

# VIROPHARMA INC

## FORM S-3/A

(Securities Registration Statement (simplified form))

Filed 10/01/99

Address	730 STOCKTON DRIVE EXTON, PA 19341
Telephone	6104587300
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Symbol	VPHM
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Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

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# SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

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Amendment No. 1 to  
**Form S-3**  
REGISTRATION STATEMENT  
Under  
The Securities Act of 1933

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## VIROPHARMA INCORPORATED

(Exact name of registrant as specified in charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

2834  
(Primary Standard Industrial  
Classification Code No.)

94-2347624  
(IRS Employer  
Identification Number)

405 Eagleview Boulevard  
Exton, Pennsylvania 19341  
(610) 458-7300

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

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**THOMAS F. DOYLE, ESQ.**  
Vice President and General Counsel  
ViroPharma Incorporated  
405 Eagleview Boulevard  
Exton, Pennsylvania 19341  
(610) 458-7300

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

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

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

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

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

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 Commission, acting pursuant to said Section 8(a), may determine.

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+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 we are not soliciting offers to buy these +  
+securities in any state where the offer or sale is not permitted. +

+++++ PROSPECTUS (Subject to  
Completion)

Issued October 1, 1999

3,000,000 Shares  
[ViroPharma Incorporated Logo]

**COMMON STOCK**

ViroPharma Incorporated is offering shares of its common stock.

Our common stock is listed on the Nasdaq National Market under the symbol "VPHM." On September 30, 1999, the reported last sale price of our common stock on the Nasdaq National Market was \$22.28 per share.

Investing in the common stock involves risks. See "Risk Factors" beginning on page 8.

**PRICE \$ A SHARE**

	Price to Public	Underwriting Discounts and Commissions	Proceeds to Company
Per Share.....	\$	\$	\$
Total.....	\$	\$	\$

ViroPharma has granted the underwriters the right to purchase up to an additional 450,000 shares to cover over-allotments.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Morgan Stanley & Co. Incorporated expects to deliver the shares to purchasers on , 1999.

**MORGAN STANLEY DEAN WITTER**

**U.S. BANCORP PIPER JAFFRAY**

, 1999

## TABLE OF CONTENTS

	Page
	----
Prospectus Summary.....	3
Risk Factors.....	8
Special Note Regarding Forward- Looking Statements.....	18
Use of Proceeds.....	18
Price Range of Common Stock.....	19
Dividend Policy.....	19
Capitalization.....	20
Dilution.....	21
Selected Financial Data.....	22

	Page
	----
Management's Discussion and Analysis of Financial Condition and Results of Operations.....	24
Business.....	29
Management.....	44
Principal Stockholders.....	46
Description of Capital Stock.....	48
Underwriters.....	52
Legal Matters.....	53
Experts.....	53
Additional Information.....	54

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You should rely only on the 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 shares of common stock 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 common stock.

## PROSPECTUS SUMMARY

You should read the following summary together with the more detailed information regarding our company and the common stock being sold in this offering appearing elsewhere in this prospectus and our financial statements and notes thereto incorporated by reference into this prospectus. Except as otherwise noted, all information in this prospectus assumes no exercise of the underwriters' overallotment option.

### VIROPHARMA

We are a pharmaceutical company dedicated to the commercialization, development and discovery of new antiviral medicines. We are focusing our current product development and discovery activities on RNA virus diseases, including viral respiratory infection, viral meningitis, hepatitis C, and respiratory syncytial virus diseases.

In September 1999, we commenced our Phase III clinical program with our lead product candidate, pleconaril, for the treatment of viral respiratory infection, or VRI, a severe form of the common cold. We are also conducting a Phase III clinical program with pleconaril for the treatment of viral meningitis.

Approximately 1,700 patients have been treated with pleconaril in clinical studies completed to date. Based on our analysis of the data from these studies, pleconaril demonstrated a clinical benefit to patients and exhibited an adverse event profile similar to that of placebo.

We believe that there are significant market opportunities for pleconaril based upon the following information that we have derived from market research:

- . each year in the United States there are more than 34 million physician visits for VRI;
- . each year in the United States there are more than 500,000 cases of viral meningitis; and
- . currently, there are no antiviral treatments for these two diseases.

