalties from product that may be payable to our collaborators.

Formation of Atugen. In 1998, we transferred our gene function identification and target validation technologies to Atugen in exchange for an equity interest in Atugen. This opportunity was attractive to us because substantial funding was available from both outside investors and the German government. This funding would not otherwise have been available to us and should allow us to benefit indirectly from Atugen's expansion of the target validation business and technology.

We will benefit from Atugen's activities in the future in several ways:

- we retain an interest in Atugen and, as of December 31, 1998, owned 49.5% of its equity,
- we have the right to develop ribozymes against targets validated by Atugen for its customers,
- we will be paid by Atugen for ribozymes and other material manufactured by us pursuant to our exclusive manufacturing rights,
- we will be paid by Atugen for a portion of our costs of prosecuting patents applicable to Atugen's business,
- we will be paid by Atugen for certain administrative and other services rendered by us to Atugen, and
- we retain the right to use the target validation and discovery technology in non-high throughput applications for our own use and in connection with limited research and development collaborations with third parties.

Financing for Atugen was accomplished through a combination of venture capital investment, an investment by us and German government grants and loans. We contributed $2.0 million in cash to Atugen. On December 31, 1998, we owned a 49.5% equity interest in Atugen. Our equity interest in Atugen is subject to dilution if additional equity is issued for any purpose, such as to raise additional capital in connection with acquisitions or in connection with stock option or similar incentive plans for Atugen employees.

We have the right to name two of six designees to Atugen's Board of Directors and the Chairman of the Board for as long as we and BB BioVentures together own a majority of Atugen's outstanding stock. Nonetheless, most corporate actions taken by Atugen require a 75% vote or consent of the holders of Atugen's outstanding stock.

Pursuant to a service agreement with Atugen, we provide a business development team which devotes 50% of its time to support Atugen's business development efforts for nine months and, at Atugen's option, for an additional three months. Our CEO, CFO and Vice President of Research, Dr. Christoffersen, Mr. Bullock and Dr. Usman, respectively, devote up to 25% of their time to Atugen activities for the first six months to ensure a smooth transfer of technology. They will make every reasonable attempt to accommodate any additional time needed by Atugen during or after the six month period.

As part of the formation, Atugen received exclusive royalty-free licenses to our extensive patents and technologies for target validation and discovery. We received a one-time $2.0 million license payment in 1999 for a portion of the licensed technology. The initial technology base includes our entire gene function identification and target validation technologies for both chemically synthesized and expressed nucleic acids, including target site selection, cell culture assays, RNA and other assays, optimized delivery vehicles and animal pharmacology.

Atugen's primary goal is to accelerate discovery and validation of human

health therapeutic targets. It will provide a variety of technologies and services to utilize information emerging from human genome sequencing efforts to determine which genes are key factors causing human disease. The significant technology base transferred from us to Atugen combined with the substantial initial capitalization should allow Atugen to improve the speed and certainty of identifying and validating new therapeutic targets both for corporate partners and for internal use. As part of the formation, Atugen acquired Transgenics Berlin-Buch GmbH in return for equity in Atugen. This transaction provides Atugen with transgenic animal capabilities, allowing early and rapid animal model assessment of the effect of inhibiting expression of a targeted gene sequence using a ribozyme. Atugen formally opened its research and administrative facilities in January 1999 on the Biomedical Research Campus of the Max Delbruck Center in Berlin-Buch, Germany.

Other licenses

An element of our business strategy is to enter into licensing agreements or other arrangements to exploit our technology. We seek licensing partners who pursue the development of drugs for human diseases and other applications of our technology which we cannot otherwise develop due to our limited resources. In the past, we have entered into the following two licenses for such activities.

Dow AgroSciences LLC. In September 1993, we entered into a collaborative research feasibility study with Dow AgroSciences LLC. The goal of the feasibility study was to demonstrate the ability of ribozymes to alter corn oil traits. Dow AgroSciences provided research support for the feasibility study conducted by us. The feasibility study was completed successfully in April 1997 and we entered into a long-term license agreement with Dow AgroSciences. The agreement provides Dow AgroSciences with a worldwide, non-exclusive license to some of our technology to commercialize oil, meal and starch products in corn and several other crops. As consideration for the long-term license agreement, 41,666 shares of our common stock held by Dow AgroSciences were returned to us. We will receive royalties on products sold; however, we do not expect to receive royalties, if any, from this license for a substantial period of time.

IntelliGene. In March 1997, we granted a worldwide exclusive license to some of our technology to IntelliGene to develop and sell diagnostics for several target diseases using ribozymes. IntelliGene is a private, venture-backed biotechnology company headquartered in Jerusalem, Israel with an office in Sudbury, Massachusetts. IntelliGene is developing diagnostic products using ribozymes created using a process called in vitro evolution. The agreement provides for IntelliGene to develop diagnostic tests initially against six infectious diseases in their laboratories in Jerusalem and elsewhere, and to develop, make and sell diagnostic products based on these tests, either alone or through sublicenses. We received a license fee and will receive royalties on product sales. We do not expect to receive royalties, if any, from this license for a substantial period of time.

Our competition

We are engaged in the rapidly changing business of developing treatments for human disease through gene modulation. Competition among entities attempting to develop gene modulation products for disease treatment is intense and is expected to increase. We face direct competition from other companies engaged in the research, development and commercialization of ribozyme-based technology as well as competition from companies attempting other methods of gene expression control, such as antisense and triplex. In addition, we compete with large pharmaceutical companies and established biotechnology firms, many of whom are developing new products for the treatment of the same diseases targeted by us. In some cases, those companies have already commenced clinical trials for their products. Many of these companies have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies and clinical trials, obtaining regulatory approvals and marketing than us. Our collaborators and licensees may be conducting research and development programs directed at the same diseases that we are targeting. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies. In addition, companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before their competitors may achieve a significant competitive advantage.

Academic institutions, governmental agencies and other public and private research organizations also conduct research, seek patent protection and establish collaborative arrangements for products and clinical development and marketing. These companies and institutions compete with us in recruiting and retaining highly qualified scientific and management personnel.

In addition, we face competition based on product efficacy, safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capability, reimbursement coverage, price and patent position.

Our patents and proprietary technology

Protecting patents and other proprietary rights is crucial to developing our business. In addition to patents, we rely upon trade secrets, know-how and continuing technological innovations in the design, synthesis, and purification of ribozymes and in nucleic acid chemistry. We also rely on licensing opportunities to develop and maintain our competitive position. It is our policy to file patent applications when appropriate to protect technology, inventions, and improvements that are considered important in the development of our business.

At the core of our technology are inventions and patents of the University of Colorado developed by Dr. Thomas R. Cech and various of his associates. Pursuant to the University's policies, these inventions and the related patents (the "Cech Technology") became the property of the University. The Cech Technology was assigned to the University's affiliate, University Research Corporation ("URC"), which in turn assigned the rights to license parts of the Cech Technology to Competitive Technologies, Inc. United States Biochemical Corporation ("USB") licensed the Cech Technology pursuant to two sublicenses. We have entered into a license with URC and sublicenses with USB and Competitive Technologies pursuant to which we have obtained the exclusive (except for non-commercial academic research) worldwide right to the Cech Technology to, among other things, make, use and sell ribozymes and ribozyme products covered by the licensed patents. The URC license and USB sublicense are fully paid. The Competitive Technologies license provides for the payment of a royalty on sales of ribozyme products covered by the licensed patents. We may grant sublicenses to the licensed technology subject to the payment to Competitive Technologies of a share of royalty income from such sublicenses or a royalty on sales from sublicensed products, methods or services, depending on the particular licensed patents involved. In addition, we must pay Competitive Technologies a share of any option fee, license fee, prepaid royalty or other "front-end" fee other than research and development funding paid in connection with such sublicense.

In September 1993, we were granted a right of first refusal to license any new inventions, improvements and patents related to ribozyme technology developed by Dr. Cech or others at the University, in exchange for payments. To maintain this right, we agreed to fund research at CU through an unrestricted grant of $750,000 payable in various installments over a five-year period. This grant has been paid in full. In addition, we have agreed to pay CU a fee for each invention accepted by us under the license.

As part of our overall intellectual property strategy, we selectively enter into agreements with academic institutions either to license pre-existing technology or to support the development of new technologies and gain the commercial rights to such new technologies.

As a result of these licenses and sublicenses, and our own internal research, we currently have the rights to 84 issued or allowed patents, and more than 100 patent applications under consideration worldwide. This includes exclusive worldwide rights to 61 patents issued in the United States, 3 patents issued in Europe, 1 patent issued in Japan and 8 patents issued in Australia. In addition, Notices of Allowance have been received for at least 11 patents from the United States Patent and Trademark Office. Six of the 61 United States issued patents, 1 European patent and 1 Japanese patent cover enzymatic RNA and the use of an enzymatic RNA to cleave a single stranded RNA (the "Cech Patents"). The Cech Patents grant us the right to exclude others from practicing ribozyme technology as it is currently known to us in the United States, Europe and Japan irrespective of the application, the method of production, the method of purification, or the ribozyme motif used. Unless extended, the Cech Patents will expire in December 2008 in the United States and December 2007 in Europe and in Japan. The additional issued patents cover both ribozyme technology (e.g., ribozyme design, synthesis, chemical modifications, delivery, ribozyme motifs, vector production, target site selection) as well as application to specific therapeutic targets.

In addition, we have filed or hold exclusive licenses to more than 100 pending United States and related foreign applications. Our patent portfolio includes approximately 40 United States applications for various areas of interest in human therapeutics and diagnostics and agricultural uses. The portfolio also includes

approximately 80 United States applications related to the chemistry, design, optimization, manufacture and delivery of ribozyme products. These patents collectively extend our ribozyme patent coverage well beyond the life of the Cech Patents.

We have filed opposition documents against two patents granted to a competitor in Europe. Opposition proceedings against two of our European and Japanese patents have been initiated by our competitors. The Japanese Opposition Division has rejected competitor oppositions, and has issued a notification that it will maintain our Japanese patent without change. The opposition proceedings against our European patent are still ongoing. In addition, we anticipate interference proceedings against some of our patents and patent applications in the United States. Our patents and applications are soundly based, but the extent of protection may vary in different countries and no assurance can be given that any patent will provide commercially significant protection or will not be challenged, invalidated, or circumvented. Litigation could prove necessary to protect our patent position, which would result in our incurring substantial costs as well as diverting our efforts. Atugen will be responsible for the patent prosecution costs for patents transferred to it.

Competitors or other patent holders could bring legal actions against us involving our patents, patent applications or rights to use proprietary technology. If any actions succeed, in addition to any potential liability for damages, we could be enjoined from selling the affected product, or be required to obtain a license in order to continue to manufacture or market the product. There can be no assurance that we would prevail in any such action or that any license required under any such patent would be made available on acceptable terms, if at all. There has been, and there will likely continue to be, significant litigation in the pharmaceutical industry regarding patent and other intellectual property rights. Any additional litigation could consume a substantial portion of the our resources regardless of the outcome.

Government regulation of our drug development activities

The development, manufacture and potential sale of therapeutics is subject to extensive regulation by United States and foreign governmental authorities. In particular, pharmaceutical products undergo rigorous preclinical and clinical testing and to other approval requirements by the FDA in the United States under the federal Food, Drug and Cosmetic Act and the Public Health Service Act and by comparable agencies in most foreign countries.

Before testing agents with potential therapeutic value in healthy human test subjects or patients may begin, stringent government requirements for preclinical data must be satisfied. The data, obtained from studies in several animal species, as well as from laboratory studies, are submitted in an IND application or its equivalent in countries outside the United States where clinical studies are to be conducted. Preclinical data must provide an adequate basis for evaluating both the safety and the scientific rationale for the initiation of clinical trials.

Clinical trials are typically conducted in three sequential phases, although these phases may overlap. In Phase I, which frequently begins with initial introduction of the compound into healthy human subjects prior to introduction into patients, the product is tested for safety, adverse affects, dosage, tolerance, absorption, metabolism, excretion and clinical pharmacology. Phase II typically involves studies in a small sample of the intended patient population to assess the efficacy of the compound for a specific indication to determine dose tolerance and the optimal dose range as well as to gather additional information relating to safety and potential adverse effects. Phase III trials are undertaken to further evaluate clinical safety and efficacy in an expanded patient population at geographically dispersed study sites to determine the overall risk-benefit ratio of the compound and to provide an adequate basis for product labeling. Each trial is conducted in accordance with certain standards under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND.

Data from preclinical and clinical trials are submitted to the FDA as an NDA for marketing approval and to other health authorities as a marketing authorization application. The process of completing clinical

trials for a new drug is likely to take a number of years and requires the expenditure of substantial resources. Preparing an NDA or marketing authorization application involves considerable data collection, verification, analysis and expense. There can be no assurance that FDA or any other health authority approval will be granted on a timely basis, if at all. The approval process is affected by a number of factors, primarily the risks and benefits

demonstrated in clinical trials as well as the severity of the disease and the availability of alternative treatments. The FDA or other health authorities may deny an NDA or marketing authorization application if the authority's regulatory criteria are not satisfied or may require additional testing or information.

Even after initial FDA or other health authority approval has been obtained, further studies, including Phase IV post-marketing studies, may be required to provide additional data on safety and will be required to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested. Also, the FDA or other regulatory authorities may require post-marketing reporting to monitor the side effects of the drug. Results of post-marketing programs may limit or expand the further marketing of the products. Further, if there are any modifications to the drug, including changes in indication, manufacturing process or labeling or a change in manufacturing facility, an application seeking approval of such changes will be required to be submitted to the FDA or other regulatory authority.

Whether or not FDA approval has been obtained, approval of a product by regulatory authorities in foreign countries must be obtained prior to commencing commercial sales of the product in such countries. The requirements governing the conduct of clinical trials and product approvals vary widely from country to country, and the time required for approval may be longer or shorter than that required for FDA approval. Although there are some procedures for unified filings for certain European countries, in general, each country at this time has its own procedures and requirements. Further, the FDA regulates the export of products produced in the United States and may prohibit the export of such products even if these are approved for sale in other countries.

In addition to FDA requirements, the National Institute of Health ("NIH") has established guidelines for research involving recombinant DNA molecules, which are utilized by us and our collaborators and licensees. These guidelines apply to all recombinant DNA research within the United States or its territories which is conducted at or supported by the NIH. Under current guidelines, proposals to conduct clinical research involving gene therapy which is supported by the NIH must be reviewed by the NIH Recombinant DNA Advisory Committee. Our vector delivery of ribozymes will need to be reviewed by this Committee.

We are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resources Conservation and Recovery Act and other present and potential future federal, state and local regulations.

Completing the multitude of steps necessary before marketing can begin requires the expenditure of considerable resources and a lengthy period of time. Delay or failure in obtaining the required approvals, clearances or permits by us, our corporate partners or our licensees would have a material adverse affect on our ability to generate sales or royalty revenue. The impact of new or changed laws or regulations cannot be predicted with any accuracy.

Our manufacturing and marketing strategies

To support our preclinical and clinical trial manufacturing requirements, we constructed manufacturing facilities that we believe comply with applicable regulatory requirements. We have also established operational quality assurance and quality control procedures. We believe that our existing facilities and those available from contract manufacturers will be satisfactory for production of ribozymes needed through clinical trials for our products currently in development.

We do not currently have the facilities or means to manufacture, market, distribute or sell on a commercial scale any of products we may develop. We will need to develop our own facilities or contract

with third parties for the manufacture of products. We have expanded our quality control and quality assurance program internally, including adopting a set of standard operating procedures designed to assure that any products manufactured by or for us are made in accordance with cGMP and other applicable domestic and foreign regulations.

In connection with establishing of our manufacturing capabilities, we have entered into agreements with Pharmacia Biotech and Protogene. In November 1995, we agreed to collaborate with Pharmacia Biotech to develop better synthesis and purification methods for the preparation of modified amidites and chimeric oligonucleotides on a large scale. The goal of the collaboration is to reduce the cost of manufacturing ribozymes and other oligonucleotides products that use amidites. Pharmacia Biotech, a subsidiary of Pharmacia & Upjohn, Inc., has

expertise in the manufacture of oligonucleotides synthesis and purification instrumentation and software. Under the terms of the collaboration, Pharmacia Biotech is providing us with synthesis instrumentation and software, research funding and milestone payments, a portion of which may be set-off against future royalties payable to us.

In December 1996, we entered into an agreement with Protogene, a private biotechnology company, to develop an instrument allowing high throughput synthesis of non-DNA oligonucleotides. Under the terms of the agreement, we have purchased an instrument manufactured by Protogene.

We expect to market and sell any products developed, at least initially, directly and through co-promotion or other licensing arrangements with third parties, including our collaborators. In some markets, we may enter into distribution or partnership agreements with pharmaceutical or biotechnology companies that have large, established sales organizations.

Our Employees

As of March 15, 1999, we had 65 full-time employees, including a technical scientific staff of 50. Our future performance depends significantly on the continued service of our key personnel. None of our employees are covered by collective bargaining arrangements. We believe our employee relations are good.

Legal Proceedings

We are not actively involved in any litigation which could reasonably be expected to have a material adverse effect on our business or the results of our operations.

Properties

We lease approximately 30,000 square feet of laboratory, manufacturing and office space at 2950 Wilderness Place, Boulder, Colorado, under an operating lease that lasts through June 2007. This facility will be sufficient to meet our needs at least through 2000.

Our Scientific Advisory Board

We are assisted in our research and development activities by our Scientific Advisory Board composed of leading scientists who meet with us several times each year to review our research and development activities, and to discuss technological advances and our business. We also have collaborative relationships with several board members that further advance our product development. Our current Scientific Advisory Board members are:

Thomas R. Cech, Ph.D. — Distinguished Professor, Department of Chemistry & Biochemistry, University of Colorado; Chairman, SAB

Gerald Joyce, M.D., Ph.D. — Professor, Department of Molecular Biology, Scripps Research Institute

Edward Mocarski, Ph.D. — Professor and Chairman, Departments of Microbiology & Immunology, Stanford University

Gary Nabel, M.D., Ph.D. — Professor, Departments of Internal Medicine and Biological Chemistry, University of Michigan

Bruce Sullenger, Ph.D. — Assistant Professor, Departments of Experimental Surgery and Genetics, Duke University

Olke C. Uhlenbeck, Ph.D. — Professor, Department of Chemistry and Biochemistry, University of Colorado

Each member has entered into an exclusive consulting agreement with Ribozyme Pharmaceuticals in the field of ribozymes and signed confidentiality and non-disclosure agreements. In 1998, they each received:

- an annual retainer of $4,000 paid quarterly,
- an honorarium of $1,000 per day for meetings attended, and

. options for 4,000 shares of our common stock, which vest ratably over three years.

MANAGEMENT

Directors and Executive Officers

The directors and executive officers of Ribozyme Pharmaceuticals are as follows:

Name	Age	Position
Ralph E. Christoffersen, Ph.D. (1)	61	Chief Executive Officer, President and Director
Lawrence E. Bullock	43	Vice President of Administration and Finance, Chief Financial Officer and Secretary
Alene A. Holzman	42	Vice President of Business Development and General Manager of Target Validation and Discovery Business
Thomas H. Rossing, M.D.	49	Vice President of Product Development
Nassim Usman, Ph.D.	39	Vice President of Research
David T. Morgenthaler (1) (2)	79	Chairman of the Board
Jeremy L. Curnock Cook (1) (3)	49	Director
Anthony B. Evnin, Ph.D. (1) (2)	58	Director
David Ichikawa (3)	46	Director
Anders P. Wiklund (2) (3)	58	Director

(1) Member of the Executive Committee.
(2) Member of the Compensation Committee.
(3) Member of the Audit Committee.

Ralph E. Christoffersen, Ph.D., has served as Chief Executive Officer, President and Director of Ribozyme Pharmaceuticals since June 1992. From 1989 to June 1992, Dr. Christoffersen was Senior Vice President and Director of U.S. Research at SmithKline Beecham Pharmaceuticals, a pharmaceutical company. From 1983 to 1989, he held senior management positions in research at The Upjohn Company, a pharmaceutical company. Prior to joining The Upjohn Company, Dr. Christoffersen served as a Professor of Chemistry and Vice Chancellor for Academic Affairs at the University of Kansas, and as President of Colorado State University. He received his Ph.D. in physical chemistry from Indiana University.

Lawrence E. Bullock has served as Vice President of Administration and Finance, Chief Financial Officer and Secretary, since January 1996. From December 1990 to January 1996, Mr. Bullock was Chief Financial Officer, Director of Finance and Administration and Secretary of La Jolla Pharmaceutical Company, a biopharmaceutical company. Mr. Bullock received his M.B.A. from the University of Utah.

Alene A. Holzman has served as Vice President of Business Development and General Manager of Target Validation and Discovery Business since April 1997. From January 1990 to March 1997, Ms. Holzman was Vice President of ChemTrak Corporation, a medical technology firm, where she was responsible for finance, business development and marketing and sales. From 1987 to 1990, she was Vice President of CytoSciences, Inc., a biomedical company, and from 1981 to 1987 she was Vice President of Marketing and Sales for Hana Biologics, Inc. (now Cell Genesys Corporation), a biotechnology firm. Ms. Holzman received her M.B.A. from the University of California at Berkeley.

Thomas H. Rossing, M.D., has served as Vice President of Product Development since July 1997. From July 1996 to July 1997, Dr. Rossing was Vice President of

Clinical Development and Regulatory Affairs at GeneMedicine, Inc., a biotechnology company. From March 1993 to July 1996, Dr. Rossing was Director of International Respiratory Clinical Research at GlaxoWellcome, a pharmaceutical company. He has also

served as Director of Clinical Pharmacology and Worldwide Regulatory Liaison at Merck Research Laboratories, a pharmaceutical company, and a staff physician at Brigham and Women's Hospital in Boston, Massachusetts. He received his M.D. degree from Harvard University. Dr. Rossing announced that he is retiring effective August 31, 1999.

Nassim Usman, Ph.D., has served as Vice President of Research since May 1996. From April 1994 until May 1996, Dr. Usman served as Director of Chemistry and Biochemistry Research at Ribozyme Pharmaceuticals and from September 1992 until April 1994 Dr. Usman served as Senior Scientist in Chemistry and Biochemistry. From January 1987 to September 1992, Dr. Usman was a Postdoctoral Fellow and Scientist in the Departments of Biology and Chemistry at the Massachusetts Institute of Technology. Dr. Usman received his Ph.D. in chemistry from McGill University.

David T. Morgenthaler has served as a director since February 1992 and was elected Chairman of the Board in December 1995. Mr. Morgenthaler was a founder of and has been Managing Partner of Morgenthaler Ventures, a private venture capital firm, since 1968. He has been a director of a number of public and private companies. Mr. Morgenthaler received his M.S. degree from the Massachusetts Institute of Technology.

Jeremy L. Curnock Cook has served as a director since July 1995. Mr. Cook is a director of Rothschild Asset Management, an investment fund, and has been responsible for the Rothschild Bioscience Unit since 1987. Mr. Cook founded the International Biochemicals Group in 1975 which he subsequently sold to Royal Dutch Shell in 1985, remaining as Managing Director until 1987. He is also a director of the International Biotechnology Trust plc, Creative BioMolecules Inc., Targeted Genetics Inc., Cantab Pharmaceuticals plc, Sugen, Inc., Cell Therapeutics, Inc., Amrad Corporation, Vanguard Medica plc, Angiotech Pharmaceuticals, Inc., Inflazyme Pharmaceuticals, Inc. and Biocompatibles International plc. Mr. Cook received an M.A. in Natural Sciences from Trinity College Dublin.

Anthony B. Evnin, Ph.D., has served as a director since February 1992. Dr. Evnin has been a General Partner of Venrock Associates, a venture capital partnership, since 1975. He is also a director of AxyS Pharmaceutical Corporation, Centocor, Inc., Opta Food Ingredients, Inc., and Triangle Pharmaceuticals, Incorporated. Dr. Evnin received his Ph.D. from the Massachusetts Institute of Technology.

David Ichikawa has served as a director since May 1998. Mr. Ichikawa has been employed by Chiron Corporation, a biotechnology company, since September 1994 and is currently Vice President of Finance and Operations of Chiron Technologies. He has also held management positions at Boehringer Mannhiem Corporation and Chiron (Cetus) Corporation. Mr. Ichikawa received his M.B.A. from the University of California at Berkeley.

Anders P. Wiklund has served as a director since August 1994. Since January 1997, Mr. Wiklund has been the principal of Wiklund International, an advisory firm to the biotechnology and pharmaceutical industries. From 1967 through 1996, Mr. Wiklund served in numerous executive positions for the Kabi and Pharmacia group of companies, including President and CEO of Kabi Vitrum Inc. and Kabi Pharmacia, Incorporated. Mr. Wiklund is also a director of Trega Bioscience, Inc., Medivir, A.B. and InSite Vision, Inc., as well as private company boards. Mr. Wiklund received a Master of Pharmacy degree from the Pharmaceutical Institute in Stockholm.

Executive Compensation

The following table summarizes the compensation paid to or earned by our Chief Executive Officer and our other four most highly compensated executive officers whose annual compensation exceeded $100,000 in 1998 ("Named Executive Officers").

Summary Compensation Table

<TABLE>
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	Annual Compensation			Long-term Compensation

Name and Principal Position	Year	Salary($)	Bonus($)	Other Annual Comp.($)	Restricted Stock Awards(#)	Shares Underlying Options Granted(#)	All Other Comp.($)
Ralph E. Christoffersen, Ph.D.	1998	285,670	50,000	37,862(1)		198,748(2)	4,998(3)
Chief Executive Officer and	1997	269,520	50,000	45,000(1)	--	129,450	4,744(3)
President	1996	247,248	--	70,000(1)	188,100(4)	97,770	153,910(4)
Lawrence E. Bullock	1998	150,800	25,000	75,883(5)	--	85,957(2)	4,998(3)
Vice President of Administration	1997	136,254	25,000	35,524(5)	--	37,500	4,744(3)
and Finance, CFO and Secretary	1996	118,433	15,000	24,993(5)	--	66,000	--
Alene A. Holzman(6)	1998	156,900	6,500	37,721(7)	--	100,000(2)	4,998(3)
Vice President of Business	1997	108,557	12,500	28,389(7)	--	80,000	3,494(3)
Development and General Manager of Target Validation and Discovery Business							
Thomas H. Rossing, M.D.(8)	1998	250,650	--	34,000(9)	--	110,624(2)	4,998(3)
Vice President of Product Development	1997	105,859	22,000	84,008(9)	--	107,500	--
Nassim Usman, Ph.D.	1998	183,038(11)	23,000	25,841(10)		99,167(2)	4,998(3)
Vice President of Research	1997	158,004	--	25,397(10)	--	45,000	4,744(3)
	1996	132,919	25,000	20,499(10)	--	53,892	--

</TABLE>

(1) Includes (a) $50,000 in 1996 and $25,000 in each of 1997 and 1998 for forgiveness of a loan made to Dr. Christoffersen for relocation expenses; and (b) $20,000 in each of 1996 and 1997 and $12,862 in 1998 to assist him with the tax liability relating to the loan forgiveness.

(2) Includes shares granted in connection with the stock option repricing in 1998. See "Stock Option Plan--Repricing." All Named Executive Officers received an option to purchase 0.75 share of common stock in exchange for an option representing one share.

(3) Matching contributions in common stock made by Ribozyme Pharmaceuticals under our 401(k) Salary Reduction Plan.

(4) Dr. Christoffersen received a bonus of $342,010, payable $153,910 in cash and $188,100 in shares of common stock (18,810 shares at our initial public offering price of $10.00 per share), upon closing of our initial public offering in April 1996.

(5) Includes (a) $9,058 and $9,641 in 1996 and 1997, respectively, representing implied interest related to an interest-free loan made to Mr. Bullock for relocation expenses; (b) $15,000 in each of 1997 and 1998 for partial forgiveness of the loan; (c) $7,883 in each of 1997 and 1998 for taxes relating to the loan; (d) $3,000 in each of 1997 and 1998 as reimbursements for dependent daycare expenses; and (e) $15,935 and $50,000, in 1996 and 1998, respectively, to reimburse Mr. Bullock for relocation expenses.

(6) Ms. Holzman joined Ribozyme Pharmaceuticals on April 1, 1997.

(7) Includes (a) $10,036 in 1997 representing implied interest related to an interest-free loan made to Ms. Holzman for relocation expenses; (b) $15,853 and $9,721 in 1997 and 1998, respectively, to reimburse Ms. Holzman for relocation expenses; (c) $25,000 in 1998 for partial forgiveness of the loan; and (d) $2,500 and $3,000 in 1997 and 1998, respectively, as reimbursements for dependent day care expenses.

(8) Dr. Rossing joined Ribozyme Pharmaceuticals on July 28, 1997.

(9) Includes (a) $14,901 in 1997 representing implied interest related to an interest-free loan made to Dr. Rossing for relocation expenses; (b) $34,000 in 1998 for partial forgiveness of the loan; and (c) $69,107 in 1997 to reimburse Dr. Rossing for relocation expenses.

(10) Includes (a) $20,499 in 1996 representing implied interest related to an interest-free loan made to Dr. Usman for relocation expenses; (b) $15,000 in each of 1997 and 1998 for partial forgiveness of the loan; (d) $7,883 in each of 1997 and 1998 for taxes relating to the loan; and (d) $2,496 in each of 1997 and 1998 as reimbursements for dependent day care expenses.

(11) Includes $13,988 in additional salary for Dr. Usman's three month temporary position as Vice President of Atugen.

Stock Option Plan

In March 1996 we amended, restated and merged our stock option plans and named the resulting plan the 1996 Stock Option Plan (the "Plan"). Currently, 1,478,493 shares of our common stock are reserved for issuance under the Plan. As of March 15, 1999, options to purchase 1,386,487 shares were outstanding under the Plan. The Plan will terminate in January 2006, unless earlier terminated by the Board of Directors. The purpose of the Plan is to:

- attract and retain qualified personnel,
- provide additional incentives to our employees, officers, directors and consultants, and
- promote the success of our business.

Under the Plan, we may grant or issue incentive stock options and supplemental (non-qualified) stock options to our consultants, employees, officers and directors.

Administration. Our Board has delegated administration of the Plan to a Compensation Committee comprised of three independent directors (see "Board Committees"). Subject to the limitations set forth in the Plan, the Board or the Compensation Committee has the authority to:

- select the persons to whom grants are to be made,
- designate the number of shares to be covered by each option,
- determine whether an option is an incentive stock option or a non-statutory stock option,
- establish vesting schedules, and
- subject to restrictions, specify the type of consideration to be paid upon exercise and to specify other terms of the options.

Terms. The maximum term of options granted under the Plan is ten years, however, the maximum term is five years for incentive options granted to a person who at that time owns 10% of the total combined voting power of all classes of stock. The aggregate fair market value of the stock with respect to which incentive stock options are first exercisable in any calendar year may not exceed $100,000 per optionee. Any portion in excess of $100,000 shall be treated as non-statutory stock options. Options granted under the Plan are non-transferable and generally expire upon the earlier of the stated expiration date or three months after the termination of an optionee's service to Ribozyme Pharmaceuticals. However, the expiration date would be 18 months in the event the optionee's employment terminates by reason of death, or 12 months in the event the optionee's employment terminates due to disability, or a longer or shorter period as may be specified in the option agreement.

Our Board has discretion in connection with a merger, consolidation, reorganization or similar corporate event where we are the surviving corporation to prescribe the terms and conditions for the modifications of the options granted under the Plan. If we are not the surviving corporation in the event of our dissolution or

liquidation, or our merger or consolidation, all outstanding options will terminate unless assumed by another corporation.

No specific vesting schedule is required under the Plan. The exercise price of incentive stock options must equal at least the fair market value of the common stock on the date of grant, except that the exercise price of incentive stock options granted to any person who at the time of grant owns stock possessing more than 10% of the combined voting power of all classes of stock must be at least 110% of the fair market value of the stock on the date of grant. The exercise price on non-statutory stock options under the Plan may be no less than 85% of the fair market value of the common stock on the date of grant.

Repricing. In September 1998 our Board of Directors approved a repricing of all employee stock options outstanding under the Plan. Pursuant to this repricing, each Named Executive Officer holding options received 0.75 option for each one option surrendered with a new vesting date and an exercise price of $3.00 per share. All non-executive employees who were option holders received one new option for each one option surrendered with a new vesting date and an exercise price of $3.00 per share. As a result of this repricing offer, 890,921 options were canceled and 747,060 options were granted effective September 18, 1998.

The following table contains information about stock options granted to each of the Named Executive Officers during 1998 under the Plan:

Option Grants in 1998

<TABLE>
<CAPTION>

	Individual Grants					
	Number of Shares Underlying Options Granted (#)(1)	% of Total Options Granted to Employees in 1998(2)	Exercise Price ($/Share)(3)	Expiration Date	Potential Realizable Value at Annual Rate of Stock Price Appreciation for Option Term(4) 5%($)	10%($)
<S>	<C>	<C>	<C>	<C>	<C>	<C>
Ralph E. Christoffersen.....	76,874(5)	6.7%	$3.00	09-18-08	145,037	367,552
	*76,874(5)	6.7	3.00	09-18-08	145,037	367,552
	22,500	2.0	5.63	12-02-08	79,665	201,887
	*22,500	2.0	5.63	12-02-08	79,665	201,887
	198,748	17.4				
Lawrence E. Bullock.....	39,395(5)	3.4	3.00	09-18-08	74,326	188,356
	*21,562(5)	1.9	3.00	09-18-08	40,681	103,093
	12,500	1.1	5.63	12-02-08	44,258	112,160
	*12,500	1.1	5.63	12-02-08	44,258	112,160
	85,957	7.5				
Alene A. Holzman.....	30,000(5)	2.6	3.00	09-18-08	56,601	143,437
	*30,000(5)	2.6	3.00	09-18-08	56,601	143,437
	20,000	1.8	5.63	12-02-08	70,814	179,455
	*20,000	1.8	5.63	12-02-08	70,814	179,455
	100,000	8.8				
Thomas H. Rossing.....	40,312(5)	3.5	3.00	09-18-08	76,056	192,741
	*40,312(5)	3.5	3.00	09-18-08	76,056	192,741
	15,000	1.3	5.63	12-02-08	53,110	134,592
	*15,000	1.3	5.63	12-02-08	53,110	134,592
	110,624	9.6				
Nassim Usman.....	44,542(5)	3.9	3.00	09-18-08	84,037	212,965
	*29,625(5)	2.6	3.00	09-18-08	55,893	141,644
	12,500	1.1	5.63	12-02-08	44,258	112,160
	*12,500	1.1	5.63	12-02-08	44,258	112,160
	99,167	8.7				

</TABLE>

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* These options become 100% vested upon the completion of various research or business performance milestones.

(1) All options, other than performance-based options which are indicated by *, vest in increments of 20% over a five-year period and first become exercisable on the first anniversary of the grant date. Options granted in connection with the stock option repricing first vest on September 18, 1999. The options are granted for a term of ten years, subject to earlier termination in events related to termination of employment.

(2) In 1998 we granted options representing an aggregate of 1,139,560 shares of our common stock to our employees, including the Named Executive Officers.

(3) The exercise price of each option was equal to the fair market value of the common stock on the date of the option grant as determined by the Board of Directors.

(4) Amounts reported in these columns show hypothetical gains that may be realized upon exercise of the options, assuming the market price of common stock appreciates at the specified annual rates of

appreciation, compounded annually over the term of the options. These numbers are calculated based upon rules promulgated by the SEC. Actual gains, if any, depend on the future performance of our common stock and overall market conditions.

(5) Shares granted in connection with the stock option repricing.

The following table contains information about the number and value of stock options held by each Named Executive Officer as of December 31, 1998. No other Named Executive Officer exercised any stock options during 1998. A stock option is "in-the-money" if the closing market price of our common stock exceeds the exercise price of the stock option. The value of "in-the-money" unexercised stock options set forth in the table represents the difference between the exercise price of these options and the closing sales price of our common stock on December 31, 1998, as reported by the Nasdaq National Market, $4.38 per share.

1998 Year-End Option Values

<TABLE>
<CAPTION>

Name	Number of Securities Underlying Unexercised Options at December 31, 1998(#) Exercisable/Unexercisable	Value of Unexercised In-the-Money Options at December 31, 1998($) Exercisable/Unexercisable
<S>	<C>	<C>
Ralph E. Christoffersen....	69,706/174,374	176,794/178,536
Lawrence E. Bullock.....	17,847/89,394	28,295/91,863
Alene A. Holzman.....	12,001/87,250	16,560/65,205
Thomas H. Rossing.....	9,000/101,624	12,420/98,841
Nassim Usman.....	28,265/85,885	47,537/84,288

</TABLE>

Employment agreements

Ralph E. Christoffersen. In May 1992, we entered into an employment agreement with Ralph E. Christoffersen, Ph.D., our President and Chief Executive Officer, which, as amended, currently provides for:

- an annual salary of $297,000,
- an annual performance-based cash bonus of up to $80,000,
- an interest-free loan of $250,000 which has been forgiven in its entirety,
- repayment of relocation expenses,
- stock options to acquire 74,444 shares of common stock at an exercise price of $0.45 per share which vest ratably over five years,
- stock options to acquire 31,446 shares of common stock at an exercise price of $0.45 per share which vested upon our completion of performance milestones,
- stock options for common stock as reflected in the tables in this "Management" section, and
- a bonus of $342,010, paid in cash and common stock upon the completion of our initial public offering in April 1996.

Dr. Christoffersen's agreement may be terminated upon his death, disability or for cause. If we terminate Dr. Christoffersen's employment, he is entitled to receive all accrued salary and benefits up to his termination and, unless he has been terminated for cause, nine months of severance pay at the same monthly rate as in effect at the time of his termination. If termination occurs after January 1, 2000, Dr. Christoffersen shall be paid a lump sum cash payment of up to $27,500.

Lawrence E. Bullock. In January 1996, we entered into an employment agreement with Lawrence E. Bullock, our Vice President of Administration and Finance, Chief Financial Officer and Secretary, which, as amended, currently provides for:

- an annual salary of $158,350,
- an annual performance-based cash bonus of up to 20% of his current salary,
- a signing bonus of $15,000,
- stock options for common stock as reflected in the tables in this "Management" section, and

- repayment of relocation expenses, including an interest-free loan of $75,000 made in 1996 and forgivable in five equal installments, grossed-up for taxes, as long as Mr. Bullock remains employed by us. The loan had an outstanding balance of $30,000 as of March 15, 1999.

If we terminate Mr. Bullock's employment without cause, he is entitled to six months' severance pay at his then current salary.

Nassim Usman, Ph.D. In May 1996, we entered into an employment agreement with Nassim Usman, Ph.D., our Vice President of Research, which, as amended, currently provides for:

- an annual salary of $177,925,
- an annual performance-based cash bonus of up to 20% of his current salary,
- stock options for common stock as reflected in the tables in this "Management" section, and
- an interest-free loan of $75,000 made in May 1996 and forgivable in five equal installments, grossed-up for taxes, as long as Dr. Usman remains employed by us. The loan had an outstanding balance of $45,000 as of March 15, 1999.

If we terminate Dr. Usman's employment without cause, he will be entitled to six months' severance pay at his then current salary.

Alene A. Holzman. In February 1997, we entered into an employment agreement with Alene A. Holzman, our Vice President of Business Development and General Manager of Target Validation and Discovery Business, which, as amended, currently provides for:

- an annual salary of $166,325,
- an annual performance-based cash bonus of up to 20% of her current salary,
- stock options for common stock as reflected in the tables in this "Management" section, and
- an interest-free loan of $75,000 made in June 1997 and forgivable in three equal installments as long as Ms. Holzman is employed by us. The loan had an outstanding balance of $50,000 as of March 15, 1999.

If we terminate Ms. Holzman's employment without cause, she is entitled to six months' severance pay at her then current salary.

Thomas H. Rossing. In July 1997, we entered into an employment agreement with Thomas H. Rossing, M.D., our Vice President of Product Development, which, as amended, currently provides for:

- an annual salary of $258,175,
- an annual performance-based cash bonus of up to 15% of his current salary,
- stock options for common stock as reflected in the tables in this "Management" section, and
- an interest-free loan of $100,000 made in September and 1997 forgivable in three equal installments as long as Dr. Rossing is employed by us. The loan had an outstanding balance of $66,000 as of March 15, 1999.

Dr. Rossing has given notice that he will retire from Ribozyme Pharmaceuticals on August 31, 1999. If we terminate Dr. Rossing's employment without cause prior to that time, he will be entitled to six months' severance pay at his then current salary.

Employee Benefits

Executive Bonus Plan. In March 1998, our Executive Bonus Plan was adopted by the Board of Directors. This Bonus Plan provides our executive officers with the opportunity to earn an annual bonus contingent upon their fulfillment of annual goals as determined by our Compensation Committee comprised of three independent directors. The Compensation Committee has complete authority to establish the goals for each executive officer, to interpret all provisions of

the Bonus Plan and to make all other determinations necessary or advisable for the administration of the Bonus Plan. The Compensation Committee may award each of our executive officers with an annual bonus comprised of one or more of the following:

- cash payment,
- stock options pursuant to our stock option plan, or
- forgiveness of any portion of the principal of interest-free loans provided to the executive officer.

Section 401(k) Plan. As part of our effort to attract and maintain high quality staff, we adopted a 401(k) Salary Reduction Plan and Trust on June 1, 1992. Our employees may make pre-tax elective contributions of up to 20% of their salary, subject to limitations prescribed by law. All contributions are paid to a trustee who invests for the benefit of members of the 401(k) Plan. In March 1997, the 401(k) Plan was amended to provide that we may match the employee's contributions with common stock. We may amend or terminate the 401(k) Plan at any time, subject to legal restrictions.

Employee Stock Purchase Plan. In March 1996, we adopted an Employee Stock Purchase Plan (the "Purchase Plan"), which authorizes the issuance of up to 300,000 share of our common stock to eligible employees. Generally, each offering lasts for twenty-four months, and purchases are made on each October 31 and April 30 during each offering. For example, the initial offering began on April 11, 1996, and terminated on April 30, 1998. Common stock is purchased for accounts of employees participating in the Purchase Plan at a price per share equal to the lower of:

- 85% of the fair market value of a share of common stock on the date of commencement of participation in the offering, or
- 85% of the fair market value of a share of common stock on the date of purchase.

Generally, all regular employees, including executive officers, may participate in the Purchase Plan and may authorize payroll deductions of up to 15% of their base compensation for the purchase of common stock under the Purchase Plan. Our Board of Directors has the authority to terminate the Purchase Plan at its discretion. As of March 1, 1999, 99,832 shares had been issued pursuant to the Purchase Plan.

Director Compensation

Fees. All non-employee directors receive a fee of:

- $1,000 per day for each Board or Committee meeting attended, and
- $500 per day for participating telephonically in a meeting of the Board or a Committee.

Stock Options. Non-employee directors may also receive stock options for 5,000 shares of our stock annually under our stock option plan. In 1997 and 1998, each non-employee director was granted an option to purchase 5,000 shares. The options vest after one year of service. In addition, Mr. Wiklund received an option to purchase 4,444 shares in June 1994, of which 1,111 shares vested immediately and the remaining 3,333 shares vest in increments of 20% over five years starting in 1995.

Board Committees

The Board has established an Audit Committee, a Compensation Committee and an Executive Committee. The Executive Committee, consisting of Messrs. Morgenthaler (Chairman) and Cook and Drs. Christoffersen and Evnin, manages and operates our business.

The Compensation Committee, consisting of Dr. Evnin (Chairman) and Messrs. Morgenthaler and Wiklund:

- reviews and recommends for Board approval grants of options pursuant to our stock option plan,
- decides salaries and incentive compensation for our employees and consultants, and
- recommends compensation for executive officers.

The Audit Committee, consisting of Messrs. Ichikawa (Chairman), Cook and Wiklund:

- recommends to the Board the selection of independent auditors,
- reviews the results and scope of the audit and other services provided by our independent auditors, and
- reviews and evaluates our audit and control functions.

Compensation Committee Interlocks

The members of our Compensation Committee have no interlocking relationships as defined under SEC regulations.

Director and Officer Indemnification and Liability

Pursuant to provisions of Delaware General Corporation Law ("DGCL"), we have adopted provisions in our certificate of incorporation which provide that our directors shall not be personally liable for monetary damages to us or our stockholders for breach of fiduciary duty as a director, except for liability:

- for any breach of the director's duty of loyalty to us or our stockholders,
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law,
- under Section 174 of the DGCL relating to improper dividends or distributions, and
- for any transaction from which the director derived an improper personal benefit.

This limitation of liability does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our bylaws authorize us to indemnify our officers, directors, employees and agents to the extent permitted by the DGCL. Pursuant to Section 145 of the DGCL, which empowers us to enter into indemnification agreements with our officers, directors, employees and agents, we have entered into separate indemnification agreements with our directors and executive officers which may, in some cases, be broader than the specific indemnification provisions contained in the DGCL. The indemnification agreements may require us to indemnify the executive officers and directors against liabilities that may arise by reason of their status or service as directors or executive officers, other than liabilities arising from acts or omissions not in good faith or willful misconduct, and to advance expenses incurred as a result of any proceeding against them as to which they could be indemnified.

There is no pending litigation or proceeding involving any of our directors, officers, employees or agents where indemnification will be required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

CERTAIN TRANSACTIONS

We believe that the following transactions were in our best interests. As a matter of policy, these transactions were, and all future transactions between Ribozyme Pharmaceuticals and any of our officers, directors or principal stockholders will be:

- approved by a majority of the independent members of our Board of Directors,
- entered into on terms no less favorable to Ribozyme Pharmaceuticals than could be obtained from unaffiliated third parties, and
- entered into in connection with bona fide business purposes.

Executive Loans. We made interest-free loans for relocation expenses to our executive officers when we hired them. We have forgiven all or a portion of the outstanding principal amount of each loan under the terms of each officer's employment agreement. See "Management--Employment Agreements."

<TABLE>
<CAPTION>

	Balance as of

Name	Loan Amount	March 15, 1999
<S>	<C>	<C>
Ralph E. Christoffersen, Ph.D.	$250,000(1)	$ 0
Lawrence E. Bullock.....	75,000(2)	30,000
Nassim Usman, Ph.D.	75,000(3)	45,000
Alene A. Holzman.....	75,000(4)	50,000
Thomas H. Rossing.....	100,000(5)	66,000

</TABLE>

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(1) $50,000 forgiven in each of June 1993, January 1995, January 1996 and January 1997, and $25,000 forgiven in each of January 1994 and January 1998.
(2) $15,000 forgiven in each of June 1997, January 1998 and January 1999.
(3) $15,000 forgiven in each of June 1997 and May 1998.
(4) $25,000 forgiven in March 1998.
(5) $34,000 forgiven in July 1998.

Chiron Transactions. Chiron and Ribozyme Pharmaceuticals granted each other licenses to technologies and agreed to undertake research activities pursuant to a collaboration agreement. Chiron purchased:

- 100,000 shares of our common stock for a purchase price of $3.60 per share,

- 107,095 shares of our Series E Preferred Stock for a purchase price of $37.35 per share, and

- a warrant at a price of $4.50 per warrant share, exercisable for 444,444 shares of our common stock for an exercise price of $40.50 per share.

In February 1996, we amended the warrant issuable to Chiron to reduce the exercise price from $40.50 per share to $22.50 per share. When we closed our initial public offering in April 1996, Chiron:

- purchased 377,202 shares of our common stock for $3,640,000 at the initial public offering price less one-half of the underwriting discount,

- paid us $1,800,000 to complete the purchase of its warrant, and

- received 35,127 additional shares of our common stock pursuant to anti-dilutive provisions.

Chiron also has a representative on our Board of Directors.

In May 1996, we entered into a second collaboration with Chiron for the use of ribozymes to characterize gene function. The collaborations give Chiron the right to develop and commercialize products that result from the collaboration, and entitle us to receive product development milestone payments and royalties on sales of commercial products. Chiron and Ribozyme Pharmaceuticals each pay a portion of the

research and development expenses of the collaboration, and we agreed to provide Chiron $1.8 million, which was paid in 1996, for research funding related to the proposed collaboration.

Schering AG Transaction. In April 1997, we entered into a research collaboration with Schering focusing on the use of ribozymes and related technologies for gene function validation. Schering AG purchased:

- 212,766 shares of our common stock for $2.5 million in May 1997, and

- 465,117 shares of our common stock for $2.5 million in 1998.

Separately, Schering AG provided loans of $2.0 million in both 1997 and 1998. We received an additional $1.0 million on this loan facility in January 1999. Schering AG will continue to provide loans of up to $2 million annually for each year through 2001, provided that the collaboration is continued in each of those years. The loans, which carry an interest rate of 8% per annum, are convertible into equity at Schering AG's option under certain circumstances. Principal and interest payments are deferred until maturity of the loans in April 2004.

In addition, Schering AG made research payments of $1.5 million in 1997 and $2.0 million in 1998 and, provided that the collaboration is continued, will make research payments of $2 million a year through 2001. All payments are subject to some restrictions, including receipt of third party consents. Upon payment of termination fees to us, the research collaboration may be terminated

at Schering AG's option at any time.

Atugen Transaction. In 1998, we and other investors formed Atugen. Financing for Atugen was accomplished through a combination of venture capital, an investment by us and German government grants and loans. We contributed $2.0 million in cash to Atugen. On December 31, 1998, we owned a 49.5% equity interest in Atugen. All five of our executive officers and two of our employees received shares of Atugen's common stock in the formation at no cost to them, for which we will receive a one-time compensation expense of approximately $81,000. Currently, these seven people hold 5.5% of Atugen's common stock.