In our first Phase III clinical trial with pleconaril for the treatment of VRI, we are administering 400 milligrams of pleconaril three times daily to otherwise healthy adolescent and adult patients with VRI. Randomized adolescent and adult patients receiving this dose in our Phase II clinical program experienced a clinical benefit and a statistically significant reduction in their disease when compared to placebo. Specifically, these patients in our Phase II study reported:

- . a 3.5 day reduction in the median time to complete elimination of disease symptoms from 14 days to 10.5 days ( $p = 0.009$ );
- . a 3.5 day reduction in the median time to patient overall wellness from 14 days to 10.5 days ( $p = 0.002$ ); and
- . statistically significant reductions in several additional endpoints, including time to elimination of runny nose, sore throat and nasal congestion.

In our Phase III clinical program with pleconaril for the treatment of viral meningitis, which commenced in July 1998, we are administering 200 milligrams of pleconaril three times daily to otherwise healthy adolescent and adult patients with viral meningitis. Randomized adolescent and adult patients receiving this dose in our Phase II/III clinical program reported, among other things, a two day reduction in the median duration of headache for pleconaril- treated patients with confirmed enteroviral meningitis from nine to seven days ( $p = 0.04$ ).

In the pediatric component of our Phase III clinical program for the treatment of viral meningitis, we are administering 2.5 milligrams/kilogram of pleconaril three times daily in otherwise healthy children between the ages of eight and 14 years with viral meningitis. Randomized children between the ages of eight and 14 years receiving this dose in our Phase II/III clinical program reported, among other things, a one day reduction in disease duration when measured by headache ( $p=0.029$ ).

Positive results from our ongoing Phase III clinical programs with pleconaril, as well as regulatory approvals, are required before pleconaril can be commercialized.

We plan to leverage the infrastructure of partners for the manufacturing and distribution of pleconaril. Our marketing plans for pleconaril include a focused medical education program involving peer-to-peer presentations and medical and scientific publications. We intend to build a specialty sales force of approximately 50 to 70 sales representatives to market pleconaril for the treatment of viral meningitis to emergency medicine, infectious disease and pediatric infectious disease physicians. We intend to identify a strategic partner to help us target primary care physicians and develop the market for pleconaril for the treatment of VRI. We also intend to add personnel to our sales force to target other physician groups.

We currently are conducting preclinical toxicology studies on product candidates VP50406 for the treatment of hepatitis C due to the hepatitis C virus and VP14637 for the treatment of diseases caused by respiratory syncytial virus, or RSV. We intend to initiate human clinical studies with both of these product candidates in early to mid-2000.

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ViroPharma was incorporated in Delaware in 1994. Our principal offices are located at 405 Eagleview Boulevard, Exton, Pennsylvania 19341, our telephone number is (610) 458-7300 and our web site is <http://www.viopharma.com>.

## THE OFFERING

Common stock offered.....	3,000,000 shares
Common stock to be outstanding after this offering..	14,576,824 shares
Over-allotment option.....	450,000 shares
Use of proceeds.....	For the further development and commercialization of pleconaril, including pre-marketing activities and hiring a targeted sales force, initiation of human clinical trials for hepatitis C and RSV disease product candidates, ongoing research and general corporate purposes, which may include capital equipment expenditures.
Dividend policy.....	We do not anticipate paying any cash dividends in the foreseeable future. In addition, our bank loan agreements restrict our ability to declare and pay cash dividends. We are obligated to pay any cash dividends paid to common stockholders to the holders of our series A convertible participating preferred stock, on an as converted basis.
Nasdaq National Market symbol.....	VPHM
Preferred stock purchase rights.....	One preferred stock purchase right will be attached to each share of common stock sold in the offering and thus the preferred stock purchase rights are also being offered by this prospectus. These rights would cause substantial dilution to any person or group who attempts to acquire a significant interest in our company without advance approval from our board of directors and thus could make an acquisition of control of our company more difficult.

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The number of shares of our common stock to be outstanding after the offering does not take into account, as of September 1, 1999:

. 579,592 options for shares of common stock available for issuance under our stock option plan;

. 1,289,123 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of \$10.11 per share;

. 2,317,329 shares of common stock issuable upon conversion of outstanding shares of series A convertible participating preferred stock, which are eligible for registration upon exercise of demand registration rights; and

. 595,000 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$9.53 per share, which are eligible for registration upon exercise of demand registration rights.