As part of the formation, Atugen received exclusive royalty-free licenses to our extensive patents and technologies for target validation and discovery. We will receive a one-time $2.0 million up-front license payment in 1999. We also will be compensated for providing management and other services to Atugen under the terms of a services agreement.

PRINCIPAL STOCKHOLDERS

The following table summarizes information regarding the beneficial ownership of our outstanding securities as of March 15, 1999 (which includes shares that may be acquired on the exercise of stock options vested or warrants exercisable through May 15, 1999), by:

- each person or group that we know owns more than 5% of the outstanding shares of common stock,
- each of our directors,
- each Named Executive Officer listed in the Summary Compensation Table, and
- all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with rules of the SEC and includes shares over which the indicated beneficial owner exercises voting and/or investment power. Shares of common stock subject to options or warrants currently exercisable or exercisable within 60 days are deemed outstanding for computing the percentage ownership of the person holding the options but are not deemed outstanding for computing the percentage ownership of any other person. Except as otherwise indicated in the footnotes to this table, we believe that each stockholder identified in the table has sole voting and investment power with respect to all shares listed opposite their names. Unless otherwise indicated, the following officers, directors and stockholders can be reached at the principal offices of Ribozyme Pharmaceuticals.

<TABLE>
<CAPTION>

Name and Address	Number of Shares Beneficially Owned	Percentage of Shares Outstanding Before Offering	Percentage of Shares Outstanding After Offering
<S>	<C>	<C>	<C>
Schering Berlin Venture Corporation..... 3400 Change Bridge Road Monteville, New Jersey 07045	1,778,727(1)	17.3%	14.7%
Chiron Corporation..... 4560 Horton Street Emeryville, California 94608	1,063,868(2)	11.1%	9.3%
International Biotechnology Trust plc..... c/o Rothschild Asset Management, Ltd. Five Arrows House St. Swithin's Lane London EC4N 8NR England	1,012,633	11.0%	9.2%
Ralph E. Christoffersen, Ph.D.	159,434(3)	1.7%	1.4%
Jeremy L. Curnock Cook.....	1,017,633(4)	11.1%	9.3%
Anthony B. Evnin, Ph.D.	320,773(5)	3.5%	2.9%

David Ichikawa.....	0(6)	0%	0%
David T. Morgenthaler.....	377,874(7)	4.1%	3.4%
Anders P. Wiklund.....	8,733(8)	*	*
Lawrence E. Bullock.....	29,606(9)	*	*
Alene Holzman.....	15,799(10)	*	*
Thomas H. Rossing, M.D.	9,899(11)	*	*
Nassim Usman, Ph.D.....	30,746(12)	*	*
Executive officers and directors as a group (10 persons).....	1,970,497(13)	21.1%	17.7%

</TABLE>

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* Less than 1%.

(1) Includes 1,100,844 shares convertible from outstanding debt assuming a conversion price of $4.88 per share.
(2) Includes 444,444 shares issuable upon exercise of warrants.
(3) Includes options to purchase 69,706 shares.
(4) Includes options to purchase 5,000 shares and 1,012,633 shares held by the International Biotechnology Trust plc, for which Rothschild Asset Management, Ltd. ("Rothschild") acts as investment advisor. Mr. Cook is a director of Rothschild but disclaims beneficial ownership of these shares.
(5) Includes options to purchase 5,000 shares, 218,022 shares held by Venrock Associates and 97,751 shares held by Venrock Associates II, L.P. Mr. Evnin is a general partner of both partnerships and disclaims beneficial ownership of these shares except to the extent of his general partnership interests.
(6) Excludes 1,063,868 shares held by Chiron. Mr. Ichikawa is employed by Chiron and disclaims beneficial ownership of those shares.
(7) Includes options to purchase 5,000 shares, 362,874 shares held by Morgenthaler Venture Partners III and 10,000 shares held by Morgenthaler Family Partnership. Mr. Morgenthaler is a general partner of both partnerships and disclaims beneficial ownership of these shares except to the extent of his general partnership interests.
(8) Includes options to purchase 8,733 shares.
(9) Includes options to purchase 21,180 shares.
(10) Includes options to purchase 12,000 shares.
(11) Includes options to purchase 9,000 shares.
(12) Includes options to purchase 28,265 shares and 532 shares owned by Dr. Usman's spouse to which Dr. Usman disclaims beneficial ownership.
(13) Includes options to purchase 163,884 shares.

DESCRIPTION OF CAPITAL STOCK

Our Certificate of Incorporation provides for authorized capital stock of 25,000,000 consisting of 20,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share. The following summary of material provisions of our common stock and preferred stock is not complete and may not contain all the information you should consider before investing in the common stock. You should carefully read our Certificate of Incorporation which is filed as an exhibit to the registration statement of which this prospectus is a part.

Common Stock

Holders of common stock are entitled to one vote per share in the election of directors and on all other matters on which stockholders are entitled or permitted to vote. Holders of common stock are not entitled to cumulative voting rights. Therefore, holders of a majority of the shares voting for the election of directors can elect all the directors. Subject to the terms of any outstanding series of preferred stock, the holders of common stock are entitled to dividends in amounts and at times as may be declared by the Board of Directors out of funds legally available therefor. See "Dividend Policy." Upon liquidation or dissolution, holders of common stock are entitled to share ratably in all net assets available for distribution to stockholders after payment of any liquidation preferences to holders of preferred stock. Holders of common stock have no redemption, conversion or preemptive rights.

Warrants

As of March 15, 1999, we had warrants outstanding to purchase an aggregate of 487,458 shares (subject to adjustment) of common stock as follows:

<TABLE>
<CAPTION>

Shares	Exercise Price	Expiration Date
<S>	<C>	<C>
9,523	$15.75	10-01-00
1,270	$15.75	N/A*
11,111	$40.50	12-28-01
16,666	$22.50	09-01-03
2,222	$22.50	12-29-05
444,444	$22.50	04-17-06
2,222	$22.50	04-17-06

</TABLE>

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* These warrants are redeemable at our option at any time upon 15 days' notice for an aggregate price of $200.

Preferred Stock

The Board of Directors has the authority to issue up to 5,000,000 shares of preferred stock and to fix the price, rights, preferences, privileges and restrictions, including voting rights, of those shares without any further vote or action by the stockholders. The rights of the holders of our common stock will be subject to, and may be adversely affected by, the rights of the holders of any preferred stock that we may issue in the future. The issuance of preferred stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, may have the effect of delaying, deferring or preventing a change in control of Ribozyme Pharmaceuticals, may discourage bids for our common stock at a premium over the market price of the common stock and may adversely affect the market price of and the voting and other rights of the holders of the common stock. We have no present plans to issue shares of preferred stock.

Convertible Debt

As of March 15, 1999, there were 1,100,844 shares of common stock issuable upon conversion of the outstanding notes payable to Schering AG, assuming amounts of $5,372,117 and a conversion price of $4.88 per share based on the closing price of our common stock on March 15, 1999. Schering AG may convert the note into shares of common stock at any time.

Delaware Anti-Takeover Law and Charter Provisions

Provisions of our Certificate of Incorporation and Bylaws are intended to enhance continuity and stability in our Board of Directors and in our policies, but might have the effect of delaying or preventing a change in control of Ribozyme Pharmaceuticals and may make more difficult the removal of incumbent management even if the transactions could be beneficial to the interests of stockholders. A summary description of these provisions is below:

Authority to Issue Preferred Stock. The Certificate of Incorporation authorizes the Board, without stockholder approval, to establish and to issue shares of one or more series of preferred stock, each series having the voting rights, divided rates, liquidation, redemption, conversion and other rights as may be fixed by the Board.

Stockholder Actions and Meetings. The Bylaws direct that special meetings of the stockholders may only be called by a majority of the members of the Board of Directors, the Chairman of the Board of Directors, the President or the holders of not less than 10% of the total voting power of all shares of our capital stock entitled to vote in the election of directors. The Bylaws further provide that stockholders' nominations to the Board of Directors and other stockholder business proposed to be transacted at stockholder meetings must be timely received by us in a proper written form which meets the prescribed content requirements.

Limitation of Director Liability. Section 102(b)(7) of the Delaware General Corporation Law ("DGCL") authorizes corporations to limit or eliminate the personal liability of directors to corporations and their stockholders for monetary damages for breach of directors' fiduciary duty of care. Although Section 102(b) does not change directors' duty of care it enables corporations to limit available relief to equitable remedies such as injunction or rescission. Our Certificate of Incorporation limits the

liability of directors to the company or its stockholders (in their capacity as directors but not in their capacity as officers) to the fullest extent permitted by Section 102(b). Specifically, our directors will not be personally liable for monetary damages for breach of a director's fiduciary duty as a director, except for liability:

- for any breach of the director's duty of loyalty to us or our stockholders,
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law,
- for unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the DGCL, or
- for any transaction from which the director derived an improper personal benefit.

Indemnification. To the maximum extent permitted by law, our Bylaws provide for mandatory indemnification of directors and permit indemnification of our officers, employees and agents against all expense, liability and loss to which they may become subject or which they may incur as a result of being or having been our director, officer, employee or agent. In addition, we must advance or reimburse directors, and may advance or reimburse officers, employees and agents for expenses incurred by them as a result of indemnifiable claims.

Section 203 of the DGCL generally provides that a stockholder acquiring more than 15% of the outstanding voting stock of a corporation subject to the statute but less than 85% of the outstanding voting stock may not engage in some business combinations with the corporation for a period of three years after the date on which the stockholder became an interested stockholder unless:

- prior to this date, the corporation's Board of Directors approved either the business combination or the transaction in which the stockholder became an interested stockholder, or
- the business combination is approved by the corporation's Board of Directors and authorized at a stockholders' meeting by a vote of at least two-thirds of the corporation's outstanding voting stock not owned by the interested stockholder.

Under Section 203, these restrictions will not apply to some business combinations proposed by an interested stockholder following the earlier of the announcement or notification of a particular extraordinary transaction involving the corporation and a person who was not an interested stockholder during the previous three years or who became an interested stockholder with the approval of the corporation's Board of Directors, if the extraordinary transaction is approved or not opposed by a majority of the directors who were directors prior to any person becoming an interested stockholder during the previous three years or were recommended for election or elected to succeed those directors by a majority of those directors.

Section 203 defines the term "business combination" to encompass a wide variety of transactions with or caused by an interested stockholder, including transactions in which the interested stockholder receives or could receive a benefit on other than a pro rata basis with other stockholders, such as mergers, asset sales, issuances of additional shares to the interested stockholder, transactions with the corporation which increase the proportionate interest in the corporation directly or indirectly owned by the interested stockholder or transactions in which the interested stockholder receives other benefits.

The provisions of Section 203, together with the ability of our Board of Directors to issue preferred stock without further stockholder action, could delay or frustrate the removal of incumbent directors or a change in control of Ribozyme Pharmaceuticals. The provisions also could discourage, impede or prevent a merger, tender offer or proxy contest, even if this event would be favorable to the interests of stockholders. Our stockholders, by adopting an amendment to the Certificate of Incorporation or Bylaws, may elect not to be governed by Section 203 effective 12 months after adoption. Neither our Certificate of Incorporation nor Bylaws currently exclude us from the restrictions imposed by Section 203.

Registration Rights

As of March 15, 1999, the holders of approximately 677,883 shares of common

stock (the "Registrable Shares") are entitled to rights with respect to the registration of their shares for offer and sale to the public under the Securities Act. Under these provisions, holders of Registrable Shares may request that we file up to two registration statements under the Securities Act to register such shares. We may also be required to effect an unlimited number of registrations on Form S-3. Further, whenever we propose to register any of our shares under the Securities Act, we must allow the holders to include all Registrable Shares to be included in the registration, subject to limitations. We are required to bear all expenses (except underwriting discounts, selling commissions and stock transfer taxes) of all registrations.

Holders of warrants that are exercisable for 487,458 shares of our common stock have the same registration rights for these shares when they are issued.

Transfer Agent

The transfer agent and registrar for the common stock is American Stock Transfer & Trust Company, New York, New York.

PLAN OF DISTRIBUTION

We will enter into a placement agency agreement with Hambrecht & Quist LLC, pursuant to which Hambrecht & Quist LLC will agree to act as placement agent in connection with the offering. Hambrecht & Quist LLC will use its best efforts to introduce Ribozyme Pharmaceuticals to selected institutional and accredited investors who will purchase the shares. Hambrecht & Quist LLC has no obligation to buy from us any of the shares.

Hambrecht & Quist LLC will solicit indications of interest from investors for the full amount of the offering. We will not request effectiveness until Hambrecht & Quist LLC has informed us that it has received indications of interest for the full amount of the offering. Investor funds will not be accepted until the registration statement is declared effective.

All investor funds will be deposited into an escrow account set up at Citibank, N.A. for the benefit of the investors. Citibank, N.A., acting as escrow agent, will invest all funds it receives in accordance with Rule 15c2-4 under the Exchange Act of 1934, as amended. Any interest collected on the funds will be returned to Ribozyme Pharmaceuticals and investors on the closing date. Before the closing date, Citibank, N.A. will notify Ribozyme Pharmaceuticals and Hambrecht & Quist LLC that all of the funds to pay for the shares have been received. We will deposit the shares with the Depository Trust Company upon receiving a notice from Citibank, N.A. The shares will then be credited to the respective accounts of the investors.

If funds are not received for all of the shares being offered, then all funds that were deposited into escrow will be returned to investors and the offering will terminate.

We have agreed to indemnify Hambrecht & Quist LLC and other persons against some liabilities under the Securities Act. Hambrecht & Quist LLC has informed us that it will not engage in overallotment, stabilizing transactions or syndicate covering transactions in connection with the offering.

We have agreed to pay Hambrecht & Quist LLC a fee equal to 8% of the proceeds of this offering; provided, however, that we will not be obligated to pay Hambrecht & Quist LLC a fee in respect of the sale of any shares offered hereby to certain specified investors. We also agreed to reimburse Hambrecht & Quist LLC for up to $150,000 for expenses that it incurs in connection with the offering.

We have agreed not to issue, and our directors and officers have also agreed that they will not, directly or indirectly, offer, sell or otherwise dispose of or arrange to dispose of any shares of common stock or any securities convertible into or exercisable for, or any rights to purchase or acquire, our common stock, for a period of 90 days after the date of the prospectus without Hambrecht & Quist LLC's prior consent.

For a period of 18 months from the date of this prospectus, we have granted Hambrecht & Quist LLC (provided this offering is completed) the right to provide us with investment banking services on an exclusive basis in all matters for which we seek such services, with certain exceptions. Furthermore, we have agreed that, if within 18 months after the termination of Hambrecht & Quist LLC's engagement, we sell shares of our common stock to investors previously identified and/or contacted by Hambrecht & Quist LLC, then we will pay Hambrecht & Quist LLC, at the time of each such sale, an amount equal to the placement agency fee described above with respect our gross proceeds from each such sale.

Affiliates of Hambrecht & Quist LLC own 16,666 warrants to purchase our common stock at an exercise price of $9.00.

LEGAL MATTERS

The validity of the common stock offered by this prospectus will be passed upon for Ribozyme Pharmaceuticals by Rothgerber Johnson & Lyons, LLP, Denver, Colorado. Legal matters in connection with this offering will be passed upon for Hambrecht & Quist LLC by Stroock & Stroock & Lavan LLP, New York, New York.

EXPERTS

The financial statements of Ribozyme Pharmaceuticals at December 31, 1998 and 1997, and for each of the three years in the period ended December 31, 1998, appearing in this prospectus and Registration Statement have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

ADDITIONAL INFORMATION

Ribozyme Pharmaceuticals is subject to the informational requirements of the Securities Exchange Act, and, accordingly, files reports, proxy statements and other information with the SEC. These reports, proxy statements and other information filed with the SEC are available for inspection and copying at the public reference facilities maintained by the SEC at Judiciary Plaza, 450 Fifth Street, N.W., Washington, DC 20549, and at the SEC's Regional Offices: 500 West Madison Street, Suite 1400, Chicago, IL 60661 and 7 World Trade Center, New York, NY 10048. The public may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC maintains a site on the World Wide Web at "http://www.sec.gov" that contains reports, proxy statements and other information regarding registrants that file electronically with the SEC. In addition, these materials and other information concerning Ribozyme Pharmaceuticals can be inspected at the National Association of Securities Dealers, Inc., 1735 K Street, N.W., Washington, DC 20006.

We have filed with the SEC a registration statement on Form S-1 under the Securities Act to register with the SEC the securities we are offering with this prospectus. This prospectus is a part of that registration statement. As allowed by SEC rules, this prospectus does not contain all of the information contained in the registration statement or the exhibits to that registration statement. For further information with respect to Ribozyme Pharmaceuticals and the common stock we are offering, you should refer to the registration statement. Statements in this prospectus concerning the contents of any contract or other document are not necessarily complete. You should refer to the copy of the contract or other document filed with the SEC as an exhibit to the registration statement. With respect to each document filed with the SEC as an exhibit to the registration statement, you should refer to the exhibit for a more complete description of the matter involved.

INDEX TO FINANCIAL STATEMENTS

<TABLE>
<CAPTION>

</TABLE>

REPORT OF INDEPENDENT AUDITORS

To the Stockholders and Board of Directors
Ribozyme Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Ribozyme Pharmaceuticals, Inc. ("the Company") as of December 31, 1998 and 1997, and the related statements of operations, stockholders' equity, and cashflows for each of the three years in the period ended December 31, 1998. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with generally accepted auditing standards. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ribozyme Pharmaceuticals, Inc. at December 31, 1998 and 1997, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 1998 in conformity with generally accepted accounting principles.

/s/ ERNST & YOUNG LLP

Denver, Colorado
February 16, 1999

RIBOZYME PHARMACEUTICALS, INC.

BALANCE SHEETS

<TABLE>
<CAPTION>

	December 31	
	1998	1997
<S>	<C>	<C>
ASSETS		
Current assets:		
Cash and cash equivalents	$ 6,511,512	$ 15,302,775
Securities available-for-sale	--	799,616
Restricted cash	--	52,669
Accounts receivable	3,898,581	8,044
Notes receivable--related parties	118,466	127,341
Prepaid expenses and other	84,766	175,549
Total current assets	10,613,325	16,465,994
Property, plant, and equipment:		
Machinery and equipment	6,478,223	5,673,115
Leasehold improvements	3,582,664	3,567,106
Office furniture and equipment	1,065,049	1,007,104
	11,125,936	10,247,325
Accumulated depreciation	(6,903,742)	(5,290,160)
	4,222,194	4,957,165
Notes receivable--related parties	162,466	231,932
Deferred patent costs, net of accumulated amortization (1998--$271,328; 1997--$171,039)	2,905,575	2,510,705
Investment in Atugen Biotechnology GmbH	860,216	--
Other assets	460,515	684,245
Total assets	$ 19,224,291	$ 24,850,041
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable--trade	$ 750,514	$ 904,681
Accrued liabilities	396,143	245,956
Deferred revenue--current portion	400,000	--
Current portion of long-term debt	498,179	2,077,771
Total current liabilities	2,044,836	3,228,408
Deferred revenue--long-term portion	1,600,000	--
Long-term debt	200,455	698,633
Convertible debt	4,344,612	2,052,889

Commitments		
Stockholders' equity:		
Voting convertible preferred stock, $.01 par value; 5,000,000 shares authorized; no shares outstanding	--	--
Common stock, $.01 par value; 20,000,000 shares authorized; 9,181,455 and 8,607,022 shares issued and outstanding in 1998 and 1997, respectively	91,815	86,070
Additional paid-in capital	84,434,213	81,424,341
Accumulated deficit	(73,422,491)	(62,504,924)
Unrealized loss on securities available-for-sale	--	(5,064)
Deferred compensation	(69,149)	(130,312)
Total stockholders' equity	11,034,388	18,870,111
Total liabilities and stockholders' equity	$ 19,224,291	$ 24,850,041

See accompanying notes.

RIBOZYME PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS

	Year ended December 31		
	1998	1997	1996
Revenues:			
Collaborative agreements	$ 8,962,813	$ 1,976,500	$ 759,122
Grant and other income	25,045	6,642	13,981
Interest income	634,569	794,968	936,397
Total revenues	9,622,427	2,778,110	1,709,500
Expenses:			
Research and development	16,941,652	15,169,731	14,188,836
General and administrative	1,812,860	1,886,108	1,943,583
Interest expense	703,711	844,365	844,661
Total expenses	19,458,223	17,900,204	16,977,080
Equity in loss of unconsolidated affiliate	1,081,771	--	--
Net loss	$(10,917,567)	$(15,122,094)	$(15,267,580)
Net loss per share	$ (1.22)	$ (2.04)	$ (2.61)
Shares used in computing net loss per share	8,978,355	7,419,650	5,844,987

See accompanying notes.

RIBOZYME PHARMACEUTICALS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Preferred Stock		Additional Paid-In	Accumulated	Unrealized Loss on	Deferred	
	Shares	Amount	Shares	Amount	Capital	Deficit	Securities	Compensation	Total
Balance at December 31, 1995	982,501	$ 9,825	2,231,960	$ 22,321	$40,725,061	$(32,115,250)	$ --	$(163,989)	$ 8,477,968
Conversion of									

preferred stock in connection with initial public offering.....	2,231,960	22,321	(2,231,960)	(22,321)	--	--	--	--	--
Issuance of common stock relating to certain antidilution rights in connection with initial public offering.....	841,279	8,412	--	--	(8,412)	--	--	--	--
Issuance of common stock for cash --initial public offering, net of issuance costs of $816,990.....	2,300,000	23,000	--	--	20,550,010	--	--	--	20,573,010
Issuance of common stock for cash --other.....	510,829	5,108	--	--	3,762,048	--	--	--	3,767,156
Payment on warrants.....	--	--	--	--	1,800,000	--	--	--	1,800,000
Issuance of common stock for employee bonus.....	18,810	188	--	--	187,912	--	--	--	188,100
Issuance of common stock under employee stock purchase plan.....	15,842	158	--	--	131,172	--	--	--	131,330
Compensation for issuance of common stock and options....	--	--	--	--	162,530	--	--	(24,913)	137,617
Issuance of common stock for services...	2,083	21	--	--	23,413	--	--	--	23,434
Issuance of common stock relating to certain royalty agreements.....	45,000	450	--	--	539,550	--	--	--	540,000
Unrealized loss on securities available-for-sale.....	--	--	--	--	--	--	(9,214)	--	(9,214)
Net loss.....	--	--	--	--	--	(15,267,580)	--	--	(15,267,580)
Comprehensive income/(loss)..									(15,276,794)
Balance at December 31, 1996.....	6,948,304	69,483	--	--	67,873,284	(47,382,830)	(9,214)	(188,902)	20,361,821
Issuance of common stock for cash --public offering, net of issuance costs of $634,796.....	1,400,000	14,000	--	--	10,551,204	--	--	--	10,565,204
Issuance of common stock for cash.....	212,766	2,128	--	--	2,497,872	--	--	--	2,500,000
Issuance of common stock for cash --under stock option plan....	30,001	300	--	--	51,404	--	--	--	51,704
Issuance of common stock under employee stock purchase									

plan.....	29,875	298	--	--	310,303	--	--	--	310,601
Issuance of common stock under 401(k) plan-stock match.....	19,409	194	--	--	155,078	--	--	--	155,272
Cancellation of common stock relating to license agreement.....	(33,333)	(333)	--	--	333	--	--	--	--
Compensation for issuance of common stock and options....	--	--	--	--	(15,137)	--	--	58,590	43,453
Net loss.....	--	--	--	--	--	(15,122,094)	--	--	(15,122,094)
Change in unrealized loss on securities available-for-sale.....	--	--	--	--	--	--	4,150	--	4,150
Comprehensive income/(loss)..									(15,117,944)
Balance at December 31, 1997.....	8,607,022	86,070	--	--	81,424,341	(62,504,924)	(5,064)	(130,312)	18,870,111
Issuance of common stock for cash.....	465,117	4,651	--	--	2,495,349	--	--	--	2,500,000
Issuance of common stock for cash --under stock option plan....	21,689	217	--	--	45,545	--	--	--	45,762
Issuance of common stock under employee stock purchase plan.....	54,115	542	--	--	307,608	--	--	--	308,150
Issuance of common stock under 401(k) plan-stock match.....	33,512	335	--	--	190,371	--	--	--	190,706
Compensation for issuance of common stock and options....	--	--	--	--	(29,001)	--	--	61,163	32,162
Change in unrealized loss on securities available-for-sale.....	--	--	--	--	--	--	5,064	--	5,064
Net loss.....	--	--	--	--	--	(10,917,567)	--	--	(10,917,567)
Comprehensive income/(loss)..									(10,912,503)
Balance at December 31, 1998.....	$9,181,455	$91,815	--	$ --	$84,434,213	$(73,422,491)	$ --	$ (69,149)	$ 11,034,388

</TABLE>

See accompanying notes.