## SUMMARY FINANCIAL DATA

The following Statement of Operations Data for the period from December 5, 1994 (inception) through December 31, 1994, and the years ended December 31, 1995, 1996, 1997 and 1998 are derived from our audited financial statements. The Statement of Operations Data for the six-month periods ended June 30, 1998 and 1999, and the Balance Sheet Data as of June 30, 1999, are derived from our unaudited financial statements which, in our opinion, have been prepared on the same basis as the audited financial statements and reflect all adjustments (consisting only of normal recurring adjustments) necessary for a fair presentation of our results of operations and financial position. Results for the six months ended June 30, 1999 are not necessarily indicative of results that may be expected for the entire year. The financial data set forth below should be read in conjunction with the sections of this prospectus entitled "Selected Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and notes thereto incorporated by reference into this prospectus. The as adjusted Balance Sheet Data column gives effect to our sale of the 3,000,000 shares of our common stock offered by this prospectus at an assumed public offering price of \$22.28 per share, less underwriting discounts and estimated offering expenses.

	Period from December 5, 1994 (inception) through December 31, 1994	Year Ended December 31,				Six Months Ended June 30,	
		1995	1996	1997	1998	1998	1999
		(in thousands, except per share data)				(unaudited)	
Statement of Operations Data:							
License fee and milestone revenue.....	\$ --	\$ --	\$ 1,000	\$ 1,500	\$ 1,500	\$ 750	\$ --
Grant revenue.....	--	91	436	--	--	--	--
Total revenues.....	--	91	1,436	1,500	1,500	750	--
Operating expenses:							
Research and development.....	76	2,931	6,695	10,929	25,130	9,637	10,095
General and administrative.....	243	1,091	1,421	3,341	4,376	1,879	2,394
Total operating expenses.....	319	4,022	8,116	14,270	29,506	11,516	12,489
Loss from operations...	(319)	(3,931)	(6,680)	(12,770)	(28,006)	(10,766)	(12,489)
Interest income, net....	--	76	285	1,320	1,604	704	720
Net loss.....	(319)	(3,855)	(6,395)	(11,450)	(26,402)	(10,062)	(11,769)
Beneficial conversion feature of preferred stock.....	--	--	--	--	--	--	4,140
Accretion of redemption value attributable to manditorily redeemable convertible preferred stock.....	--	19	1,597	--	--	--	--
Net loss allocable to common stockholders....	\$(319)	\$(3,874)	\$(7,992)	\$(11,450)	\$(26,402)	\$(10,062)	\$(15,909)
Net loss per share allocable to common stockholders:							
Basic.....		\$ (4.67)	\$ (3.89)	\$ (1.13)	\$ (2.30)	\$ (.88)	\$ (1.38)
Diluted.....		\$ (3.52)	\$ (3.44)	\$ (1.13)	\$ (2.30)	\$ (.88)	\$ (1.38)
Shares used in computing net loss per share allocable to common stockholders:							
Basic.....		829	2,053	10,093	11,486	11,479	11,564
Diluted.....		1,099	2,324	10,093	11,486	11,479	11,564

As of June 30, 1999

	Actual	As Adjusted
	(in thousands)	
	(unaudited)	
Balance Sheet Data:		
Cash, cash equivalents and short-term investments.....	\$ 20,583	\$ 83,681
Other current assets.....	320	320
	-----	-----
Total current assets.....	20,903	84,001
Equipment and leasehold improvements, net.....	2,654	2,654
Other assets.....	675	675
	-----	-----
Total assets.....	\$ 24,232	\$ 87,330
	=====	=====
Accounts payable, accrued expenses and other current		
liabilities.....	\$ 7,257	\$ 7,257
Loans payable--current.....	200	200
	-----	-----
Total current liabilities.....	7,457	7,457
Loans payable--non-current.....	1,782	1,782
	-----	-----
Total liabilities.....	9,239	9,239
	-----	-----
Preferred stock.....	2	2
Common stock.....	23	29
Additional paid-in capital.....	75,228	138,320
Deferred compensation.....	(121)	(121)
Unrealized gains on available for sale securities.....	51	51
Deficit accumulated during the development stage.....	(60,190)	(60,190)
	-----	-----
Total stockholders' equity.....	14,993	78,091
	-----	-----
Total liabilities and stockholders' equity.....	\$ 24,232	\$ 87,330
	=====	=====

## RISK FACTORS

You should carefully consider the risks described below before making an investment decision. The risks described below are not the only ones facing our company. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations.

Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment.

This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks faced by us described below and elsewhere in this prospectus.

We depend heavily on the success of our lead product candidate, pleconaril, which is still in clinical trials and may never be approved for commercial use. If we are unable to commercialize pleconaril, our business and results of operations will be harmed.

We have invested a significant portion of our time and financial resources since our inception in the development of pleconaril and anticipate that for the foreseeable future our ability to achieve profitability will be solely dependent on its successful commercialization. Many factors could negatively affect the success of our efforts to develop and commercialize pleconaril, including:

- . significant delays in our clinical trials;
- . significant increases in the costs of our clinical trials;
- . negative, inconclusive or otherwise unfavorable results from our clinical trials;
- . an inability to obtain, or delay in obtaining, regulatory approval for the commercialization of pleconaril;
- . an inability to manufacture pleconaril in commercial quantities at acceptable cost; and
- . a failure to achieve market acceptance of pleconaril.

If we are unable to commercialize pleconaril, our business and results of operations will be harmed.

We have incurred losses since inception and anticipate that we will incur continued losses for the foreseeable future. We do not have a current source of product revenue and may never be profitable.

We are a development stage company with no current source of product revenue. We have incurred losses in each year since our inception in 1994. As of June 30, 1999, we had an accumulated deficit of approximately \$60.2 million. We do not know when or if we will achieve product revenue. We expect to incur such losses at an increasing rate over at least the next several years, primarily due to expected increases in our research and development expenses, further clinical trials of our most advanced product candidate, pleconaril (including any significant additional studies for approval in the European Union, if any are required), and milestone payments that may be payable under the terms of our agreement with Sanofi-Synthelabo for pleconaril. Also, we expect to incur expenses related to our marketing and market research activities for pleconaril, our development of a marketing and sales staff and further research and development related to other product candidates. Our ability to achieve profitability is dependent on a number of factors, including our ability to develop and obtain regulatory approvals for our product candidates, successfully commercialize those product candidates, which may include entering into collaborative agreements for product development and commercialization, and secure contract manufacturing and distribution and logistics services. We do not know when or if we will complete our product development efforts, receive regulatory approval of any of our product candidates or successfully commercialize any approved products. As a result, we are unable to predict the extent of any future losses or the time required to achieve profitability, if at all.

Our long term success depends upon our ability to develop additional drug product candidates. If our drug discovery and development programs are not successful, our business, and results of operations will be harmed.

We are performing preclinical research on product candidates for the treatment of hepatitis C and RSV diseases. We also are seeking to discover additional product candidates for the treatment of these and other RNA virus diseases. Drug discovery and research for RNA virus diseases is a new and challenging area. We cannot be certain that our efforts in this regard will lead to commercially viable products. Moreover, we have not submitted Investigational New Drug Applications, or INDs, for these products, which are required before we can begin clinical trials on the products. We are not sure that we will submit INDs for the treatment of hepatitis C and RSV as planned, or whether FDA will permit us to proceed with clinical trials. These product candidates are in the early stages of development, and we may abandon further development efforts before the products reach clinical trials. We do not know what the cost to manufacture these products in commercial quantities will be, or the dose required to treat patients. We do not know whether any of these early-stage development products ultimately will be shown to be safe and effective. Moreover, governmental authorities may enact new legislation or regulations that could limit or restrict our development efforts. If we are unable to successfully discover new product candidates or develop our early- stage product candidates, our business and results of operations will be harmed.

None of our product candidates is approved for commercial use. If our product candidates do not receive regulatory approval, or if we are unable to maintain regulatory compliance, we will be limited in our ability to commercialize these products, and our business and results of operations will be harmed.