RIBOZYME PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

<TABLE>
<CAPTION>

	Year ended December 31		
	1998	1997	1996

<S>	<C>	<C>	<C>
Operating activities			
Net loss	$(10,917,567)	$(15,122,094)	$(15,267,580)
Adjustments to reconcile net loss to net cash used by operating activities:			
Depreciation	1,670,825	1,665,044	1,648,435
Amortization	92,107	74,051	40,747
Equity in loss of unconsolidated affiliate	1,081,771	--	--
Write-off of deferred patent costs	11,836	93,557	--
Compensation related to common stock and options	278,150	280,177	889,151
Compensation related to issuance of affiliate's stock	81,000	--	--
Compensation for forgiveness of notes receivable--related parties	126,466	92,466	92,466
Loss on sale of securities available-for-sale	--	--	13,140
Gain on sale of investment in corporate partner	(25,045)	--	--
Loss (gain) on disposal of equipment	541	(1,126)	--
Accrued interest included in convertible debt	291,723	52,889	--
Changes in operating assets and liabilities:			
Accounts receivable	(3,890,537)	65,978	(55,962)
Prepaid expenses and other	90,783	38,168	(55,882)
Other assets	(18,087)	(277,807)	(29,260)
Accounts payable--trade	(154,167)	351,777	3,866
Accrued liabilities	150,186	29,340	130,226
Deferred revenue	2,000,000		
Deferred gain	--	(5,515)	(27,130)
Net cash used by operating activities	(9,130,015)	(12,663,095)	(12,617,783)
Investing activities			
Additions to property, plant, and equipment	(936,395)	(2,213,311)	(1,541,412)
Additions to deferred patent costs	(506,994)	(660,581)	(558,895)
Sale (purchase) of investment in corporate partner	275,045	--	(250,000)
Proceeds from sale of equipment	--	2,600	--
Net sales of securities available-for-sale	804,680	3,748,005	(1,058,590)
Investment in unconsolidated affiliate	(2,022,987)	--	--
Transfer of restricted cash	52,669	242,733	914,528
Loan repayments--related parties	1,875	3,000	56,625
Loan advances--related parties	(50,000)	(175,000)	(156,500)
Net cash (used) provided by investing activities	(2,382,107)	947,446	(2,594,244)
Financing activities			
Net proceeds from sale of shares of common stock and of warrants	2,798,630	13,346,056	26,271,496
Payments under loan facilities	(2,077,771)	(1,480,677)	(1,316,027)
Borrowings under loan facilities	2,000,000	2,254,460	1,162,242
Payments on capital lease obligations	--	(152,093)	(768,014)
Net cash provided by financing activities	2,720,859	13,967,746	25,349,697
Net (decrease) increase in cash and cash equivalents	(8,791,263)	2,252,097	10,137,670
Cash and cash equivalents at beginning of year	15,302,775	13,050,678	2,913,008
Cash and cash equivalents at end of year	$ 6,511,512	$ 15,302,775	$ 13,050,678

</TABLE>

See accompanying notes.

1. Summary of Significant Accounting Policies

Description of Business

Ribozyme Pharmaceuticals, Inc. ("RPI" or the "Company") was founded in 1992 to capitalize on the broad potential of ribozymes for use in the development of human therapeutics and therapeutic target validation services. To date, the Company has engaged in the research and development of its ribozyme technology and has experienced significant operating losses in each fiscal year since inception. The Company has not generated any revenue from the commercialization of its ribozyme technology and it expects to continue to incur significant operating losses over at least the next several years.

During 1998, the Company formed Atugen Biotechnology GmbH ("Atugen"), a German company located in Berlin. Atugen's primary goal is to utilize RPI's proprietary ribozyme and related technologies and accelerate gene function validation and discovery of human health therapeutic targets. Financing for Atugen was accomplished through a combination of venture capital, an investment by RPI and German government grants and loans. As part of the formation, Atugen received exclusive licenses to RPI patents and technologies for target validation and discovery. In addition, in 1998 Atugen acquired Transgenics Berlin-Buch GmbH ("Transgenics") in exchange for Atugen common stock, which allowed access to DNA "chip" technologies. As of December 31, 1998, the Company owned 49.5% of the Atugen voting stock and accounts for its investment in Atugen using the equity method. RPI plans to retain ownership in and have other on-going business relationships with Atugen.

Capital Requirements and Management's Plans

The Company incurred a net loss of $10,917,567 for the year ended December 31, 1998 and has a accumulated deficit of $73,422,491 at December 31, 1998.

Development of the Company's products will require a commitment of substantial additional funds to conduct the costly and time-consuming research, preclinical and clinical testing necessary to bring its proposed products to market and to establish manufacturing and marketing capabilities. The Company's future capital requirements will depend on many factors, including, among others, the progress of the Company's research, development and drug discovery efforts, the ability of the Company to establish collaborative arrangements for clinical testing, progress with preclinical studies and clinical trials, the time and costs involved in obtaining regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, competing technological and market developments, changes in the Company's existing research relationships, determination as to the commercial potential of the Company's potential products, effective commercialization activities and arrangements, and the cost and availability of third-party financing for capital expenditures.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Net Loss Per Share

In 1997, the Financial Accounting Standards Board (FASB) issued Statement No. 128, Earnings per Share (SFAS 128). SFAS 128 replaced the calculation of primary and fully diluted earnings per share with

basic and diluted earnings per share. Unlike primary earnings per share, basic earnings per share excludes any potentially dilutive securities. Diluted earnings per share is very similar to the previously reported fully diluted earnings per share. No restatement of prior periods is necessary as the

potentially dilutive securities have been excluded from the computation as their effect is antidilutive.

Prior to April 11, 1996, pursuant to Securities and Exchange Commission Staff Accounting Bulletins and Staff Policy, all convertible securities issued prior to the Company's initial public offering, even if antidilutive, have been included in the basic loss per share calculation as if they were outstanding.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with a maturity of three months or less to be cash equivalents. The Company's cash equivalents are comprised of certificates of deposit, money market funds, and investment securities with maturities of three months or less.

Property, Plant, and Equipment

Property, plant, and equipment is stated at cost. Depreciation is computed by the straight-line method over the estimated useful lives of the assets. Useful lives of laboratory equipment and furniture are estimated at five years and all computer equipment is estimated at three years. Leasehold improvements and equipment subject to financing obligations are amortized on a straight-line basis over the shorter of their estimated useful lives or the term of the lease.

Deferred Patent Costs

The Company capitalizes legal costs directly incurred in pursuing patent applications as deferred patent costs. When such applications result in an issued patent, the related costs are amortized over the remaining legal life of the patents, using the straight-line method. On a quarterly basis, the Company reviews its issued patents and pending patent applications, and if it determines to abandon a patent application or that an issued patent no longer has economic value, the unamortized balance in deferred patent costs relating to that patent is immediately expensed.

It is possible the above estimates of future economic life of the Company's commercialization revenues, the amount of anticipated future commercialization revenues, or both, will be reduced significantly in the near term due to alternative technologies developed by other biotechnology or pharmaceutical companies. As a result, the carrying amount of deferred patent costs may be reduced in the future.

Revenue Recognition

Revenues recognized under the Company's collaborative research agreements and grants are recorded as earned ratably over the term of the agreements.

Research and Development Expenses

Research and development costs are expensed as incurred.

New Accounting Pronouncements

In 1997 the FASB issued Statement of Financial Accounting Standards No. 130 Reporting Comprehensive Income, and Statement of Financial Accounting Standards No. 131, Disclosures About Segments of an Enterprise and Related Information, both of which were adopted by the Company during

1998. As a result of the adoption of Statement 130, the Company has reported comprehensive income (loss) as a component of the Statement of Stockholders' Equity. There was no change in the Company's financial reporting as a result of the adoption of Statement 131.

Reclassifications

Certain amounts in the December 31, 1997 financial statements were reclassified to conform with the December 31, 1998 presentation. These reclassifications had no impact on the reported results of operations.

2. Securities Available-for-Sale

Management has determined that at December 31, 1998 all marketable securities held by the Company were cash and cash equivalents. At December 31, 1997

management determined that certain marketable securities held by the Company at December 31, 1997 were available-for-sale. Securities available-for-sale are carried at fair value, with unrealized gains and losses reported as a component stockholders' equity. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in investment income. Realized gains and losses and declines in value judged to be other-than-temporary on securities available-for-sale are included in investment income. Interest and dividends on securities available-for-sale are included in investment income. The cost of securities sold is based on the specific identification method. There were no gross realized gains or losses on sales of securities available-for-sale in 1998 or 1997.

3. Long-Term Debt

Long-term debt as of December 31 consists of the following:

<TABLE>
<CAPTION>

	1998	1997
<S>	<C>	<C>
Equipment loan (I)	$ --	$ 263,301
Tenant interest loan (II)	--	496,066
Tenant improvement and equipment loan (II)	--	972,703
Equipment loan (III)	698,634	1,044,334
Convertible debt (IV)	4,344,612	2,052,889
	$5,043,246	$4,829,293

</TABLE>

I. During 1994, the Company obtained a tenant improvement loan of $1,000,000 for leasehold improvements and an equipment loan to purchase up to $1,500,000 of equipment. The interest rate on borrowings under these loan facilities was 10.00% at December 31, 1997. The agreement required monthly principal and interest payments through August 1998, at which time the loan was paid in full.

II. In April 1995, the Company obtained a loan of $1,000,000 collateralized by its tenant interest and certain existing leasehold improvements, and an additional loan to purchase up to $1,500,000 of leasehold improvements and equipment. The terms of the agreement call for fixed monthly principal and interest payments through October 1998, assuming the Company exercised a prepayment option. In December 1998, the Company exercised the prepayment option and paid off the loan at its carrying amount.

III. In December 1995, the Company negotiated an additional equipment credit facility of $2,000,000 with a financial institution. The facility commitment was terminated on June 30, 1997. The agreement requires monthly principal and interest payments through April 2000, at which time a final payment of $283,328 is due in full. The interest rate on these borrowings was 12% at December 31, 1998 and 1997.

IV. In April 1997, the Company entered into a collaboration agreement with a corporate partner whereby, among other items, the Company may borrow from the partner up to $2.0 million annually for each of the next five years. The loans are collaterallized 50% by equipment purchases. The loans

carry an interest rate of 8% per annum and under certain circumstances are convertible into equity at the option of the corporate partner. Principal and interest payments on the loans are deferred until maturity of the loans which is in April 2004. The collaboration and loan facility may be terminated at the option of the partner any time.

Cash paid for interest for the years ended December 31, 1998, 1997 and 1996 was $411,988, $791,476 and $844,661, respectively. At December 31, 1998 the carrying amounts of the Company's long-term debt approximates fair value as all borrowings bear interest rates which are comparable to the current market rate for such borrowings.

All assets acquired under the above loan facilities represent collateral for the amounts outstanding. In addition, the Company was required to maintain

minimum cash balances in the form of certificates of deposit with a financial institution, in the amount of $0 and $52,669 at December 31, 1998 and 1997, respectively. These amounts are presented as restricted cash in the accompanying balance sheets.

As of December 31, 1998, maturities of long-term debt are as follows:

<TABLE>
<CAPTION>

	Amount
<S>	<C>
1999	$ 498,179
2000	200,455
2001	--
2002	--
2003	--
Thereafter	4,344,612
	$5,043,246

</TABLE>

4. Leases

The Company leases office space under a noncancelable operating lease which was extended until June 2007. Total rent expense, including miscellaneous laboratory equipment rentals, was $493,188, $443,796 and $496,774 in 1998, 1997 and 1996 respectively.

The Company's lease commitments at December 31, 1998 are as follows:

<TABLE>
<CAPTION>

	Operating Lease
<S>	<C>
1999	$ 478,516
2000	363,480
2001	363,480
2002	363,480
2003	363,480
2004 and thereafter	1,272,180
	$3,204,616

</TABLE>

5. Stockholders' Equity

In April 1996, the Company completed an initial public offering of its common stock, whereby 2,300,000 shares of the Company's common stock were sold at $10.00 per share, resulting in net proceeds of approximately $20.6 million. As a result of the Company's initial public offering, all preferred shares outstanding were converted into an aggregate of 2,231,960 shares of common stock.

Upon consummation of the initial public offering the Company sold 377,202 shares of common stock to Chiron Corporation ("Chiron") for $3,640,000. Additionally, the Company received $1,800,000 from Chiron to complete the purchase of warrants to purchase 444,444 shares of common stock, issued concurrently with the IPO.

The Company adopted an Employee Stock Purchase Plan (the "Purchase Plan"), authorizing the issuance of 300,000 shares pursuant to purchase rights granted to employees of the Company. The Purchase Plan provides a means by which employees purchase common stock of the Company through payroll deductions. The Purchase Plan is implemented by offerings of rights to eligible employees. Generally, each offering is twenty-four months' duration with purchases occurring on each October 31 and April 30 during each offering (except that April 30, 1996 was not a purchase date). Common stock is purchased for accounts of employees participating in the Purchase Plan at a price per share equal to

the lower of (i) 85% of the fair market value of a share of common stock on the date of commencement of participation in the offering or (ii) 85% of the fair market value of a share of common stock on the date of purchase. Generally all regular employees, including executive officers, may participate in the Purchase Plan and may authorize payroll deduction of up to 15% of their base compensation for the purchase of stock under the plan. The Company's Board of Directors has the authority to terminate the Purchase Plan at its discretion. Shares are deemed issued for accounting purposes in the year the shares are purchased.

Pursuant to an antidilution agreement (the "Antidilution Agreement") with a founder of the Company, the Company agreed to issue additional shares to this individual so that he would maintain a 5% interest in the fully diluted equity of the Company until the occurrence of one of several events, including the Company's initial public offering. Accordingly, effective April 11, 1996, 115,506 shares were issued related to the Antidilution Agreement which represented the founder's 5% interest in the Company. No additional rights under the Antidilution Agreement exist.

Below is a summary of common stock reserved by the Company at December 31, 1998 for issuance upon the exercise of the various options, warrants and the 401(k) and purchase plans.

<TABLE>
<CAPTION>

	Shares
<S>	<C>
Stock option plans	1,479,173
Employee stock purchase plan	200,168
Employee 401(k) stock match	247,079
Warrants at $15.75 per share	10,793
Warrants at $40.50 per share	11,111
Warrants at $22.50 per share	465,554
	2,413,878

</TABLE>

The Company's ability to pay dividends is restricted by the terms of its tenant improvement and equipment loan facility agreements.

6. Stock Option Plans

The Company has established a Non-Qualified Stock Option Plan and an Incentive Stock Option Plan (collectively, the "Plans"), under which it is authorized to grant stock options to purchase up to 1,317,154 shares of the Company's common stock to eligible employees, consultants, and other individuals, as defined in the Plans. In May 1997, the Company's shareholders approved an additional 350,000 shares of the Company's common stock to be reserved for issuance pursuant to the Plans. Options to purchase the Company's common stock are exercisable at a price as determined by the Board of Directors at the time the

option is granted, which shall not be less than 100% of the fair market value (110% in the case of 10 percent shareholders) at the date of grant. Vesting rights are determined by the Board of Directors at the time the option is granted and generally the options become exercisable at twenty percent at the end of each of years one through five. If not exercised, the options expire after ten years. The Board of Directors has also granted certain employees options vesting upon achievement of certain contingent milestone events.

During the third quarter of 1998, the Company offered a repricing of existing stock options to all of its current employees. Pursuant to the offer, all non-executive employees were allowed to exchange each existing stock option for a newly priced stock option one for one, with the new stock options having an exercise price equal to the current market price of the underlying common stock. If exchanged, the vesting term would start over beginning on the date of exchange. A similar offer was given to all executives, except the options were exchanged at a one for .75 ratio. As a result of the offer, 890,921 options were canceled and 747,060 options were granted, effective September 18, 1998.

The Company has elected to follow Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees (APB 25), and related Interpretations

in accounting for its employee stock options because, as discussed below, the alternative fair value accounting provided for under FASB Statement of Financial Accounting Standards No. 123, Accounting for Stock-Based Compensation (SFAS 123), requires use of option valuation models that were not developed for use in valuing employee stock options. Under APB 25, if the exercise price of the Company's employee stock options equals the market price of the underlying stock on the date of grant, no compensation expense is recognized. During 1998, 1997 and 1996, the Company recorded $32,162, $43,453 and $137,617, respectively, of compensation relating to the grant of stock options and the Antidilution Agreement, all of which relates to pre-IPO issuances which have been deferred until vesting has been completed.

Pro forma information regarding net income and earnings per share is required by SFAS 123, which also requires that the information be determined as if the Company has accounted for its employee stock options under the fair value method of SFAS 123. The fair value for these options was estimated at the date of grant using a Black-Scholes option pricing model with the following weighted-average assumptions for 1998, 1997 and 1996, respectively: risk-free interest rates of 4.7%, 6.4% and 6.3%; a dividend yield of 0%; volatility factors of the expected market price of the Company's common stock of .967, .638 and .566; and a weighted-average expected life of the option of 6 years. The weighted average fair value of stock options granted during 1998, 1997 and 1996 was $4.04, $5.88 and $6.59, respectively.

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the options' vesting period. The Company's pro forma information follows:

<TABLE>
<CAPTION>

	1998	1997	1996
<S>	<C>	<C>	<C>
Pro forma net loss	$(11,948,280)	$(16,153,548)	$(15,554,890)
Pro forma loss per share	(1.33)	(2.18)	(2.66)

</TABLE>

Because the SFAS 123 method of accounting has not been applied to options granted prior to January 1, 1995, the resulting pro forma net loss may not be representative of that to be expected in future years.

Changes in stock options for the years ended December 31, 1998 and 1997 were as follows:

<TABLE>
<CAPTION>

	Options	Exercise Price
<S>	<C>	<C>
Outstanding at December 31, 1995	367,838	$ .45--$ 5.40
Options granted	508,652	$ 2.70--$ 19.00
Options exercised/canceled	(197,067)	$ .45--$ 5.40
Outstanding at December 31, 1996	679,423	$ .45--$ 19.00
Options granted	604,300	$ 7.50--$ 13.50
Options exercised/canceled	(64,833)	$ .45--$ 19.00
Outstanding at December 31, 1997	1,218,890	$ .45--$ 15.25
Options granted	1,174,560	$ 3.00--$ 8.13
Options exercised/canceled	(1,045,878)	$ .45--$ 15.25
Outstanding at December 31, 1998	1,347,572	$ .45--$ 12.78

	==========

</TABLE>

The weighted average exercise price of options outstanding at December 31, 1998, 1997 and 1996 was $4.21 and $9.31 and $8.93, respectively.

Stock options vest as follows:

<TABLE>
<CAPTION>

	Options
<S>	<C>
Currently exercisable	258,279
1999	219,492
2000	176,592
2001	159,938
2002	149,583
2003 and thereafter	172,160
Contingent vesting	211,528
Total	1,347,572

</TABLE>

7. Collaborative Agreements

Parke-Davis

In April 1993, the Company entered into a research and development collaboration agreement with the Parke-Davis division of the Warner-Lambert Corporation ("Parke-Davis"), whereby Parke-Davis was to partially fund the research and development costs incurred by the Company in developing and commercializing ribozyme-based products for application to the treatment of osteoarthritis and other diseases. Pursuant to the Parke-Davis agreement, Parke-Davis purchased 100,100 shares of Series C preferred stock at a price of $29.97 per share in 1993, 27,777 shares of Series C preferred stock at a price of $36.00 per share in 1994, and 40,160 shares of Series F preferred stock at $37.35 per share in 1995, for a

total equity investment of $5,500,000. All preferred shares were converted into 168,037 shares of common stock upon the Company's initial public offering.

Also pursuant to the collaboration agreement, through December 31, 1996, Parke-Davis provided $1,700,000 research and development funding to the Company. As of June 30, 1997, the collaboration agreement has been completed.

In March 1998, the Company entered into a Target Validation agreement with Parke-Davis. The agreement gives Parke-Davis access to the Company's proprietary ribozyme technology which will assist Parke-Davis in determining which genes are valid therapeutic targets. Under the terms of the contract, the Company will design and synthesize ribozymes against target genes designated by Parke-Davis and perform various studies to determine the level of gene expression inhibition achieved. Parke-Davis will fund the research and may provide milestone payments or success fees to the Company if Parke-Davis uses the information to derive compounds to take into development.

Dow Agrosciences

In September 1993, the Company entered into a research and development study with Dow Agrosciences (the "Feasibility Study") to demonstrate the stable integration and the effective use of ribozymes to alter corn composition. Pursuant to the terms of the Feasibility Study, Dow Agrosciences reimbursed the Company for all of its expenses related to the Feasibility Study and, in 1994, purchased 41,666 shares of Series D preferred stock at a price of $36.00 per share, for a total equity investment of $1,500,000. All preferred shares were converted into 41,666 shares of common stock upon completion of the Company's initial public offering.

The Feasibility Study was completed in 1997 and the parties entered into a long-term license agreement for the development and commercialization of ribozymes to the targets of interest. As consideration for the long-term license agreement, 41,666 shares of common stock held by Dow Agrosciences were returned to the Company. The Company canceled 33,333 of the shares and reissued

the remaining 8,333 shares to CTI as a consideration of royalty, due to the license transaction.

Chiron

In July 1994, the Company entered into a research and development collaboration agreement with Chiron to research, develop and market products directed towards five genetic targets, and all human clinical indications associated with those targets. The Company and Chiron will share equally in the costs and profits of any jointly developed products. In addition, Chiron may, at its option, finance the Company's portion of its Phase II and Phase III drug development costs for mutually approved programs. The Company retains the option to reacquire its rights by reimbursing Chiron for such development costs plus a predetermined risk premium. The term of the research program is five years, with the terms of the agreement to be extended if products are jointly developed. As part of this agreement, Chiron committed to make a $10,000,000 equity investment in the Company. The components of this investment are:

In 1994, Chiron purchased 100,000 shares of the Company's common stock at a price of $3.60 per share, or $360,000; also in 1994 Chiron purchased 107,095 shares of Series E preferred stock at a price of $37.35 per share, or $4,000,000. In 1996, the Company issued Chiron immediately upon the closing of the Company's initial public offering a warrant to purchase 444,444 shares of the Company's common stock which is exercisable at a price of $22.50 per share, for an aggregate purchase price of $4.50 per warrant share. In 1994, Chiron paid the Company $0.45 per warrant share, or $200,000. The balance of the warrant purchase price, $1,800,000, or $4.05 per warrant share, was paid to the Company upon completion of its initial public offering. Further, Chiron purchased 377,202 common

shares with an aggregate value of $3,640,000 upon completion of the Company's initial public offering, at the initial public offering price less one-half of the underwriting discount. Chiron also has a designated Board member on the Company's Board of Directors. All preferred shares were converted into 142,222 shares of common stock upon completion of the Company's initial public offering.

In May 1996, the Company entered into a collaboration with Chiron for the use of ribozymes to characterize gene function. The collaboration gives Chiron the right to develop and commercialize products that result from the collaboration, and would entitle RPI to receive product development milestone payments and royalties on sales of any such commercial products. Chiron and RPI each pay a portion of the research and development expenses of the collaboration, and the Company provided Chiron $1,800,000 in 1996 for research funding related to the collaboration.

In September 1998, the Company received a $2.5 million option payment from Chiron related to the possible joint product development of ANGIOZYME. In December 1998, Chiron paid the final option payment of $2.5 million to guarantee its position as a joint collaborator for the development of ANGIOZYME. In addition, and coinciding with the second option payment, Chiron agreed to share equally in the costs of product development of ANGIOZYME. In 1998, the Company recorded $1,048,138 in revenues related to Chiron product development payments.

Pharmacia Biotech AB

In November 1995, the Company and Pharmacia Biotech AB entered into a collaboration and license agreement for the improvement of production scale synthesis of RNA and chimeric oligonucleotides. The goal of the collaboration is to reduce the cost of manufacturing ribozymes and other oligonucleotide products. Pharmacia Biotech AB will provide research funding, synthesis support and instrumentation, while RPI will receive royalties on the sales of modified RNA oligonucleotides and non-DNA primer support. As of December 31, 1998, the Company has received $731,500 in funding pursuant to the agreement.

Schering AG, Berlin

On April 9, 1997, the Company entered into a research collaboration with Schering AG, Berlin, ("Schering AG") focusing on the use of ribozymes for therapeutic target validation, as well as the development of ribozymes as therapeutic agents. The collaboration will utilize the special selectivity of ribozymes to validate new molecular therapeutic targets and to discover new therapeutic agents based on those targets. The Company will provide its

expertise in ribozyme design, synthesis and delivery, and Berlex Laboratories, Inc., a U.S. subsidiary of Schering AG ("Berlex") will provide candidate targets, cell culture screens, animal models and development and commercialization expertise to the collaboration. The Company anticipates that hundreds of potential targets may be examined over a five year period with Berlex having the option to commercialize products from any validated targets.

Schering AG made an equity investment in the Company in May 1997 of $2.5 million in exchange for 212,766 shares of common stock, and made an additional equity investment of $2.5 million for 465,117 shares in April 1998. Separately, Schering AG provided a loan of $2.0 million in 1997, and subsequently $2.0 million in 1998. Schering AG will continue to provide loans of up to $2.0 million annually for each of the next three years, provided that the collaboration is continued in each of those years. Amounts not used in any calendar year may be carried forward to future years. According to the terms of the Company's agreement with Schering AG, 50% of any borrowings on the line of credit must be collateralized by equipment purchases. The loans, which carry an interest rate of 8% per annum, are convertible into equity at the option of Schering AG under certain circumstances. At December 31, 1998, the outstanding borrowings of $4.3 million were convertible into approximately 992,000 shares of the Company's common

stock. Principal and interest payments are deferred until maturity of the loans which is in April 2004. In addition, Schering AG made research payments of $2.0 million and $1.5 million in 1998 and 1997, respectively. Provided that the collaboration is continued, Schering AG will make research payments of $2 million a year for each year through April 2001. The Company may earn success fees upon product development milestones and will manufacture synthetic ribozyme products and receive royalties on sales of both ribozyme and non-ribozyme products resulting from the collaboration. All such payments are subject to some restrictions, including receipt of certain third party consents. Upon payment of termination fees paid to the Company, the research collaboration may be terminated at Schering AG's option any time.

Roche Bioscience

In May 1998, the Company entered into a Target Validation agreement with Roche Bioscience. The agreement gives Roche Bioscience access to the Company's proprietary ribozyme technology which will assist Roche Bioscience in determining which genes are valid therapeutic targets. Under the terms of the contract, the Company will design and synthesize ribozymes against target genes designated by Roche Bioscience and perform various studies to determine the level of gene expression inhibition achieved. Roche Bioscience will fund the research and may provide milestone payments or success fees to the Company if Roche Bioscience uses the information to derive compounds to take into development.

8. Commitments and Contingency

At the core of the Company's technology are inventions and patents of the University of Colorado ("CU") which were developed by Dr. Thomas R. Cech and various associates of Dr. Cech. Pursuant to the policies of CU, these inventions and the patents issued thereon, (the "Cech Technology") became the property of CU. The Cech Technology was assigned to CU's affiliate, University Research Corporation ("URC"), which in turn assigned the rights to license certain of the Cech Technology to Competitive Technologies, Inc. ("CTI"), formerly known as University Patents, Inc. United States Biochemical Corporation ("USB") licensed the Cech Technology pursuant to two sublicenses. One of these sublicenses was for the Cech Technology held by CTI. In November 1996, USB assigned to the Company its rights under the sublicense from CTI and the Company entered into an amended and restated license with CTI. The Company also has obtained a license from URC and a sublicense from USB for other Cech Technology held by URC. The CTI license, URC license and USB sublicense together grant the Company the exclusive (except for non-commercial academic research) worldwide right, among other things, to make, use and sell RNA enzymes covered by licensed patents and products incorporating them. The URC license and USB sublicense are fully paid. The CTI license provides for the payment of a royalty on sales of products incorporating RNA enzymes, covered by licensed patents, and for certain minimum annual royalties. The Company may grant sublicenses to the licensed technology subject to the payment to CTI of a share of royalty income from such sublicenses or a royalty on sales from sublicensed products, methods or services, depending on the particular licensed patents involved. In addition, the Company must pay CTI a share of any option fee, license fee, prepaid royalty or other "front-end" fee other than research

and development funding paid in connection with such sublicense. At the Company's discretion, the payment may be in either cash or equity.

During 1993, the Company was granted the right of first refusal to license any new inventions, improvements and patents related to ribozyme technology developed by Dr. Cech or others at CU, in exchange for certain payments. In order to maintain the right of first refusal, the Company agreed to fund research at CU through an unrestricted grant of $750,000 payable in various installments over a five year period commencing in September 1993. URC made an investment of approximately $41,000 for 46,188 shares of the Company's common stock upon entering into the agreement.

During 1996, the Company eliminated the royalty arrangement in exchange for 45,000 shares of its common stock. The Company recognized expense related to the exchange of $540,000 during 1996. The Company's final payment under the above unrestricted grant was $113,000, which was paid in 1998.

The Company is involved in legal proceedings which have arisen in the ordinary course of business. In the opinion of management the outcome of these legal proceedings will not have a material adverse impact on the Company's financial position or operations.

9. Related Party Transactions

At December 31, 1998, 1997 and 1996, the Company had a total of $280,932, $320,000, and $225,000, respectively, of non-interest bearing loans due from officers. The balances may be forgiven by the Company under certain employment agreement provisions. The loan balances are forgivable or payable to the Company under various terms not to exceed 5 years. The Company forgave $126,466, $80,000 and $85,000 of these loans during each of the years ending December 31, 1998, 1997 and 1996, respectively.

10. Formation of Atugen, an unconsolidated German Affiliate

In 1998, the Company transferred its gene function and target validation business and technology to Atugen, a separately funded German affiliate. Financing for Atugen was accomplished through an equity investment of $2.0 million from RPI, a venture capital investment of $7.0 million and a commitment by the German government to provide grants and loans of up to $10.0 million. As a result, at December 31, 1998, RPI retained a 49.5% ownership in Atugen. In connection with its formation, Atugen received exclusive royalty-free licenses to RPI patents and technologies for target validation and discovery in exchange for a one-time $2.0 million payment which was received by RPI in January 1999. The entire amount of this one-time payment has been deferred as of December 31, 1998 and will be amortized over the five-year term of the license agreement and reflected in the Company's equity in earnings or loss of this unconsolidated affiliate.

According to a service agreement executed by both parties, RPI will provide management support, technologies, facilities and reagents to Atugen for reasonable fees. RPI will retain rights to develop ribozyme therapeutic agents against targets validated by Atugen.

In 1998, RPI gave to its officers and certain other employees stock representing a 5.5% interest in the newly formed Atugen at no personal cost to the individuals. As a result, the Company's 1998 Statement of Operations includes $81,000 of compensation related to the share grant.

11. Income Taxes

The Company accounts for income taxes in accordance with Statement of Financial Accounting Standard No. 109, Accounting for Income Taxes (SFAS 109). Under the provisions of SFAS 109, a deferred tax liability or asset (net of a valuation allowance) is provided in the financial statements by applying the provisions of applicable tax laws to measure the deferred tax consequences of temporary differences that will result in net taxable or deductible amounts in future years as a result of events recognized in the financial statements in the current or preceding years.

At December 31, 1998, the Company has the following net operating loss and tax credit carryforwards for income tax purposes:

Expiration Date	Net Operating Losses	Research and Development Credits	State Investment Credits
1999	$ --	$ --	$14,000
2000	--	--	11,000
2001	--	--	6,000
2007	3,506,000	101,000	--
2008	7,363,000	185,000	--
2009	9,239,000	316,000	--
2010	11,953,000	139,000	--
2011	15,125,000	181,000	--
2012	15,291,000	297,000	--
2018	11,248,000	298,000	--
Total	$73,725,000	$1,517,000	$31,000

The Tax Reform Act of 1986 contains provisions that limit the utilization of net operating loss and tax credit carryforwards if there has been a "change of ownership" as described in Section 382 of the Internal Revenue Code. Such a change of ownership may limit the Company's utilization of its net operating loss and tax credit carryforwards, and could have been triggered by the Company's initial public offering or by subsequent sales of securities by the Company or its shareholders.

The components of the Company's deferred tax assets and liabilities as of December 31, 1998 and 1997 are as follows:

	1998	1997
Deferred tax assets:		
Net operating loss carryforwards	$ 27,499,000	$ 23,324,000
Research and development and state investment credit carryforwards	1,516,000	1,102,000
Depreciation	639,000	618,000
Other	62,000	12,000
	29,716,000	25,056,000
Valuation allowance	(28,610,000)	(24,097,000)
Net deferred tax assets	1,106,000	959,000
Deferred tax liabilities:		
Deferred patent costs	1,084,000	936,000
Other	22,000	23,000
Total deferred tax liabilities	1,106,000	959,000
	$ --	$ --

11. Employee Savings Plan

The Company has a 401(k) plan which allows participants to contribute 1% to 15% of their salary, subject to eligibility requirements and annual limits. The Board may, at its sole discretion, approve matching contributions with the Company's common stock. In both 1998 and 1997, the Board approved a 50% common stock match equal to total participant deferrals made in each respective year.

The Company stock match is subject to vesting restrictions.

12. Subsequent Event

In March 1999, the Company entered into a collaboration with Eli Lilly and Company ("Lilly") to conduct research, development and commercialization of HEPTAZYME, the Company's ribozyme for the treatment of hepatitis C virus ("HCV") infection. Under the terms of the agreement, the Company will receive approximately $9.2 million in 1999, which includes initial fees, funding for research and clinical trial expenses, and an equity investment. In addition, the Company may receive success fees related to various development milestones and royalties on future sales of products developed related to the collaboration. Lilly will receive the exclusive worldwide commercialization rights to products that result from this collaboration, including the HEPTAZYME product. The Company has retained certain rights to manufacture HEPTAZYME products resulting from the collaboration.

ANGIOZYME/TM/ and HEPTAZYME/TM/ are trademarks of Ribozyme Pharmaceuticals.

1,800,000 Shares

[LOGO OF RPI APPEARS HERE]

Common Stock

PROSPECTUS

HAMBRECHT & QUIST LLC

, 1999

You should rely only on information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the common stock or possession or distribution of this prospectus in any such jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to

inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses Of Issuance And Distribution

The following table sets forth the various expenses in connection with the distribution and sale of the securities being registered which will be paid by us. All amounts are estimates except for the SEC registration fee:

<TABLE>

<S>	<C>
SEC registration fee	$ 2,390
Printing and mailing expenses	$ 40,000
Nasdaq listing fee	$ 17,500
Legal fees and expenses	$ 75,000
Accounting fees and expenses	$ 40,000
TOTAL	$174,890

</TABLE>

Item 14. Indemnification Of Directors And Officers

Article XI of our Bylaws provides for indemnification of our directors to the fullest extent permitted by law, as now in effect or later amended. Article XI of our Bylaws also permits the indemnification to the same extent of our officers, employees or agents if, and to the extent, authorized by the Board of Directors. In addition, the Bylaws provide for indemnification against expenses incurred by a director to be paid by us at reasonable intervals in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of the director or officer to repay such amount if it shall be ultimately determined that he is not entitled to be indemnified by us. The Bylaws further provide for a contractual cause of action on the part of our directors for indemnification claims that have not been paid by us.

Article VI of our Certificate of Incorporation, as amended, limits under certain circumstances the liability of our directors for a breach of their fiduciary duty as directors. These provisions do not eliminate the liability of a director (1) for a breach of the director's duty of loyalty to us or our stockholders, (2) for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law, (3) under Section 174 of the General Corporate Law of the State of Delaware ("DGCL") (relating to the declaration of dividends and purchase or redemption of shares in violation of the DGCL) or (4) for any transaction from which the director derived an improper personal benefit.

Section 145 of the DGCL contains provisions regarding indemnification, among others, of officers and directors. Section 145 of the DGCL provides in relevant part:

> (a) A corporation shall have power to indemnify 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 the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that the person's conduct was unlawful.

(b) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

(c) To the extent that a present or former director or officer of a corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in subsections (a) and (b) of this section, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith.

(d) Any indemnification under subsections (a) and (b) of this section (unless ordered by a court) shall be made by the corporation only as authorized in the specific case upon a determination that indemnification of the present or former director, officer, employee or agent is proper in the circumstances because the person has met the applicable standard of conduct set forth in subsections (a) and (b) of this section. Such determination shall be made, with respect to a person who is a director or officer at the time of such determination, (1) by a majority vote of the directors who are not parties to such action, suit or proceeding, even though less than a quorum, or (2) by a committee of such directors designated by majority vote of such directors, 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.

Delaware law also permits a corporation to purchase and maintain insurance on behalf of any person who is or was a director or officer against any liability asserted against him and incurred by him in such capacity or arising out of his status as such, whether or not the corporation has the power to indemnify him against that liability under Section 145 of the DGCL.

We also have provided liability insurance for each director and officer for losses arising from claims or charges made against them while acting in their capacities as our directors or officers.

The above discussion of our corporate documents is not intended to be exhaustive and is respectively qualified in its entirety by our corporate documents.

Item 15. Recent Sale Of Unregistered Securities

The following table sets forth the Ribozyme Pharmaceuticals' sales of unregistered securities for the past three years. All transactions listed below involved the issuance of common stock and options to acquire shares of common stock prior to commencement of the offering described in the foregoing prospectus. No underwriters were employed with respect to the sale of any of the securities listed below. All shares were issued in reliance upon Section 4(2) and/or 3(b) of the Securities Act.

<TABLE>
<CAPTION>

Securities Issued	Purchaser	Date Acquired	Consideration
<S>	<C>	<C>	<C>
212,776 shares of common stock.....	Schering AG	May 1997	$2,500,000
465,117 shares of common stock.....	Schering AG	May 1998	$2,500,000

</TABLE>

Item 16. Exhibits And Financial Statement Schedules

(a) Exhibits

<TABLE>
<CAPTION>

Number	Description
<C>	<S>
1.1	Form of Placement Agency Agreement dated , 1999, between Ribozyme Pharmaceuticals and Hambrecht & Quist LLC
1.2	Form of Escrow Agreement dated , 1999, between Ribozyme Pharmaceuticals Hambrecht & Quist LLC and Citibank, N.A.
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10.40	Amended and Restated License Agreement dated November 20, 1996, between Ribozyme Pharmaceuticals, University Research Corporation, University of Colorado and United States Biochemical Corporation(3)*
10.41	Amended and Restated Sublicense Agreement dated November 20, 1996, between Ribozyme Pharmaceuticals and United States Biochemical Corporation(3)*
10.42	Amended and Restated License Agreement dated November 20, 1996, between Ribozyme Pharmaceuticals and Competitive Technologies, Incorporated(3)*
10.43	Memorandum of Understanding dated March 1, 1996, between Ribozyme Pharmaceuticals and DowElanco(1)
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10.54	Research, License, Supply and Royalty Agreement between Schering Aktiengesellschaft and Ribozyme Pharmaceuticals dated April 9, 1997(4)*
10.55	Purchase Agreement dated April 9, 1997, among Ribozyme Pharmaceuticals, Schering Berlin Venture Corporation and Schering Aktiengesellschaft(4)*
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10.57	Employment Agreement dated July 5, 1997, between Ribozyme Pharmaceuticals and Thomas Rossing(5)
10.58	Executive Bonus Plan dated March 27, 1998(6)
10.59	Research, Collaboration and License Agreement dated May 19, 1998, between Ribozyme Pharmaceuticals and Roche Bioscience, a division of Syntex (U.S.A.) Inc.(7)*
10.60	Employment Agreement dated September 8, 1998, between Ribozyme

Pharmaceuticals and Nassim Usman(8)

10.61 Participation Agreement dated August 31, 1998, as amended, and related documents between Ribozyme Pharmaceuticals and Atugen Biotechnology GmbH(9)**

</TABLE>

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Number	Description
<C>	<S>
10.62	Research Collaboration and License Agreement dated March 17, 1999, between Ribozyme Pharmaceuticals and Eli Lilly and Company***
23.1	Consent of Ernst & Young LLP, Independent Auditors
23.2	Consent of Rothgerber Johnson & Lyons LLP (included in Exhibit 5.1)
24.1	Power of attorney (included on the signature page of this Registration Statement)

</TABLE>

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* Ribozyme Pharmaceuticals has applied for and received confidential treatment with respect to portions of these exhibits.
** Ribozyme Pharmaceuticals has applied for confidential treatment with respect to portions of these exhibits.
*** To be filed by amendment.

(1) Documents incorporated by reference herein to certain exhibits to Ribozyme Pharmaceuticals' Form SB-2 Registration Statement, File No. 333-1908-D.
(2) Documents incorporated by reference herein to certain exhibits to Ribozyme Pharmaceuticals' Form 10-QSB for the quarter ended June 30, 1996.
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(b) Financial Statement Schedules

All schedules have been omitted because they are not applicable or not required or the required information is included in the financial statements or notes thereto.

Item 17. Undertakings

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 SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 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 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;

(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.

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 provision described under Item 20 or otherwise, the registrant has been advised that in the opinion of the SEC 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, the registrant certifies that it has reasonable grounds to believe that it meets all the requirements for filing on Form S-1 and has duly caused this Form S-1 Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in Boulder, Colorado, on March 25, 1999.

Ribozyme Pharmaceuticals, Inc.

By: /s/ Ralph E. Christoffersen
Ralph E. Christoffersen, Ph.D.
Chief Executive Officer and President

In accordance with the requirements of the Securities Act of 1933, as amended, this Form S-1 Registration Statement has been signed below by the following persons in the capacities and on the dates indicated. Each of the following persons hereby appoints Ralph E. Christoffersen and Lawrence E. Bullock and each of them, as his attorney-in-fact to (1) execute and file amendments to this Registration Statement, (2) request acceleration of the effective date of or withdraw from the registration process this Registration Statement, or (3) take any other action regarding this Registration Statement as such attorneys-in-fact, or either of them, may deem appropriate.

<TABLE>
<CAPTION>

Signature	Title	Date
<S>	<C>	<C>
/s/ Ralph E. Christoffersen Ralph E. Christoffersen, Ph.D.	Chief Executive Officer and President (Principal Executive Officer)	March 25, 1999
/s/ Lawrence E. Bullock Lawrence E. Bullock	Vice President, Administration Finance, Chief Financial Officer and Secretary (Principal Financial and Accounting	March 25, 1999

	Officer)	
/s/ David T. Morgenthaler David T. Morgenthaler	Chairman of the Board of Directors	March 25, 1999
/s/ Jeremy C. Cook Jeremy C. Cook	Director	March 25, 1999
/s/ Anthony B. Evnin Anthony B. Evnin, Ph.D.	Director	March 25, 1999
/s/ David Ichikawa David Ichikawa	Director	March 25, 1999
/s/ Anders Wiklund Anders Wiklund	Director	March 25, 1999

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10.59 Research, Collaboration and License Agreement dated May 19, 1998, between Ribozyme Pharmaceuticals and Roche Bioscience, a division of Syntex (U.S.A.) Inc.(7)*

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EXHIBIT 1.1

[DRAFT]

RIBOZYME PHARMACEUTICALS, INC.

1,800,000 Shares of Common Stock, $0.01 par value per share

PLACEMENT AGENCY AGREEMENT

April __, 1999

HAMBRECHT & QUIST LLC
One Bush Street
San Francisco, CA 94104,
As Placement Agent

Dear Sir or Madam:

Ribozyme Pharmaceuticals, Inc., a Delaware corporation (the "Company"), proposes to issue and sell 1,800,000 shares (the "Shares") of common stock, par value $.01 per share (the "Common Stock"), to certain investors (collectively, the "Investors"). The Company desires to engage you as its placement agent (the "Placement Agent") in connection with such issuance and sale. The Shares are more fully described in the Registration Statement (as hereinafter defined).

The Company hereby confirms as follows its agreements with the Placement Agent.

1. Agreement to Act as Placement Agent. On the basis of the representations, warranties and agreements of the Company herein contained and subject to all the terms and conditions of this Agreement, the Placement Agent agrees to act as the Company's exclusive placement agent in connection with the issuance and sale, on a best efforts basis, by the Company of the Shares to the Investors. The Company shall pay to the Placement Agent 8.0% of the proceeds received by the Company from the sale of the Shares as set forth on the cover page of the Prospectus (as hereinafter defined); provided, however, that the Company shall not be obligated to pay the Placement Agent a fee in respect of sales to the investors identified on Schedule 1 to this Agreement.

2. Delivery and Payment. Concurrently with the execution and

delivery of this Agreement, the Company, the Placement Agent, and Citibank N.A., as escrow agent (the "Escrow Agent"), shall enter into an Escrow Agreement substantially in the form of Exhibit A attached hereto (the "Escrow Agreement"), pursuant to which an escrow account will be established, at the Company's expense, for the benefit of the Investors (the "Escrow Account"). Prior to the Closing Date (defined below), (i) each of the Investors will deposit an amount equal to the price per Share as shown on the cover page of the Prospectus (as hereinafter defined)

multiplied by the number of Shares purchased by it in the Escrow Account, and (ii) the Escrow Agent will notify the Company and the Placement Agent in writing whether the Investors have deposited in the Escrow Account funds in the amount equal to the proceeds of the sale of all of the Shares offered hereby (the "Requisite Funds") into the Escrow Account. At 10:00 a.m., New York City time, on April __, 1999, or at such other time on such other date as may be agreed upon by the Company and the Placement Agent but in no event prior to the date on which the Escrow Agent shall have received all of the Requisite Funds (such date is hereinafter referred to as the "Closing Date"), the Escrow Agent will release the Requisite Funds from the Escrow Account for collection by the Company and the Placement Agent as provided in the Escrow Agreement and the Company shall deliver the Shares to the Investors, which delivery may be made through the facilities of the Depository Trust Company. The closing (the "Closing") shall take place at the office of Stroock & Stroock & Lavan LLP, 180 Maiden Lane, New York, New York 10038. All actions taken at the Closing shall be deemed to have occurred simultaneously.

Certificates evidencing the Shares shall be in definitive form and shall be registered in such names and in such denominations as the Placement Agent shall request by written notice to the Company. For the purpose of expediting the checking and packaging of certificates for the Shares, the Company agrees to make such certificates available for inspection at least 24 hours prior to delivery to the Investors.

3. Representations and Warranties of the Company. The Company represents and warrants and covenants to the Placement Agent that:

(a) A registration statement (Registration No. 333-_____) on Form S-1 relating to the Shares, including a preliminary prospectus relating to the Shares and such amendments to such registration statement as may have been required to the date of this Agreement, has been prepared by the Company, under the provisions of the Securities Act of 1933, as amended (the "Act"), and the rules and regulations (collectively referred to as the "Rules and Regulations") of the Securities and Exchange Commission (the "Commission") thereunder, and has been filed with the Commission. The Commission has not issued any order preventing or suspending the use of the Prospectus or the Preliminary Prospectus (as defined below). The term "Preliminary Prospectus" as used herein means a preliminary prospectus relating to the Shares as contemplated by Rule 430 or Rule 430A ("Rule 430A") of the Rules and Regulations included at any time as part of the registration statement. Copies of such registration statement and

amendments and of each related Preliminary Prospectus have been delivered to the Placement Agent. If such registration statement has not become effective, a further amendment to such registration statement, including a form of final prospectus, necessary to permit such registration statement to become effective will be filed promptly by the Company with the Commission. If such registration statement has become effective, a final prospectus relating to the Shares containing information permitted to be omitted at the time of effectiveness by Rule 430A will be filed by the Company with the Commission in accordance with Rule 424(b) of the Rules and Regulations promptly after execution and delivery of this Agreement. The term "Registration Statement" means the registration statement as amended at the time it becomes or became effective (the "Effective Date"), including all material

incorporated by reference therein and any information deemed to be included by Rule 430A. The term "Prospectus" means the prospectus relating to the Shares as first filed with the Commission pursuant to Rule 424(b) of the Rules and Regulations or, if no such filing is required, the form of final prospectus relating to the Shares included in the Registration Statement at the Effective Date, in either case, including all material, if any, incorporated by reference therein.

(b) On the date that any Preliminary Prospectus was filed with the Commission, the date the Prospectus is first filed with the Commission pursuant to Rule 424(b) (if required), at all times subsequent to and including the Closing Date and when any post-effective amendment to the Registration Statement becomes effective or any amendment or supplement to the Prospectus is filed with the Commission, the Registration Statement, each Preliminary Prospectus and the Prospectus (as amended or as supplemented if the Company shall have filed with the Commission any amendment or supplement thereto), including the financial statements included in the Prospectus, did or will comply with all applicable provisions of the Act and the Rules and Regulations and did or will contain all statements required to be stated therein in accordance with the Act and the Rules and Regulations. On the Effective Date and when any post-effective amendment to the Registration Statement becomes effective, no part of the Registration Statement or any such amendment did or will contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein not misleading. At the Effective Date, at the date the Prospectus or any amendment or supplement to the Prospectus is filed with the Commission and at the Closing Date the Prospectus did not or will not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading. The Company has not distributed any offering material in connection with the offering or sale of the Common Stock, other than the Registration Statement, the Preliminary Prospectus and the Prospectus.