We have not received regulatory approval to commercialize pleconaril or any of our other product candidates. We will need to complete preclinical and clinical testing of each of our product candidates before submitting marketing applications. Negative, inconclusive or inconsistent clinical trial results could prevent regulatory approval, increase the cost and timing of regulatory approval or require additional studies or a filing for a narrower indication. FDA recently enacted new regulations requiring the development and submission of pediatric use data for new drug products. Our failure to obtain this data, or to obtain a delay of, or exemption from this requirement could adversely affect our chances of receiving regulatory approval, or could result in regulatory or legal enforcement actions.

The development of any of our product candidates is subject to many risks, including the risk that:

- . the product candidate is found to be ineffective or unsafe;
- . the clinical test results for a product candidate delay or prevent regulatory approval;
- . the product candidate cannot be developed into a commercially viable product;
- . the product candidate is difficult to manufacture;
- . the product candidate later is discovered to cause adverse effects that prevent widespread use, require withdrawal from the market, or serve as the basis for product liability claims;
- . third party competitors hold proprietary rights that preclude us from marketing the product; and
- . third party competitors market a more clinically effective or more cost- effective product.

Even if we believe that clinical data demonstrate the safety and efficacy of our product, regulators may disagree with us, which could delay, limit or prevent the approval of our product candidates. As a result, we may not obtain the labeling claims we believe are necessary or desirable for the promotion of those products. In addition, regulatory approval may take longer than we expect as a result of a number of factors, including failure to qualify for priority review of our application. For example, the regulatory approval process may delay the launch of pleconaril for the treatment of viral meningitis beyond the year 2000. All statutes and regulations governing the approval of our product candidates are subject to change in the future. These changes may increase the time or cost of regulatory approval, limit approval, or prevent it completely.

Even if we receive regulatory approval for our product candidates, the later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions, including withdrawal of the product from the market. Approval of a product candidate may be conditioned upon certain limitations and restrictions as to the drug's use, or upon the conduct of further studies, and may be subject to continuous review. After approval of a product, we will have significant ongoing regulatory compliance obligations, and if we fail to comply with these requirements, we could be subject to penalties, including:

- . warning letters;
- . fines;
- . product recalls;
- . withdrawal of regulatory approval;
- . operating restrictions;
- . injunctions; and
- . criminal prosecution.

If we are unable to commercialize our products as anticipated, our business and results of operations will be harmed. Our license with Sanofi-Synthelabo makes Sanofi-Synthelabo responsible for seeking regulatory approval for and marketing pleconaril outside the United States and Canada. If Sanofi-Synthelabo fails to diligently and successfully pursue these activities, our business and results of operations will be harmed.

We will need to conduct clinical studies of all of our product candidates. These studies are costly, time consuming and unpredictable. Any unanticipated costs or delays in our clinical studies could harm our business, financial condition and results of operations.

Our lead candidate, pleconaril, is in Phase III trials for treatment of VRI and viral meningitis. We have other product candidates for treatment of hepatitis C and RSV disease in preclinical development. We must complete significant research and development, laboratory testing, and clinical testing on these product candidates before we submit marketing applications in the United States and abroad. These studies and trials can be very costly and time-consuming. In addition, we rely on third party contract research organizations to perform significant aspects of our studies and clinical trials, introducing additional sources of risk into our program.

The rate of completion of clinical trials depends upon many factors, including the rate of enrollment of patients. The acute nature of our disease targets, the fact that some of these diseases have peak incidence rates during certain times of the year, and the difficulties in anticipating where disease outbreaks will occur, may affect patient enrollment in our clinical trials. If we are unable to accrue sufficient clinical patients during the appropriate period, we may need to delay our clinical trials and incur significant additional costs. In addition FDA or Institutional Review Boards may require us to delay, restrict, or discontinue our clinical trials on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Even if we complete our clinical trials, we may be unable to submit a New Drug Application to the FDA as scheduled. If submitted, a New Drug Application would require FDA approval before we could commercialize the product described in the application.

The cost of human clinical trials varies dramatically based on a number of factors, including:

- . the order and timing of clinical indications pursued;
- . the extent of development and financial support from corporate collaborators;
- . the number of patients required for enrollment;
- . the difficulty of obtaining clinical supplies of the product candidate; and
- . the difficulty in obtaining sufficient patient populations and clinicians.

All statutes and regulations governing the conduct of clinical trials are subject to change in the future, which could affect the cost of our clinical trials. Any unanticipated costs or delays in our clinical studies could harm our business, financial condition and results of operations.