(c) The Company is, and at the Closing Date will be, duly organized, validly existing and in good standing under the laws of Delaware. The

Company has no subsidiaries. The Company has, and at the Closing Date will have, full power and authority to conduct all the activities conducted by it, to own or lease all the assets owned or leased by it and to conduct its business as described in the Registration Statement and the Prospectus (or, if the Prospectus is not in existence, in the most recent Preliminary Prospectus). The Company is, and at the Closing Date will be, duly licensed or qualified to do business and in good standing as a foreign organization in all jurisdictions in which the nature of the activities conducted by it or the character of the assets owned or leased by it makes such licensing or qualification necessary, except where the failure to be so licensed or qualified will not have a material adverse effect on the ability of the Company to carry on its business as presently conducted. Except as disclosed in the Registration Statement and on Schedule 3(c) to this Agreement, the Company does not own, and at the Closing Date will not own, directly or indirectly, any shares of stock or any other equity or long-term debt securities of any corporation or have any equity interest in any firm, partnership, joint venture, association or other entity. Complete and correct copies of the articles or certificate of incorporation and of the bylaws of the Company and all

amendments thereto have been delivered to the Placement Agent, and no changes therein will be made subsequent to the date hereof and prior to the Closing Date. Atugen Biotechnology GmbH ("Atugen") has been duly organized or formed and is validly existing as a corporation in good standing under the laws of its jurisdiction of formation. Atugen is duly qualified and in good standing as a foreign corporation in each jurisdiction in which the character or location of its properties (owned, leased or licensed) or the nature or conduct of its business makes such qualification necessary, except for those failures to be so qualified or in good standing which will not have a material effect on Atugen. All of the shares of issued capital stock set forth on Schedule 3(c) as owned by the Company are owned free and clear of any lien, encumbrance, claim, security interest, restriction on transfer, shareholders' agreement, voting trust other defect of title whatsoever.

(d) The issued and outstanding shares of capital stock of the Company have been validly issued, are fully paid and nonassessable and, other than as set forth in the Registration Statement, are not subject to any preemptive or similar rights. Except as set forth in the Registration Statement and the Prospectus such shares are not subject to any preemptive or similar rights. The Company has an authorized, issued and outstanding capitalization as set forth in the Prospectus as of the dates referred to therein. The description of the securities of the Company in the Registration Statement and the Prospectus is, and at the Closing Date will be, complete and accurate in all respects. Except as set forth in the Registration Statement and the Prospectus, as of the date referred to therein, the Company did not have outstanding any options to purchase, or any rights or warrants to subscribe for, or any securities or obligations convertible into, or exchangeable for, or any contracts or commitments to issue or sell, any shares of capital stock or other securities.

(e) The Company has full legal right, power and authority to enter into this Agreement and perform the transactions contemplated hereby. This Agreement has been duly authorized and validly executed and delivered by the Company and is a legal, valid and binding agreement of the Company enforceable against the Company in accordance with its terms, subject to the effect of applicable bankruptcy, insolvency or similar laws affecting creditors' rights generally and equitable principles of general applicability. The Escrow Agreement has been duly authorized and validly executed and delivered by the Company and is a legal, valid and binding agreement of the Company enforceable against the Company in accordance with its terms, subject to the effect of applicable bankruptcy, insolvency or similar laws affecting creditors' rights generally and equitable principles of general applicability.

(f) The issuance and sale of the Shares have been duly authorized by the Company, and the Shares, when issued and paid for in accordance with this Agreement, will be duly and validly issued, fully paid and nonassessable and will not be subject to preemptive or similar rights. The holders of the Shares will not be subject to personal liability by reason of being such holders. The Shares, when issued, will conform in all material respects to the description thereof set forth in the Prospectus.

(g) The financial statements and the related notes included in the Registration Statement and the Prospectus present fairly, in all material respects, the financial

condition of the Company as of the dates thereof and the results of its operations and cash flows at the dates and for the periods covered thereby in conformity with generally accepted accounting principles ("GAAP"). No other financial statements or schedules of the Company or any other entity are required by the Act or the Rules and Regulations to be included in the Registration Statement or the Prospectus. Ernst & Young LLP (the "Accountants"), who have reported on such financial statements and schedules, are independent accountants with respect to the Company as required by the Act and the Rules and Regulations. The financial statements of the Company and the related notes and schedules included in the Registration Statement and the Prospectus have been prepared in conformity with the requirements of the Act and the Rules and Regulations and present fairly the information shown therein.

(h) The Company maintains a system of internal accounting controls sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorization; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any

differences.

(i) Subsequent to the respective dates as of which information is given in the Registration Statement and the Prospectus and prior to the Closing Date, except as set forth in or contemplated by the Registration Statement and the Prospectus, (i) there has not been and will not have been any change in the capitalization of the Company other than non-material changes in the ordinary course of business, or any material adverse change in the business, properties, business prospects, condition (financial or otherwise) or results of operations of the Company arising for any reason whatsoever, (ii) the Company has not incurred nor will it incur any material liabilities or obligations, direct or contingent, nor has the Company entered into nor will it enter into any material transactions other than pursuant to this Agreement, the Registration Statement and the transactions referred to herein and therein and (iii) the Company has not and will not have paid or declared any dividends or other distributions of any kind on any class of its capital stock.

(j) Any real property and buildings held under lease to the Company are held or leased by the Company under valid, binding and enforceable leases conforming to the description thereof set forth in or incorporated by reference into the Registration Statement and the Prospectus, with such exceptions as do not materially interfere with the use made and proposed to be made of such property and buildings by the Company.

(k) The Company is not, nor upon completion of the transactions contemplated herein will it be, an "investment company" or an "affiliated person" of, or "promoter" or "principal underwriter" for, an "investment company," as such terms are defined in the Investment Company Act of 1940, as amended (the "Investment Company Act").

(l) Except as set forth or referred to in the Registration Statement and the Prospectus, there are no actions, suits or proceedings pending, or to the Company's knowledge, threatened against or affecting the Company or any of its officers in their capacity as such, before or by any Federal or state court, commission, regulatory body, administrative agency or other governmental body, domestic or foreign, which is reasonably expected by management of the Company to materially adversely affect the business, properties, prospects, condition (financial or otherwise) or results of operations of the Company.

(m) The Company has, and at the Closing Date will have, (i) all governmental licenses, permits, consents, orders, approvals and other authorizations necessary to carry on its business as presently conducted except where the failure to have such governmental licenses, permits, consents, orders, approvals and other authorizations would not have a material adverse effect on the business, properties, prospects, condition (financial or otherwise) or results of operation of the Company, (ii) complied with all laws, regulations and orders applicable to either it or its business, except where the failure to

so comply would not have a material adverse effect on the business, properties, prospects, condition (financial or otherwise) or results of operations of the Company, and (iii) performed all its obligations required to be performed, and is not, and at the Closing Date will not be, to the Company's best knowledge, in default, under any indenture, mortgage, deed of trust, voting trust agreement, loan agreement, bond, debenture, note agreement, lease, contract or other agreement or instrument (collectively, a "contract or other agreement") to which it is a party or by which its property is bound or affected, except as otherwise set forth in the Registration Statement and the Prospectus and except where such default would not have a material adverse effect on the business, properties, prospects, condition (financial or otherwise) or results of operations of the Company, and, to the Company's best knowledge, no other party under any material contract or other agreement to which it is a party is in default in any respect thereunder. The Company is not in violation of any provision of its organizational or governing documents.

(n) The Company has all corporate power and authority to enter into this Agreement and the Escrow Agreement, and to carry out the provisions and conditions hereof and thereof, and all consents, authorizations, approvals and orders required in connection herewith and therewith have been obtained, except such as have been obtained, such as may be required under state securities or Blue Sky Laws or the by-laws and rules of the National Association of Securities Dealers, Inc. (the "NASD").

(o) Neither (i) the issuance, offering and sale of the Shares pursuant hereto, nor (ii) the compliance by the Company with the other provisions hereof require the consent, approval, authorization, registration or qualification of or with any governmental authority, except such as have been obtained, such as may be required under state securities or Blue Sky laws or the bylaws and rules of the NASD and, if the Registration Statement is not effective under the Act as of the time of execution hereof, such as may be required (and shall be obtained as provided in this Agreement) under the Act.

(p) Neither the execution of this Agreement or the Escrow Agreement, nor the issuance, offering or sale of the Shares, nor the consummation of any of the

transactions contemplated herein or in the Escrow Agreement, nor the compliance by the Company with the terms and provisions hereof or thereof will conflict with, or will result in a breach of, any of the terms and provisions of, or has constituted or will constitute a default under, or has resulted in or will result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to the terms of any contract or other agreement to which the Company may be bound or to which any of the property or assets of the Company is subject, except such conflicts, breaches or defaults as may have been waived; nor will such action result in any violation of the provisions of the Company's organizational or governing documents, or any statute or any order, rule or regulation applicable to the Company or of any

court or of any federal, state or other regulatory authority or other government body having jurisdiction over the Company.

(q) There is no document or contract of a character required to be described in the Registration Statement or the Prospectus or to be filed as an exhibit to the Registration Statement which is not described or filed as required. All such contracts to which the Company is a party have been duly authorized, executed and delivered by the Company, constitute valid and binding agreements of the Company, and are enforceable against the Company in accordance with the terms thereof, subject to the effect of applicable bankruptcy, insolvency or similar laws affecting creditors' rights generally and equitable principles of general applicability.

(r) No statement, representation or warranty made by the Company in this Agreement or made in any certificate or document required by this Agreement or the Escrow Agreement to be delivered to the Placement Agent, the Investors or the Escrow Agent was or will be, when made, inaccurate, untrue or incorrect in any material respect.

(s) The Company and its directors, officers or controlling persons have not taken, directly or indirectly, any action intended, or which might reasonably be expected, to cause or result, under the Act or otherwise, in, or which has constituted, stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Common Stock.

(t) No holder of securities of the Company has rights to the registration of any securities of the Company as a result of the filing of the Registration Statement, other than rights which are not exercisable due to the Placement Agent's determination to include only securities sold directly from the Company, except for such rights as have been waived or those other rights which have been disclosed to the Placement Agent.

(u) The Common Stock is currently listed on the Nasdaq National Market (the "NNM").

(v) The Company is not involved in any material labor dispute nor is any such dispute known by the Company to be threatened.

(w) Except as set forth in the Registration Statement and the Prospectus, the business, operations of the Company have been and are being conducted in compliance with all applicable laws, ordinances, rules, regulations, licenses, permits, approvals, plans, authorizations or requirements relating to occupational safety and health, or pollution, or protection of health or the environment (including, without limitation, those relating to emissions, discharges, releases or threatened releases of pollutants, contaminants or hazardous or toxic substances, materials or wastes into ambient air, surface water, groundwater or land, or relating to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or

handling of chemical substances, pollutants, contaminants or hazardous or toxic substances, materials or wastes, whether solid, gaseous or liquid in nature) of any governmental department, commission, board, bureau, agency or instrumentality of the United States, any state or political subdivision thereof, or any foreign jurisdiction, and all applicable judicial or administrative agency or regulatory decrees, awards, judgments and orders relating thereto, except where the failure to be in such compliance will not, individually or in the aggregate, have a material adverse effect on the ability of the Company to carry on its business as presently conducted; and the Company has not received any notice from any governmental instrumentality or any third party alleging any material violation thereof or liability thereunder (including, without limitation, liability for costs of investigating or remediating sites containing hazardous substances and/or damages to natural resources).

(x) Except as disclosed in or specifically contemplated by the Registration Statement, (i) the Company owns or has obtained valid and enforceable licenses or options for the inventions, patent applications, patents, trademarks (both registered and unregistered), tradenames, copyrights and trade secrets necessary for the conduct of the Company's business as currently conducted and as the Registration Statement indicates the Company contemplates conducting (collectively, the "Intellectual Property"); and (ii) to the Company's knowledge (for each of the following subsections (a) through (e)): (a) there are no third parties who have any ownership rights to any Intellectual Property that is owned by, or has been licensed to, the Company for the products and services described in the Registration Statement that would preclude the Company from conducting its businesses as currently conducted and as the Registration Statement indicates the Company contemplates conducting, except for the ownership rights of the owners of the Intellectual Property licensed or optioned by the Company; (b) there are currently no sales of any products that would constitute an infringement by third parties of any Intellectual Property owned, licensed or optioned by the Company; (c) there is no pending or threatened action, suit, proceeding or claim by others challenging the rights of the Company in or to any Intellectual Property owned, licensed or optioned by the Company; (d) there is no pending or threatened action, suit, proceeding or claim by others challenging the validity or scope of any Intellectual Property owned, licensed or optioned by the Company, other than non-material claims; and (e) there is no pending or threatened action, suit, proceeding or claim by others that the Company infringe or otherwise violate any patent, trademark, copyright, trade secret or other proprietary right of others, other than non-material claims.

(y) The Company has filed all necessary federal, state and foreign income and franchise tax returns and has paid or accrued all taxes shown as due thereon, and the Company

has no knowledge of any tax deficiency which has been or might be asserted or threatened against it which could have a material adverse effect on the

business, properties, prospects, condition (financial or otherwise) or results of operations of the Company.

(aa) On the Closing Date, all stock transfer or other taxes (other than income taxes) which are required to be paid in connection with the sale and transfer of the Shares to be sold hereunder will be, or will have been, fully paid or provided for by the Company and all laws imposing such taxes will be or will have been fully complied with.

(bb) The Company maintains insurance of the types and in the amounts that the Company reasonably believes is adequate for its business, including, but not limited to, insurance covering all real and personal property owned or leased by the Company against theft, damage, destruction, acts of vandalism and all other risks customarily insured against by similarly situated companies, all of which insurance is in full force and effect.

(cc) The Company has not at any time since its incorporation, directly or indirectly, (i) made any unlawful contribution to any candidate for public office, or failed to disclose fully any contribution in violation of law, or (ii) made any payment to any federal or state governmental officer or official, or other person charged with similar public or quasi-public duties, other than payments required or permitted by the laws of the United States or any jurisdiction thereof.

(dd) The Company has initiated a review and assessment of all areas within its business and operations that could be adversely affected by the "Year 2000 Problem" (that is, the risk that computer applications used by the Company may be unable to recognize and perform properly date-sensitive functions involving certain dates prior to and any date after December 31, 1999). Based on the foregoing, the Company believes that the computer applications that are currently material to its business and operations are reasonably expected to be able to perform properly date-sensitive functions for all dates before and after January 1, 2000, except to the extent that a failure to do so would not reasonably be expected to have a material adverse effect on the business, properties, prospects, condition (financial or otherwise) or results of operations of the Company.

(ee) Each officer and director of the Company listed on Exhibit B hereto has delivered to the Placement Agent an agreement in the form of Attachment A hereto to the effect that he or she will not, for a period of 90 days after the date hereof, without the prior written consent of the Placement Agent, offer to sell, sell, contract to sell, grant any option to purchase or otherwise dispose (or announce any offer, sale, grant of any option to purchase or other disposition) of any shares of capital stock, directly or indirectly, of the Company or securities convertible into, or exchangeable or exercisable for, shares of capital stock of the Company.

(ff) The Company has delivered to the Placement Agent an agreement in the form of Attachment B hereto to the effect that it will not, for a period of 90 days after the date hereof, without the prior written consent of the Placement Agent, offer to sell, sell, contract to sell, grant any option to

purchase or otherwise dispose (or announce any offer, sale, grant of

any option to purchase or other disposition) of any shares of capital stock of the Company or securities convertible into, or exchangeable or exercisable for, shares of capital stock of the Company, except with respect to the issuance of shares of Common Stock upon the exercise of stock options and warrants outstanding as of the date hereof the and the issuance of Common Stock or stock options under any benefit plan of the Company.

4. Agreements of the Company. The Company covenants and agrees with the Placement Agent as follows:

(a) The Company will not, either prior to the Effective Date or thereafter during such period as the Prospectus would be required by law to be delivered in connection with sales of the Shares by an underwriter or dealer, file any amendment or supplement to the Registration Statement or the Prospectus, unless a copy thereof shall first have been submitted to the Placement Agent within a reasonable period of time prior to the filing thereof and the Placement Agent shall not have objected thereto in good faith.

(b) The Company will use its best efforts to cause the Registration Statement to become effective, and will notify the Placement Agent promptly, and will confirm such advice in writing, (1) when the Registration Statement has become effective and when any post-effective amendment thereto becomes effective, (2) of any request by the securities or other governmental authority (including, without limitation, the Commission) of any jurisdiction for amendments or supplements to the Registration Statement or the Prospectus or for additional information, (3) of the issuance by any securities or other governmental authority (including, without limitation, the Commission) of any jurisdiction of any stop order suspending the effectiveness of the Registration Statement or the initiation of any proceedings for that purpose or the threat thereof, (4) of the happening of any event during the period mentioned in Section 4(a) that in the judgment of the Company makes any statement made in the Registration Statement or the Prospectus untrue or that requires the making of any changes in the Registration Statement or the Prospectus in order to make the statements therein, in light of the circumstances in which they are made, not misleading and (5) of receipt by the Company or any representative or attorney of the Company of any other communication from the securities or other governmental authority (including, without limitation, the Commission) of any jurisdiction relating to any of the Registration Statement, any Preliminary Prospectus or the Prospectus. If at any time any securities or other governmental authority (including, without limitation, the Commission) of any jurisdiction shall issue any order suspending the effectiveness of the Registration Statement, the Company will make every reasonable effort to obtain the withdrawal of such order at the earliest possible moment. If the Company has omitted any information from the Registration Statement, pursuant to Rule 430A, it will use its best efforts to comply with the provisions of and make all

requisite filings with the Commission pursuant to said Rule 430A and to notify the Placement Agent promptly of all such filings.

(c) If, at any time when a Prospectus relating to the Shares is required to be delivered under the Act, any event occurs as a result of which the Prospectus, as then amended or supplemented, would, in the judgment of counsel to the Company or counsel to the

Placement Agent, include any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, or the Registration Statement, as then amended or supplemented, would, in the judgment of counsel to the Company or counsel to the Placement Agent, include any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein not misleading, or if for any other reason it is necessary, in the judgment of counsel to the Company or counsel to the Placement Agent, at any time to amend or supplement the Prospectus or the Registration Statement to comply with the Act or the Rules and Regulations, the Company will promptly notify the Placement Agent and, subject to Section 4(a) hereof, will promptly prepare and file with the Commission, at the Company's expense, an amendment to the Registration Statement or an amendment or supplement to the Prospectus that corrects such statement or omission or effects such compliance and will deliver to the Placement Agent, without charge, such number of copies thereof as the Placement Agent may reasonably request. The Company consents to the use of the Prospectus or any amendment or supplement thereto by the Placement Agent.

(d) The Company will furnish to the Placement Agent and its counsel, without charge, (i) one signed copy of the registration statement described in Section 3(a) hereof and each pre-effective amendment thereto, including financial statements and schedules, and all exhibits thereto and (ii) so long as a prospectus relating to the Shares is required to be delivered under the Act, as many copies of each Preliminary Prospectus or the Prospectus or any amendment or supplement thereto as the Placement Agent may reasonably request.

(e) The Company will comply with all the undertakings contained in the Registration Statement.

(f) Prior to the sale of the Shares to the Investors, the Company will cooperate with the Placement Agent and its counsel in connection with the registration or qualification of the Shares for offer and sale under the state securities or Blue Sky laws of such jurisdictions as the Placement Agent may request; provided, that in no event shall the Company be obligated to qualify to do business in any jurisdiction where it is not now so qualified or to take any action which would subject it to general service of process in any jurisdiction where it is not now so subject.

(g) The Company will make generally available to holders of its

securities, as soon as may be practicable, but in no event later than the last day of the fifteenth full calendar month following the calendar quarter in which the Effective Date falls, a consolidated earnings statement (which need not be audited but shall be in reasonable detail) for a period of 12 months ended commencing after the Effective Date, and satisfying the provisions of Section 11(a) of the Act (including Rule 158 of the Rules and Regulations).

(h) The Company will not at any time, directly or indirectly, take any action intended, or which might reasonably be expected, to cause or result in, or which will

constitute, stabilization of the price of the Shares to facilitate the sale or resale of any of the Shares.

(i) The Company will apply the net proceeds from the offering and sale of the Shares in the manner set forth in the Prospectus under the caption "Use of Proceeds."

5. Expenses. Whether or not the transactions contemplated by this Agreement are consummated or this Agreement is terminated, the Company will pay all costs and expenses incident to the performance of the obligations of the Company under this Agreement, including but not limited to costs and expenses of or relating to (1) the preparation, printing and filing of the Registration Statement (including each pre- and post-effective amendment thereto) and exhibits thereto, each Preliminary Prospectus, the Prospectus and any amendment or supplement to the Prospectus, including all fees, disbursements and other charges of counsel to the Company, (2) the preparation and delivery of certificates representing the Shares, (3) furnishing (including costs of shipping and mailing) such copies of the Registration Statement (including all pre- and post-effective amendments thereto), the Prospectus and any Preliminary Prospectus, and all amendments and supplements to the Prospectus, as may be requested for use in connection with the direct placement of the Shares, (4) the listing of the Common Stock on the NMS, (5) any filings required to be made by the Placement Agent with the NASD, and the fees, disbursements and other charges of counsel for the Placement Agent in connection therewith, (6) the registration or qualification of the Shares for offer and sale under the securities or Blue Sky laws of such jurisdictions designated pursuant to Section 4(f), including the reasonable fees, disbursements and other charges of counsel to the Placement Agent in connection therewith and the preparation and printing of preliminary, supplemental and final Blue Sky memoranda, (7) fees, disbursements and other charges of counsel to the Company and (8) the fees of the Escrow Agent. The Company shall reimburse the Placement Agent, on a fully accountable basis, for all travel, legal and other out-of-pocket expenses incurred in connection with the engagement hereunder, up to a maximum of $[150,000].

6. Conditions of the Obligations of the Placement Agent. The

obligations of the Placement Agent hereunder are subject to the following conditions:

(a) Notification that the Registration Statement has become effective shall be received by the Placement Agent not later than 5:00 p.m., New York City time, on the date of this Agreement or at such later date and time as shall be consented to in writing by the Placement Agent and all filings required by Rule 424 of the Rules and Regulations and Rule 430A shall have been made.

(b) (i) No stop order suspending the effectiveness of the Registration Statement shall have been issued, and no proceedings for that purpose shall be pending or threatened by any securities or other governmental authority (including, without limitation, the Commission), (ii) no order suspending the effectiveness of the Registration Statement or the qualification or registration of the Shares under the securities or Blue Sky laws of any jurisdiction shall be in effect and no proceeding for such purpose shall be pending before or

threatened or contemplated by any securities or other governmental authority (including, without limitation, the Commission), (iii) any request for additional information on the part of the staff of any securities or other governmental authority (including, without limitation, the Commission) shall have been complied with to the satisfaction of the staff of the Commission or such authorities and (iv) after the date hereof no amendment or supplement to the Registration Statement or the Prospectus shall have been filed unless a copy thereof was first submitted to the Placement Agent and the Placement Agent did not object thereto in good faith, and the Placement Agent shall have received certificates of the Company, dated the Closing Date and signed by the President and Chief Executive Officer or the Chairman of the Board of Directors of the Company, and the Chief Financial Officer of the Company, to the effect of clauses (i), (ii) and (iii).

(c) Since the respective dates as of which information is given in the Registration Statement and the Prospectus, (i) there shall not have been a material adverse change in the general affairs, business, business prospects, properties, management, condition (financial or otherwise) or results of operations of the Company, whether or not arising from transactions in the ordinary course of business, in each case other than as set forth in or contemplated by the Registration Statement and the Prospectus and (ii) the Company shall not have sustained any material loss or interference with its business or properties from fire, explosion, flood or other casualty, whether or not covered by insurance, or from any labor dispute or any court or legislative or other governmental action, order or decree, which is not set forth in the Registration Statement and the Prospectus, if in the judgment of the Placement Agent any such development makes it impracticable or inadvisable to consummate the sale and delivery of the Shares to Investors at the public offering price.

(d) Since the respective dates as of which information is given

in the Registration Statement and the Prospectus, there shall have been no litigation or other proceeding instituted against the Company or any of its officers or directors in their capacities as such, before or by any Federal, state or local court, commission, regulatory body, administrative agency or other governmental body, domestic or foreign, which litigation or proceeding is reasonably expected by management to materially and adversely affect the business, properties, business prospects, condition (financial or otherwise) or results of operations of the Company.

(e) Each of the representations and warranties of the Company contained herein shall be true and correct in all material respects at the Closing Date, as if made on such date, and all covenants and agreements herein contained to be performed on the part of the Company and all conditions herein contained to be fulfilled or complied with by the Company at or prior to the Closing Date shall have been duly performed, fulfilled or complied with in all material respects.

(f) The Placement Agent shall have received an opinion, dated the Closing Date (or such other date as may be set forth in a representation or warranty), of Rothgerber Johnson & Lyons LLP, as counsel to the Company, in form and substance reasonably satisfactory to the Placement Agent.

(g) Concurrently with the execution and delivery of this Agreement, or, if the Company elects to rely on Rule 430A, on the date of the Prospectus, the Accountants shall have furnished to the Placement Agent a letter, dated the date of its delivery (the "Original Letter"), addressed to the Placement Agent and in form and substance satisfactory to the Placement Agent, confirming that (i) they are independent public accountants with respect to the Company within the meaning of the Act and the Rules and Regulations; (ii) in their opinion, the financial statements and any supplementary financial information included in the Registration Statement and examined by them comply as to form in all material respects with the applicable accounting requirements of the Act and the Rules and Regulations; (iii) on the basis of procedures, not constituting an examination in accordance with generally accepted auditing standards, set forth in detail in the Original Letter, a reading of the latest available interim financial statements of the Company, inspections of the minute books of the Company since the latest audited financial statements included in the Prospectus, inquiries of officials of the Company responsible for financial and accounting matters and such other inquiries and procedures as may be specified in the Original Letter to a date not more than five days prior to the date of the Original Letter, nothing came to their attention that caused them to believe that: (A) as of a specified date not more than five days prior to the date of the Original Letter, there have been any changes in the capital stock of the Company or any increase in the long-term debt of the Company, or any decreases in net current assets or net assets or other items specified by the Placement Agent, or any increases in any items specified by the Placement Agent, in each case as compared with amounts shown in the latest balance sheet included in the Prospectus, except in each case for changes, increases or decreases which

the Prospectus discloses have occurred or may occur or which are described in the Original Letter; and (B) for the period from the date of the latest financial statements included in the Prospectus to the specified date referred to in Clause (A), there were any decreases in revenues or the total or per share amounts of net income or other items specified by the Placement Agent, or any increases in any items specified by the Placement Agent, in each case as compared with the comparable period of the preceding year and with any other period of corresponding length specified by the Placement Agent, except in each case for decreases or increases which the Prospectus discloses have occurred or may occur or which are described in the Original Letter; and (iv) in addition to the examination referred to in their reports included in the Prospectus and the procedures referred to in clause (iii) above, they have carried out certain specified procedures, not constituting an examination in accordance with generally accepted auditing standards, with respect to certain amounts, percentages and financial information specified by the Placement Agent, which are derived from the general accounting, financial or other records of the Company, as the case may be, which appear in the Prospectus or in Part II of, or in exhibits or schedules to, the Registration Statement, and have compared such amounts, percentages and financial information with such accounting, financial and other records and have found them to be in agreement. At the Closing Date, the Accountants shall have furnished to the Placement Agent a letter, dated the date of its delivery, which shall confirm, on the basis of a review in accordance with the procedures set forth in the Original Letter, that nothing has come to their attention during the period from the date of the Original Letter referred to in the prior sentence to a date (specified in the letter) not more than five days prior to the Closing Date which would

require any change in the Original Letter if it were required to be dated and delivered at the Closing Date.

(h) The Placement Agent shall have received an opinion, dated the Closing Date, of Lyon & Lyon LLP, patent counsel for the Company, in form and substance satisfactory to the Placement Agent as to certain intellectual property matters referenced in the Registration Statement.

(i) At the Closing Date, there shall be furnished to the Placement Agent a certificate, dated the date of its delivery, signed by each of the Chief Executive Officer and the Chief Financial Officer of the Company, in form and substance satisfactory to the Placement Agent to the effect that to each of such person's knowledge:

(i) Each signer of such certificate has carefully examined the Registration Statement and the Prospectus and (A) as of the date of such certificate, (x) the Registration Statement does not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein not misleading and (y) the Prospectus does not contain any untrue statement of a material fact or omit to state a material fact required to be stated

therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading and (B) since the Effective Date no event has occurred as a result of which it is necessary to amend or supplement the Prospectus in order to make the statements therein not untrue or misleading in any material respect.

(ii) Each of the representations and warranties of the Company contained in this Agreement were, when originally made, and are, at the time such certificate is delivered, true and correct in all material respects.

(iii) Each of the covenants required herein to be performed by the Company on or prior to the date of such certificate has been duly, timely and fully performed and each condition herein required to be complied with by the Company on or prior to the delivery of such certificate has been duly, timely and fully complied with.

(iv) No stop order suspending the effectiveness of the Registration Statement or of any part thereof has been issued and no proceedings for that purpose have been instituted or are contemplated by the Commission.

(v) Subsequent to the date of the most recent financial statements in the Prospectus, there has been no material adverse change in the financial position or results of operations of the Company, except as set forth in or contemplated by the Prospectus.

(j) The Shares shall be qualified for sale in such states as the Placement Agent may reasonably request, each such qualification shall be in effect and not subject to any stop order or other proceeding on the Closing Date; provided that in no event

shall the Company be obligated to qualify to do business in any jurisdiction where it is not now so qualified or to take any action which would subject it to taxation or general service of process in any jurisdiction where it is not now so subject.

(k) The Company shall have furnished to the Placement Agent such certificates, in addition to those specifically mentioned herein, as the Placement Agent may have reasonably requested as to the accuracy and completeness at the Closing Date of any statement in the Registration Statement or the Prospectus, as to the accuracy at the Closing Date of the representations and warranties of the Company as to the performance by the Company of its obligations hereunder, or as to the fulfillment of the conditions concurrent and precedent to the obligations hereunder of the Placement Agent.

(l) The Placement Agent shall have received the letters referred

to in Section 3 hereof substantially in the form of Attachments A and B.

7. Indemnification.

(a) The Company shall indemnify and hold harmless the Placement Agent, the directors, officers, employees and agents of the Placement Agent and each person, if any, who controls the Placement Agent within the meaning of Section 15 of the Act or Section 20 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), from and against any and all losses, claims, liabilities, expenses and damages, joint or several, (including any and all investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in settlement of, any action, suit or proceeding or any claim asserted), to which it, or any of them, may become subject under the Act or other Federal or state statutory law or regulation, at common law or otherwise, insofar as such losses, claims, liabilities, expenses or damages arise out of or are based on (i) any untrue statement or alleged untrue statement made by the Company in Section 3 of this Agreement, (ii) any untrue statement or alleged untrue statement of any material fact contained in (A) any Preliminary Prospectus, the Registration Statement or the Prospectus or any amendment or supplement to the Registration Statement or the Prospectus and (B) any application or other document, or any amendment or supplement thereto, executed by the Company based upon written information furnished by or on behalf of the Company filed in any jurisdiction in order to qualify the Shares under the securities or Blue Sky laws thereof or filed with the Commission or any securities association or securities exchange (each, an "Application") or (iii) the omission or alleged omission to state in any Preliminary Prospectus, the Registration Statement or the Prospectus or any supplement to the Registration Statement or the Prospectus or any Application a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances in which they were made, not misleading; provided, however, that the Company will not be liable to the extent that such loss, claim, liability, expense or damage arises from the sale of the Shares in the public offering to any person and is based solely on an untrue statement or omission or alleged untrue statement or omission made in reliance on and in conformity with information relating to the Placement Agent furnished in writing to the Company by the Placement Agent expressly for inclusion in the Registration Statement, any Preliminary Prospectus or the Prospectus; and provided further, that such indemnity with respect to any Preliminary

Prospectus shall not inure to the benefit of any Placement Agent (or any person controlling such Placement Agent) from whom the person asserting any such loss, claim, damage, liability or action purchased Shares which are the subject thereof to the extent that any such loss, claim, damage or liability (i) results from the fact that such Placement Agent failed to send or give a copy of the Prospectus (as amended or supplemented) to such person at or prior to the confirmation of the sale of such Shares to such person in any case where such

delivery is required by the Act and (ii) arises out of or is based upon an untrue statement or omission of a material fact contained in such Preliminary Prospectus that was corrected in the Prospectus (or any amendment or supplement thereto), unless such failure to deliver the Prospectus (as amended or supplemented) was the result of noncompliance by the Company with Section 5(d). This indemnity agreement will be in addition to any liability which the Company may otherwise have. The Company will not, without the prior written consent of the Placement Agent (which will not be unreasonably withheld), settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action, suit or proceeding in respect of which indemnification may be sought hereunder (whether or not such Placement Agent or any person who controls such Placement Agent within the meaning of Section 15 of the Act or Section 20 of the Exchange Act is a party to each claim, action, suit or proceeding), unless such settlement, compromise or consent includes an unconditional release of the Placement Agent and each such controlling person from all liability arising out of such claim, action, suit or proceeding.

(b) The Placement Agent will indemnify and hold harmless the Company, each person, if any, who controls the Company within the meaning of Section 15 of the Act or Section 20 of the Exchange Act, each director of the Company and each officer of the Company who signs the Registration Statement to the same extent as the foregoing indemnity from the Company to the Placement Agent, but only insofar as losses, claims, liabilities, expenses or damages arise out of or are based on any untrue statement or omission or alleged untrue statement or omission made in reliance on and in conformity with information relating to the Placement Agent furnished in writing to the Company by the Placement Agent expressly for use in the Registration Statement, any Preliminary Prospectus or the Prospectus. This indemnity agreement will be in addition to any liability that the Placement Agent might otherwise have. The Company acknowledges that, for all purposes under this Agreement, the statements set forth under the heading "Plan of Distribution" in any Preliminary Prospectus and the Prospectus constitute the only information relating to the Placement Agent furnished in writing to the Company by the Placement Agent expressly for inclusion in the Registration Statement, any Preliminary Prospectus or the Prospectus.

(c) Any party that proposes to assert the right to be indemnified under this Section 7 will, promptly after receipt of notice of commencement of any action against such party in respect of which a claim is to be made against an indemnifying party or parties under this Section 7, notify each such indemnifying party of the commencement of such action, enclosing a copy of all papers served, but the omission so to notify such indemnifying party will not relieve it from any liability that it may have to any indemnified party under the foregoing provisions of this Section 7 unless, and only to the extent that, such omission results in the forfeiture of substantive rights or defenses by the indemnifying party. If any such action

is brought against any indemnified party and it notifies the indemnifying party

of its commencement, the indemnifying party will be entitled to participate in and, to the extent that it elects by delivering written notice to the indemnified party promptly after receiving notice of the commencement of the action from the indemnified party, jointly with any other indemnifying party similarly notified, to assume the defense of the action, with counsel reasonably satisfactory to the indemnified party, and after notice from the indemnifying party to the indemnified party of its election to assume the defense, the indemnifying party will not be liable to the indemnified party for any legal or other expenses except as provided below and except for the reasonable costs of investigation subsequently incurred by the indemnified party in connection with the defense. The indemnified party will have the right to employ its own counsel in any such action, but the fees, expenses and other charges of such counsel will be at the expense of such indemnified party unless (1) the employment of counsel by the indemnified party has been authorized in writing by the indemnifying party, (2) the indemnified party has reasonably concluded (based on advice of counsel) that a conflict exists (based on advice of counsel to the indemnified party) between the indemnified party and the indemnifying party that would prevent the counsel selected by the indemnifying party from representing the indemnified party (in which case the indemnifying party will not have the right to direct the defense of such action on behalf of the indemnified party) or (3) the indemnifying party has not in fact employed counsel to assume the defense of such action within a reasonable time after receiving notice of the commencement of the action, in each of which cases the reasonable fees, disbursements and other charges of counsel will be at the expense of the indemnifying party or parties. It is understood that the indemnifying party or parties shall not, in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the reasonable fees, disbursements and other charges of more than one separate firm admitted to practice in such jurisdiction at any one time for all such indemnified party or parties. All such fees, disbursements and other charges will be reimbursed by the indemnifying party promptly as they are incurred. The Company will not, without the prior written consent of the Placement Agent (which consent will not be unreasonably withheld), settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action, suit or proceeding in respect of which indemnification has been sought hereunder (whether or not the Placement Agent or any person who controls the Placement Agent within the meaning of Section 15 of the Act or Section 20 of the Exchange Act is a party to such claim, action, suit or proceeding), unless such settlement, compromise or consent includes an unconditional release of the Placement Agent and each such controlling person from all liability arising out of such claim, action, suit or proceeding. An indemnifying party will not be liable for any settlement of any action or claim effected without its written consent (which consent will not be unreasonably withheld).

(d) In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in the foregoing paragraphs of this Section 7 is applicable in accordance with its terms but for any reason is held to be unavailable from the Company or the Placement Agent, the Company and the Placement Agent will contribute to the total losses, claims, liabilities, expenses and damages (including any investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in

settlement of, any action, suit or proceeding or any claim asserted, but after deducting any contribution received by the Company from persons other than the Placement Agent such

as persons who control the Company within the meaning of the Act or the Exchange Act, officers of the Company who signed the Registration Statement and directors of the Company, who also may be liable for contribution) to which the Company and the Placement Agent may be subject in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and the Placement Agent on the other. The relative benefits received by the Company on the one hand and the Placement Agent on the other shall be deemed to be in the same proportion as the total net proceeds from the offering (before deducting Company expenses) received by the Company as set forth in the table on the cover page of the Prospectus bear to the fee received by the Placement Agent hereunder. If, but only if, the allocation provided by the foregoing sentence is not permitted by applicable law, the allocation of contribution shall be made in such proportion as is appropriate to reflect not only the relative benefits referred to in the foregoing sentence but also the relative fault of the Company, on the one hand, and the Placement Agent on the other, with respect to the statements or omissions which resulted in such loss, claim, liability, expense or damage, or action in respect thereof, as well as any other relevant equitable considerations with respect to such offering. Such relative fault shall be determined by reference to whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or the Placement Agent, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Placement Agent agree that it would not be just and equitable if contributions pursuant to this Section 7(d) were to be determined by pro rata allocation or by any other method of allocation which does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, liability, expense or damage, or action in respect thereof, referred to above in this Section 7(d) shall be deemed to include, for purpose of this Section 7(d), any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this Section 7(d), the Placement Agent shall not be required to contribute any amount in excess of the fee received by it, and no person found guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) will be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 7(d), any person who controls a party to this Agreement within the meaning of the Act or the Exchange Act will have the same rights to contribution as that party, and each officer of the Company who signed the Registration Statement will have the same rights to contribution as the Company, subject in each case to the provisions hereof. Any party entitled to contribution, promptly after receipt of notice of commencement of any action against such party in respect of which a claim for contribution may be made under this Section 7(d), will notify any such party or

parties from whom contribution may be sought, but the omission so to notify will not relieve the party or parties from whom contribution may be sought from any other obligation it or they may have under this Section 7(d). No party will be liable for contribution with respect to any action or claim settled without its written consent (which consent will not be unreasonably withheld).

8. Termination.

(a) The obligations of the Placement Agent under this Agreement may be terminated at any time prior to the Closing Date, by notice to the Company from the Placement Agent, without liability on the part of the Placement Agent to the Company if, prior to delivery and payment for the Shares, in the sole judgment of the Placement Agent (i) trading in the Common Stock of the Company shall have been suspended by the Commission or by the NNM, (ii) trading in securities generally on the NNM shall have been suspended or limited or minimum or maximum prices shall have been generally established on any of such exchanges, or additional material governmental restrictions, not in force on the date of this Agreement, shall have been imposed upon trading in securities generally by any of such exchanges or by order of the Commission or any court or other governmental authority, (iii) a general banking moratorium shall have been declared by Federal or New York State authorities, or (iv) any material adverse change in the financial or securities markets in the United States or any outbreak or material escalation of hostilities or declaration by the United States of a national emergency or war or other calamity or crisis shall have occurred, the effect of any of which is such as to make it, in the sole judgment of the Placement Agent, impracticable or inadvisable to market the Shares on the terms and in the manner contemplated by the Prospectus.

(b) The obligations of the parties under this Agreement shall be automatically terminated in the event that notice is given to the Escrow Agent as determination prior to the close of business on the date scheduled for receipt of the Requisite Funds, that the Requisite Funds have not been deposited by the Investors into the Escrow Account by the close of business on the Closing Date.

(c) If this Agreement shall be terminated pursuant to any of the provisions hereof (otherwise than pursuant to Section 8(b), or if the sale of the Shares provided for herein is not consummated because any condition to the obligations of the Placement Agent set forth herein is not satisfied or because of any refusal, inability or failure on the part of the Company to perform any agreement herein or comply with any provision hereof, the Company will, subject to demand by you, reimburse you for all out-of-pocket expenses incurred in connection herewith.

9. Right of First Refusal.

(a) For a period of 18 months from the date hereof, the Company grants the Placement Agent the right (provided the financing contemplated in this agreement is completed) to provide investment banking services to the Company on an exclusive basis in all matters for which investment banking services are sought by the Company (such right, the "Right of First Refusal"). For these purposes, investment banking services shall include, without limitation, (i) acting as lead manager for any underwritten public offering; (ii) acting as exclusive placement agent or financial advisor in connection with any private offering of securities of the Company; and (iii) acting as financial advisor in connection with any sale or other transfer by the Company, directly or indirectly, of a majority or controlling portion of its capital stock or assets to another entity, any purchase or other transfer by another entity, directly or indirectly, of a majority or controlling portion of the capital stock or assets of the Company, and any merger or consolidation of the Company with another entity. The Placement Agent shall notify the Company of its intention to exercise the Right of First Refusal within 15 business days following notice in writing by the Company. Any decision by the Placement Agent to act in any such capacity shall be contained in separate agreements, which agreements would contain, among other matters, provisions for customary fees for transactions of similar size and nature, as may be mutually agreed upon, and indemnification of the Placement Agent and its affiliates and shall be subject to general market conditions. If the Placement Agent declines to exercise the Right of First Refusal, the Company shall have the right to retain any other person or persons to provide such services on terms and conditions which are not materially more favorable to such other person or persons than the terms declined by the Placement Agent.

(b) If within [18] months after the termination of the Placement Agent's engagement hereunder, shares of Common Stock are sold by the Company through a placement to investors previously identified and/or contacted by the Placement Agent in its capacity as placement agent hereunder, then the Company shall pay the Placement Agent, at the time of each such sale, an amount equal to the Placement Fee with respect to the gross proceeds to the Company from each such sale.

10. Notices. Notice given pursuant to any of the provisions of this
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Agreement shall be in writing and, unless otherwise specified, shall be mailed or delivered (a) if to the Company, at the office of the Company, 2950 Wilderness Place, Boulder, CO 80301, Attention: Larry Bullock or (b) if to the Placement Agent, at the office of Hambrecht & Quist LLC, One Bush Street, San Francisco, CO 94104, Attention: Shelly D. Guyer. Any such notice shall be effective only upon receipt. Any notice under Section 7 may be made by facsimile or telephone, but if so made shall be subsequently confirmed in writing.

11. Survival. The respective representations, warranties,
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agreements, covenants, indemnities and other statements of the Company and the

Placement Agent set forth in this Agreement or made by or on behalf of them, respectively, pursuant to this Agreement shall remain in full force and effect, regardless of (i) any investigation made by or on behalf of the Company, any of its officers or directors, the Placement Agent or any controlling person

referred to in Section 7 hereof and (ii) delivery of and payment for the Shares. The respective agreements, covenants, indemnities and other statements set forth in Sections 5 and 7 hereof shall remain in full force and effect, regardless of any termination or cancellation of this Agreement.

12. Successors. This Agreement shall inure to the benefit of and shall be binding upon the Placement Agent, the Company and their respective successors and legal representatives, and nothing expressed or mentioned in this Agreement is intended or shall be construed to give any other person any legal or equitable right, remedy or claim under or in respect of this Agreement, or any provisions herein contained, this Agreement and all conditions and provisions hereof being intended to be and being for the sole and exclusive benefit of such persons and for the benefit of no other person except that (i) the indemnification and contribution contained in Sections 7(a) and (d) of this Agreement shall also be for the benefit of the directors, officers, employees and agents of the Placement Agent and any person or persons who control the Placement Agent within the meaning of Section 15 of the Act or Section 20 of the Exchange Act and (ii) the indemnification and contribution contained in Sections 7(b) and (d) of this Agreement shall also be for the benefit of the directors of the Company, the officers of the Company who have signed the Registration Statement and any person or persons who control the Company within the meaning of Section 15 of the Act or Section 20 of the Exchange Act. No Investor shall be deemed a successor because of such purchase.

13. Applicable Law. The validity and interpretations of this Agreement, and the terms and conditions set forth herein, shall be governed by and construed in accordance with the laws of the State of New York, without giving effect to any provisions relating to conflicts of laws.

14. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

15. Entire Agreement. This Agreement constitutes the entire understanding between the parties hereto as to the matters covered hereby and supersedes all prior understandings, written or oral, relating to such subject matter.

Please confirm that the foregoing correctly sets forth the agreement between the Company and the Placement Agent.

Very truly yours,

RIBOZYME PHARMACEUTICALS, INC.

By: _____
Name:
Title:

Confirmed as of the date first above mentioned:

HAMBRECHT & QUIST LLC

By: _____
Name:
Title:

EXHIBIT A

ESCROW AGREEMENT

EXHIBIT B

LOCK UP LETTERS

ATTACHMENT A

Hambrecht & Quist LLC
One Bush Street

San Francisco, CA 94104

Ladies and Gentlemen:

Reference is made to a Placement Agency Agreement (the "Placement Agency Agreement"), which will be executed between Ribozyme Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and Hambrecht & Quist LLC (the "Placement Agent").

In consideration of the Placement Agency Agreement, the undersigned hereby agrees not to, without the prior written consent of the Placement Agent, offer to sell, sell, contract to sell, grant any option to purchase or otherwise dispose of any shares, directly or indirectly, of the Company's Common Stock, par value $.01 per share (the "Common Stock"), owned by the undersigned for a period of 90 days after the date of the Placement Agency Agreement. Notwithstanding the foregoing, the undersigned may transfer any or all of the shares of Common Stock owned by him, either during his lifetime or on death, by gift, will or intestate succession to his immediate family or to a trust the beneficiaries of which are exclusively the undersigned and/or a member or members of his immediate family; provided however that any such successor shall agree to be bound by the provisions hereof.

It is understood that, if the Company notifies you that it does not intend to proceed with the issuance and sale of Shares (as defined in the Placement Agency Agreement) pursuant to the Placement Agency Agreement, if the Placement Agency Agreement does not become effective, or if the Placement Agency Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated prior to payment for and delivery of the Shares, the undersigned will be released from his obligations under this letter agreement.

Dated: April   , 1999

Very truly yours,

ATTACHMENT B

Hambrecht & Quist LLC
One Bush Street
San Francisco, CA 94104

Ladies and Gentlemen:

Reference is made to a Placement Agency Agreement (the "Placement Agency Agreement"), which will be executed between Ribozyme Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and Hambrecht & Quist LLC (the "Placement Agent").

In consideration of the Placement Agency Agreement, the undersigned hereby agrees not to, without the prior written consent of the Placement Agent, offer, sell or otherwise dispose of any shares , directly or indirectly, of the Company's Common Stock, par value $.01 per share (the "Common Stock"), owned by the undersigned for a period of 90 days after the date of the Placement Agency Agreement except with respect to the issuance of shares of Common Stock upon the exercise of stock options and warrants outstanding as of the date hereof and the issuance of Common Stock or stock options under any benefit plan of the Company.

It is understood that, if the Company notifies you that it does not intend to proceed with the issuance and sale of Shares (as defined in the Placement Agency Agreement) pursuant to the Placement Agency Agreement, if the Placement Agency Agreement does not become effective, or if the Placement Agency Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated prior to payment for and delivery of the Shares, the undersigned will be released from his obligations under this letter agreement.

Dated: April   , 1999

Very truly yours,

RIBOZYME PHARMACEUTICALS, INC.

Name:
Title:

EXHIBIT 1.2

FORM OF ESCROW AGREEMENT

ESCROW AGREEMENT, dated as of April , 1999, by and among Ribozyme Pharmaceuticals, Inc., a Delaware corporation (the "Company"), Hambrecht & Quist LLC (the "Placement Agent") and Citibank N.A., a national banking institution incorporated under the laws of the United States of America (the "Escrow Agent").

WHEREAS, the Company proposes to sell an aggregate of 1,800,000 shares of its common stock, par value $0.01 per share (the "Shares"), for an aggregate of $, all as described in the Company's registration statement on Form S-1 (Registration No. 333-) (which, together with all amendments or supplements thereto is referred to herein as the "Registration Statement");

WHEREAS, the Shares are being offered by the Company to investors whom the Placement Agent has introduced to the Company, pursuant to registration under the Securities Act of 1933, as amended, and pursuant to registration or exemptions from registration under state securities laws;

WHEREAS, the offering of the Shares will terminate on April , 1999 (the "Closing Date"), and, if subscriptions for the total number of Shares being offered pursuant to the Registration Statement have not been received by the Company on or before the Closing Date, no Shares will be sold and all payments made by subscribers will be refunded by the Escrow Agent with interest earned thereon, if any; and

WHEREAS, with respect to all subscription payments received from subscribers, the Company proposes to establish an escrow account with the Escrow Agent at the office of its Escrow Administration, 120 Wall Street, New York, New York 10043, Attention: .

NOW THEREFORE, it is agreed as follows:

1. Establishment of Escrow. The Escrow Agent hereby agrees to receive and disburse the proceeds from the offering of the Shares and any interest earned thereon in accordance herewith.

2. Deposit of Escrowed Property. The Placement Agent, on behalf of the subscribers for the Shares, shall from time to time, but in no event later than 12:00 noon on the date following the date of receipt by the Placement Agent, cause to be wired to or deposited with, or, cause the subscribers for the Shares to wire or deposit with, the Escrow Agent funds or checks of the subscribers delivered in payment for Shares (the "Escrowed Property"). Any checks delivered to the Escrow Agent pursuant to the terms hereof shall be made payable to or endorsed to the order of the Escrow Agent. The Escrow Agent upon receipt of such checks shall present such checks for payment to the drawee-bank under such checks. Any checks not honored by the drawee-bank thereunder after the first presentment for payment shall be returned to the Placement Agent, on behalf of such subscriber, in the same manner notices are delivered pursuant to Section 6. Upon receipt of funds or checks from the Placement Agent, the Escrow Agent shall credit such funds and the amount of such checks to a non-interest-bearing account (the "Escrow Account") held by the Escrow Agent. If following the credit of the amount of any check to the Escrow Account such check is dishonored, the Escrow Agent, if such dishonored check amount shall have been invested pursuant to Section 3, shall liquidate to the extent of such dishonored check amount such investments and debit the Escrow Account for the amount of such dishonored check plus, if any, the amount of interest and other income earned with respect to any investment of such dishonored check

amount.

3. Investment of Escrowed Property. The Escrow Agent on the second business day ("business day" defined for purposes of this Escrow Agreement as any day which is not a Saturday, a Sunday or a day on which banks or trust companies in the City and State of New York are authorized or obligated by law, regulation or executive order to remain closed) succeeding (unless such deposit is made in

federal or other immediately available or "same day" funds, in which case, on the business day next succeeding) the credit of any subscription proceeds to the Escrow Account pursuant to Section 2 and until release of such proceeds in accordance with the terms hereof, shall deposit such proceeds in a Citibank Money Market Deposit Account, pursuant to Rule 15c2-4 promulgated by the Securities and Exchange Commission under the Securities Exchange Act of 1934, as amended, in accordance with the terms set forth on Exhibit A hereto (made a part of this Escrow Agreement as if herein set forth). The Escrow Agent shall in no event be liable for any loss resulting from any change in interest rates applicable to proceeds invested pursuant to this Section. Interest on proceeds invested pursuant to this section shall accrue from the date of investment of such proceeds until the termination of such investment pursuant to the terms hereof and shall be paid as set forth in Section 5.

4. List of Subscribers. The Placement Agent shall furnish or cause to be furnished to the Escrow Agent, at the time of each deposit of funds or checks pursuant to Section 2, a list, substantially in the form of Exhibit B hereto, containing the name of, the address of, the number of Shares subscribed for by, the subscription amount delivered to the Escrow Agent on behalf of, and the social security or taxpayer identification number, if applicable, of each subscriber whose funds are being deposited, and to which is attached a completed W-9 form (or, in the case of any subscriber who is not a United States citizen or resident, a W-8 form) for each listed subscriber. The Escrow Agent shall notify the Placement Agent and the Company of any discrepancy between the subscription amounts set forth on any list delivered pursuant to this Section 4 and the subscription amounts received by the Escrow Agent. The Escrow Agent is authorized to revise such list to reflect the actual subscription amounts received and the release of any subscription amounts pursuant to Section 5.

5. Withdrawal of Subscription Amounts.

(a) If the Escrow Agent shall receive a notice, substantially in the form of Exhibit C hereto (an "Offering Termination Notice"), from the Company, the Escrow Agent shall (i) promptly after receipt of such Offering Termination Notice and the clearance of all checks received by the Escrow Agent as Escrowed Property, liquidate any investments that shall have been made pursuant to Section 3 and send to each subscriber listed on the list held by the Escrow Agent pursuant to Section 4 whose total subscription amount shall not have been released pursuant to paragraph (b) or (c) of this Section 5, in the manner set forth in paragraph (e) of this Section 5, a check to the order of such subscriber in the amount of the remaining subscription amount held by the Escrow Agent as set forth on such list held by the Escrow Agent, and (ii) promptly after the fourth business day of the month immediately following the month in which the investments made pursuant to Section 3 were terminated pursuant to this paragraph, send, in the manner set forth in paragraph (e) of this Section 5, a check to the order of each such subscriber in the amount of interest and other income earned and not yet paid with respect to any investment of such subscriber's funds. The Escrow Agent shall notify the Company and the Placement Agent of the distribution of such funds to the subscribers.

(b) In the event that (i) the Shares have been subscribed for and funds

in respect thereof shall have been deposited with the Escrow Agent on or before the Closing Date and (ii) no Offering Termination Notice shall have been delivered to the Escrow Agent, the Company and the Placement Agent, shall deliver to the Escrow Agent a joint notice, substantially in the form of Exhibit D hereto (a "Closing Notice"), designating the date on which Shares are to be sold and delivered to the subscribers thereof as the "Closing Date", which date shall not be earlier than the clearance of any checks received by the Escrow Agent as Escrowed Property, the proceeds of which are to be distributed on such Closing Date, and identifying the subscribers and the number of Shares to be sold to each thereof on such Closing Date. Such Closing Notice, unless the parties otherwise agree, shall be delivered not less than two (2) nor more than five (5) business days prior to such Closing Date. The Escrow Agent, after receipt of such Closing Notice and the clearance of such checks:

(i) on or prior to the Closing Date identified in such Closing Notice, shall liquidate any investments that shall have been made pursuant to Section 3 to the extent of the subscription amount to be distributed pursuant to the immediately succeeding clause (ii);

(ii) on such Closing Date, pay to the Company and the Placement Agent, in federal or other immediately available funds and otherwise in the manner and amount specified by the Company and the Placement Agent in such Closing Notice, an amount equal to the aggregate of the subscription amounts paid by the subscribers identified in such Closing Notice for the Shares to be sold on such Closing Date as set forth on the list held by the Escrow Agent pursuant to Section 4; and

(iii) promptly after the fourth business day of the month immediately following the month in which the investments made pursuant to Section 3 were terminated pursuant to such Closing Notice, shall send, in the manner set forth in paragraph (e) of this Section 5, a check to the order of each subscriber identified in such Closing Notice in the amount of interest and other income earned and not yet paid with respect to any investment of each such subscriber's funds distributed on such Closing Date. At the time of such transfer, the Escrow Agent shall identify in writing to the Company and the Placement Agent the amount of the interest earned for the account of each subscriber and the date such subscription was received.

(c) If at any time and from time to time prior to the release of any subscriber's total subscription amount pursuant to paragraph (a) or (b) of this Section 5 from escrow, the Company shall deliver to the Escrow Agent a notice, substantially in the form of Exhibit E hereto (a "Subscription Termination Notice"), to the effect that any or all of the subscriptions of such subscriber have been rejected by the Company (a "Rejected Subscription"), the Escrow Agent (i) promptly after receipt of such Subscription Termination Notice and, if such subscriber delivered a check in payment of its Rejected Subscription, after the clearance of such check, shall liquidate, to the extent of the sum of such subscriber's Rejected Subscription amount as set forth in the Subscription Termination Notice, any investments that shall have been made pursuant to Section 3 and send to such subscriber, in the manner set forth in paragraph (e) of this Section 5, a check to the order of such subscriber in the amount of such Rejected Subscription amount, and (ii) promptly after the fourth business day of the month immediately following the month in which the investments made pursuant to Section 3 were terminated pursuant to this paragraph, shall send to such subscriber, in the manner set forth in paragraph (e) of this Section 5, a check to the order of such subscriber in the amount of interest and other income earned and not yet paid with respect to any

investment of such subscriber's Rejected Subscription amount. At the time of such transfer, the Escrow Agent shall identify in writing to the Company and the Placement Agent the amount of the interest earned for the account of each subscriber and the date such subscription was received.

(d) On a date following the transfer of any interest earned for the account of each subscriber pursuant to Section 5(a), (b) or (c), but not later than December 31, 1999, the Escrow Agent shall provide each subscriber with tax form 1099 setting forth the amount of such interest.

(e) For the purposes of this Section 5, any check that the Escrow Agent shall be required to send to any subscriber shall be sent to such subscriber by first class mail, postage prepaid, at such subscriber's address furnished to the Escrow Agent pursuant to Section 4.

6. Notices. Any notice or other communication required or permitted to be given hereunder shall be in writing and shall be (a) delivered by hand or (b) sent by mail, registered or certified, with proper postage prepaid, and addressed as follows:

if to the Company, to:

Ribozyme Pharmaceuticals, Inc.
2950 Wilderness Place
Boulder, Colorado 80301
Attention: Larry E. Bullock
Facsimile: (303) 449-6995

with a copy to:

Rothgerber Johnson & Lyons LLP
1200 17th Street, Suite 3000
Denver, Colorado 80202-5839
Attention: Herbert H. Davis III
Facsimile: (303) 623-9560

if to the Placement Agent, to:

Hambrecht & Quist LLC
One Bush Street
San Francisco, California 94104
Attention: Shelly D. Guyer
Facsimile: (415) 439-3479

with a copy to:

Stroock & Stroock & Lavan LLP
180 Maiden Lane
New York, New York 10038-4982
Attention: Anna T. Pinedo, Esq.
Facsimile: (212) 806-6006

if to the Escrow Agent, to:

Citibank, N.A.
120 Wall Street
New York, New York 10043
Attention: Facsimile: (212)

or to such other address as the person to whom notice is to be given may have previously furnished to the others in the above-referenced manner. All such

notices and communications, if mailed, shall be effective when deposited in the mails, except that notices and communications to the Escrow Agent and notices of changes of address shall not be effective until received.

7. Concerning the Escrow Agent. To induce the Escrow Agent to act hereunder, it is further agreed by the Company and Placement Agent that:

(a) The Escrow Agent shall not be under any duty to give the Escrowed Property held by it hereunder any greater degree of care than it gives its own similar property and shall not be required to invest any funds held hereunder except as directed in this Escrow Agreement. Uninvested funds held hereunder shall not earn or accrue interest.

(b) This Escrow Agreement expressly sets forth all the duties of the Escrow Agent with respect to any and all matters pertinent hereto. No implied duties or obligations shall be read into this Escrow Agreement against the Escrow Agent. The Escrow Agent shall not be bound by the provisions of any agreement among the other parties hereto except this Escrow Agreement.

(c) The Escrow Agent shall not be liable, except for its own gross negligence or willful misconduct, and, except with respect to claims based upon such gross negligence or willful misconduct that are successfully asserted against the Escrow Agent, and the other parties hereto shall jointly and severally indemnify and hold harmless the Escrow Agent (and any successor Escrow Agent) from and against any and all losses, liabilities, claims, actions, damages and expenses, including reasonable attorneys' fees and disbursements, arising out of and in connection with this Escrow Agreement. Without limiting the foregoing, the Escrow Agent shall in no event be liable in connection with its investment or reinvestment of any cash held by it hereunder in good faith, in accordance with the terms hereof, including without limitation any liability for any delays (not resulting from gross negligence or willful misconduct) in the investment or reinvestment of the Escrowed Property, or any loss of interest incident to any such delays.

(d) The Escrow Agent shall be entitled to rely upon any order, judgment, certification, demand, notice, instrument or other writing delivered to it hereunder without being required to determine the authenticity or the correctness of any fact stated therein or the propriety or validity of the service thereof. The Escrow Agent may act in reliance upon any instrument or signature believed by it in good faith to be genuine and may assume, if in good faith, that any person purporting to give notice or receipt or advice or make any statement or execute any document in connection with the provisions hereof has been duly authorized to do so.

(e) The Escrow Agent may act pursuant to the advice of counsel with respect to any matter relating to this Escrow Agreement and shall not be liable for any action taken or omitted in good faith and in accordance with such advice.

(f) The Escrow Agent does not have any interest in the Escrowed Property deposited hereunder but is serving as escrow holder only. Any payments of income from the Escrow Account shall be subject to withholding regulations then in force with respect to United States taxes. The parties hereto will provide the Escrow Agent with appropriate W-9 forms for tax I.D., number certification, or non-resident alien certifications.

This paragraph (f) and paragraph (c) of this Section 7 shall survive notwithstanding any termination of this Escrow Agreement or the resignation of the Escrow Agent.

(g) The Escrow Agent makes no representation as to the validity, value, genuineness or the collectibility of any security or other document or instrument held by or delivered to it.

(h) The Escrow Agent shall not be called upon to advise any party as to the wisdom of selling or retaining or taking or refraining from any action with respect to any securities or other property deposited hereunder.

(i) The Escrow Agent (and any successor escrow agent) at any time may be discharged from its duties and obligations hereunder by the delivery to it of notice of termination signed by both the Company and the Placement Agent or at any time may resign by giving written notice to such effect to the Company and the Placement Agent. Upon any such termination or resignation, the Escrow Agent shall deliver the Escrowed Property to any successor escrow agent jointly designated by the other parties hereto in writing, or to any court of competent jurisdiction if no such successor escrow agent is agreed upon, whereupon the Escrow Agent shall be discharged of and from any and all further obligations arising in connection with this Escrow Agreement. The termination or resignation of the Escrow Agent shall take effect on the earlier of (i) the appointment of a successor (including a court of competent jurisdiction) or (ii) the day that is 30 days after the date of delivery: (A) to the Escrow Agent of the other parties' notice of termination or (B) to the other parties hereto of the Escrow Agent's written notice of resignation. If at that time the Escrow Agent has not received a designation of a successor escrow agent, the Escrow Agent's sole responsibility after that time shall be to keep the Escrowed Property safe until receipt of a designation of successor escrow agent or a joint written disposition instruction by the other parties hereto or any enforceable order of a court of competent jurisdiction.

(j) The Escrow Agent shall have no responsibility for the contents of any writing of any third party contemplated herein as a means to resolve disputes and may rely without any liability upon the contents thereof.

(k) In the event of any disagreement among or between the other parties hereto and/or the subscribers of the Shares resulting in adverse claims or demands being made in connection with the Escrowed Property, or in the event that the Escrow Agent in good faith is in doubt as to what action it should take hereunder, the Escrow Agent shall be entitled to retain the Escrowed Property until the Escrow Agent shall have received (i) a final and non-appealable order of a court of competent jurisdiction directing delivery of the Escrowed Property or (ii) a written agreement executed by the

other parties hereto and consented to by the subscribers directing delivery of the Escrowed Property, in which event the Escrow Agent shall disburse the Escrowed Property in accordance with such order or agreement. Any court order referred to in (i) above shall be accompanied by a legal opinion by counsel for the presenting party satisfactory to the Escrow Agent to the effect that said court order is final and non-appealable. The Escrow Agent shall act on such court order and legal opinion without further question.

(l) As consideration for its agreement to act as Escrow Agent as herein described, the Company agrees to pay the Escrow Agent fees determined in accordance with the terms set forth on Exhibit F hereto (made a part of this Escrow Agreement as if herein set forth). In addition, the Company agrees to reimburse the Escrow Agent for all reasonable expenses, disbursements and advances incurred or made by the Escrow Agent in performance of its duties hereunder (including reasonable fees, expenses and disbursements of its counsel).

(m) The other parties hereto irrevocably (i) submit to the jurisdiction of any New York State or federal court sitting in New York City in any action or proceeding arising out of or relating to this Escrow Agreement, (ii) agree that all claims with respect to such action or proceeding shall be heard and determined in such New York State or federal court and (iii) waive, to the fullest extent possible, the defense of an inconvenient forum. The other parties hereby consent to and grant any such court jurisdiction over the persons of such parties and over the subject matter of any such dispute and agree that delivery or mailing of process or other papers in connection with any such action or proceeding in the manner provided hereinabove, or in such other manner as may be permitted by law, shall be valid and sufficient service thereof.

(n) No printed or other matter in any language (including, without limitation, the Registration Statement, notices, reports and promotional material) which mentions the Escrow Agent's name or the rights, powers, or duties of the Escrow Agent shall be issued by the other parties hereto or on such parties' behalf unless the Escrow Agent shall first have given its specific written consent thereto. The Escrow Agent hereby consents to the use of its name and the reference to the escrow arrangement in the Registration Statement.

8. Miscellaneous.

(a) This Escrow Agreement shall be binding upon and inure solely to the benefit of the parties hereto and their respective successors and assigns, heirs, administrators and representatives, and the subscribers of the Shares and shall not be enforceable by or inure to the benefit of any other third party except as provided in paragraph (i) of Section 7 with respect to the termination of, or resignation by, the Escrow Agent. No party may assign any of its rights or obligations under this Escrow Agreement without the written consent of the other parties.

(b) This Escrow Agreement shall be construed in accordance with and governed by the internal law of the State of New York (without reference to its rules as to conflicts of law).

(c) This Escrow Agreement may only be modified by a writing signed by all of the parties hereto and consented to by the subscribers of the Shares adversely affected by such modifications. No waiver hereunder shall be effective unless in a writing signed by the party to be charged.

(d) This Escrow Agreement shall terminate upon the payment pursuant to Section 5 of all amounts held in the Escrow Account.

(e) The section headings herein are for convenience only and shall not affect the construction thereof. Unless otherwise indicated, references to Sections are to Sections contained herein.

(f) This Escrow Agreement may be executed in one or more counterparts but all such separate counterparts shall constitute but one and the same instrument; provided that, although executed in

counterparts, the executed signature pages of each such counterpart may be affixed to a single copy of this Agreement which shall constitute an original.

IN WITNESS WHEREOF, the parties hereto have caused this Escrow Agreement to be executed as of the day and year first above written.

Ribozyme Pharmaceuticals, Inc.

By: _____

Name: _____

Title: _____

Hambrecht & Quist Llc

By: _____

Name: _____

Title: _____

Citibank, N.A.

By: _____

Name: _____

Title: _____

EXHIBIT A

Citibank Insured Money Market Deposit Accounts

Deposits/Withdrawals may be made to the Citibank Money Market Deposit Account ("MMDA") established under the Escrow Agreement to which this Exhibit is attached only through the Escrow Account. All transaction and balance reporting of the MMDA will be included as part of the Escrow Account Statement. Activity in the MMDA will be reflected as the equivalent of dollars on deposit in a Citibank Money Market Deposit Account. Deposits/Withdrawals to the MMDA will be made only as permitted by the Escrow Agreement to which this Exhibit is attached. The MMDA has certain regulatory restrictions as well as some minimum requirements:

1. By regulation, Citibank, N.A. is required to reserve the right to require seven days' prior notice of any withdrawals of funds from an account; provided, however, that, if Citibank, N.A. elects to exercise its right to require seven days' prior notice, it shall exercise such right as to all such accounts established.

2. A daily balance of $10,000 must be maintained on deposit in the MMDA. If the MMDA should fall below $10,000 on any day, Citibank, N.A. will be authorized to transfer the remaining balance to the Escrow Account.

3. Rates will be determined by Citibank, N.A. and can be determined by calling your custody account officer.

4. Balances up to $100,000 (total on deposit at Citibank, N.A.) are FDIC-insured.

EXHIBIT B

SUMMARY OF CASH RECEIVED
NEW PARTICIPANT DEPOSIT

Date:
Deposit Date: List Number:
Investment Date: Page of
Batch Number: Approved By:
JOB#:

For Bank use only

TITLE:

<TABLE>
<CAPTION>

Name	Deposit	Number of Shares	Address	Tax ID No./ Social Security No.		For Bank Use Only
<S>	<C>	<C>	<C>	<C>		<C>
						Tax Code Exempt (Y/N) W-9 (yr) NRA W-8 (yr) 1008 (87)
Broker	Misc.			Misc. II	Misc. III	Tax Code Exempt (Y/N) W-2 (yr) NRS W-8 (yr) 1008 (87)
Broker	Misc.			Misc. II	Misc. III	Tax Code Exempt (Y/N) W-2 (yr) NRS W-8 (yr) 1008 (87)
Broker	Misc.			Misc. II	Misc. III	Tax Code Exempt (Y/N) W-2 (yr) NRA W-8 (yr) 1000 (87)
Broker	Misc.			Misc. II	Misc. III	

</TABLE>

EXHIBIT C

[Form of Offering Termination Notice]

April , 1999

Citibank, N.A.
Corporate Trust
Escrow Administration
120 Wall Street, 13th Floor
New York, New York 10043

Attention:

Dear :

Pursuant to Section 5(a) of the Escrow Agreement dated as of April , 1999 (the "Escrow Agreement"), among Ribozyme Pharmaceuticals, Inc., (the

"Company"), Hambrecht & Quist LLC and you, the Company hereby notifies you of the termination of the offering of the Shares (as that term is defined in the Escrow Agreement) and directs you to make payments to subscribers as provided for in Section 5(a) of the Escrow Agreement.

Very truly yours,

Ribozyme Pharmaceuticals, Inc.

By: _____

Name: _____

Title: _____

EXHIBIT D

[Form of Closing Notice]

April , 1999

Citibank, N.A.
Corporate Trust
Escrow Administration
120 Wall Street, 13th Floor
New York, New York 10043

Attention:

Ladies and Gentlemen:

Pursuant to Section 5(b) of the Escrow Agreement dated as of April , 1999 (the "Escrow Agreement"), among Ribozyme Pharmaceuticals, Inc. (the "Company"), Hambrecht & Quist LLC and you, the Company hereby certifies that it has received subscriptions for the Shares (as that term is defined in the Escrow Agreement) and the Company will sell and deliver Shares to the subscribers thereof at a closing to be held on April , 1999 (the "Closing Date"). The names of the subscribers concerned, the number of Shares subscribed for by each of such subscribers and the related subscription amounts are set forth on Schedule I annexed hereto.

Please accept these instructions as standing instructions for the closing to be held on the Closing Date. The parties hereto certify that they do not wish to have a call back regarding these instructions.

We hereby request that the aggregate subscription amount be paid to the Placement Agent and us as follows:

1. To the Company, $;

2. To Hambrecht & Quist LLC, $; and

3. To the Escrow Agent, $.

These instructions may be executed in any number of counterparts, each of which shall be deemed to be an original, and all of which together shall constitute one and the same instrument.

Very truly yours,

Ribozyme Pharmaceuticals, Inc.

By: _____

Name: _____

Title: _____

Hambrecht & Quist LLC

By: _____

Name: _____

Title: _____

SCHEDULE I

<TABLE>
<CAPTION>

Name of Subscriber	Number of Shares	Subscription Amount
<S>	<C>	<C>

</TABLE>

EXHIBIT E

[Form of Subscription Termination Notice]

April , 1999

Citibank, N.A.
Corporate Trust
Escrow Administration
120 Wall Street, 13th Floor
New York, New York 10043

Attention:

Dear _____:

Pursuant to Section 5(c) of the Escrow Agreement dated as of April , 1997 (the "Escrow Agreement"), among Ribozyme Pharmaceuticals, Inc. (the "Company"), Hambrecht & Quist LLC and you, the Company hereby notifies you that the following subscription(s) have been rejected:

<TABLE>
<CAPTION>

	Amount of	Dollar

Name of Subscriber	Subscribed Shares Rejected	Amount of Rejected Subscription
<S>	<C>	<C>

</TABLE>

Very truly yours,

Ribozyme Pharmaceuticals, Inc.

By: _____
Name:
Title:

EXHIBIT F

Fee to Citibank N.A.: $_____

EXHIBIT 5.1

Ribozyme Pharmaceuticals, Inc.
Attn: Board of Directors
2950 Wilderness Place
Boulder, Colorado 80301

Dear Sirs:

You have requested our opinion in connection with the Registration Statement on Form S-1 ("Registration Statement") which is expected to be filed by Ribozyme Pharmaceuticals, Inc. on March 26, 1999, with respect to the offer and sale of 1,800,000 shares of a single class of common stock. We have reviewed such corporate documents and have made such investigation of Colorado law as we have deemed necessary. Based upon that review and investigation, it is our opinion that when the shares referred to above are issued in the manner described in the Registration Statement, said shares will be authorized, fully paid and non-assessable.

We consent to the use in the Registration Statement of our name and the statement with respect to our firm under the heading "Legal Matters" in the related prospectus.

Sincerely yours,

ROTHGERBER JOHNSON & LYONS, LLP

/s/ Rothgerber Johnson & Lyons, LLP

March 25, 1999

EXHIBIT 23.1

CONSENT OF INDEPENDENT AUDITORS

We consent to the reference to our firm under the captions "Selected Financial Data" and "Experts" and to the use of our report dated February 16, 1999, in the Registration Statement on Form S-1 and related prospectus of Ribozyme Pharmaceuticals, Inc. for the registration of 1,800,000 shares of its common stock.

/s/ ERNST & YOUNG LLP

Denver, Colorado
March 25, 1999