Even if we obtain positive preclinical or clinical trial results initially, future clinical trial results may not be similarly positive. As a result, ongoing and contemplated clinical testing, if permitted by governmental authorities, may not demonstrate that a product candidate is safe and effective in the patient population and for the disease indications for which we believe it will be commercially advantageous to market the product. The failure of our clinical trials to demonstrate the safety and efficacy of our desired indications could harm our business, financial condition and results of operations.

We do not have any marketing or sales experience and will need to develop marketing and sales capabilities to successfully commercialize our product candidates. If we are unable to do so, our business and results of operations will be harmed.

We currently are developing a marketing staff and do not have a sales staff. We will need both to successfully commercialize any of our product candidates, including pleconaril. We intend to establish a specialty sales force for viral meningitis and to use a third-party sales and marketing partner for VRI. The development of a marketing and sales capability will require significant expenditures, management resources and time. We may be unable to build such a sales force, the cost of establishing such a sales force may exceed any product revenues, or our marketing and sales efforts may be unsuccessful. We may not be able to find a suitable sales and marketing partner for VRI. If we are unable to successfully establish a sales and marketing capability in a timely manner or find suitable sales and marketing partners, our business and results of operations will be harmed. Even if we are able to develop a sales force or find a suitable marketing partner, we may not successfully penetrate the markets for any of our proposed products.

We currently depend and will in the future depend on third parties to manufacture our products and product candidates, including pleconaril. If these manufacturers fail to meet our requirements and the requirements of regulatory authorities, our business, financial condition and results of operations will be harmed.

We do not have the internal capability to manufacture commercial quantities of pharmaceutical products under the FDA's current Good Manufacturing Practices. We entered into agreements with SELOC France for the manufacture of pleconaril bulk drug substance and the development of a process for commercial scale production of pleconaril. In addition, SELOC France will assist us in the preparation of certain documentation that will be required in connection with our New Drug Application for pleconaril. We also have entered into agreements with Patheon, Inc. for the manufacture of oral liquid and solid formulations of pleconaril drug product. Other than the production of validation batches, these manufacturers have not delivered commercial quantities of pleconaril bulk drug substance or drug product to us yet, and we cannot be certain that they will be able to deliver commercial quantities of pleconaril bulk drug substance or drug product on a timely basis. If SELOC France or Patheon, Inc. is unable to satisfy our requirements and we are required to find an additional or alternative source of supply, there may be additional cost and delay in product development and commercialization of pleconaril.

We are also evaluating manufacturing alternatives for the commercial manufacture of drug substance and drug product. The FDA requires pre-approval inspection for all commercial manufacturing sites. We may not be able to identify and qualify alternative manufacturers on a timely basis, if at all.

We have used an oral liquid formulation of pleconaril in our clinical trials, and we have also developed oral solid, suspension and intranasal formulations of pleconaril. A delay in manufacturing validation batches, or a failure to negotiate agreements with manufacturers, will delay product development and commercialization and could harm our business, financial condition and results of operations. The chemical stability of the oral solid formulation must be tested. We also may need to demonstrate that the oral solid formulation is bioequivalent to the oral liquid formulation. A delay in the required stability testing or in manufacturing validation batches, or a failure to demonstrate chemical stability or any required bioequivalence will prevent or delay the

commercialization of the oral solid formulation of pleconaril. The suspension and intranasal formulations of pleconaril have not been used in any of our clinical trials to date.

Any contract manufacturers that we may use must adhere to the FDA's regulations on current Good Manufacturing Practices, which are enforced by the FDA through its facilities inspection program. These facilities must pass a plant inspection before the FDA will issue a pre-market approval of the product. The manufacture of product at these facilities will be subject to strict quality control, testing and recordkeeping requirements. Moreover, while we may choose to manufacture products in the future, we have no experience in the manufacture of pharmaceutical products for clinical trials or commercial purposes. If we decide to manufacture products, we would be subject to the regulatory requirements described above. In addition, we would require substantial additional capital and would be subject to delays or difficulties encountered in manufacturing pharmaceutical products. No matter who manufactures the product, we will be subject to continuing obligations regarding the submission of safety reports and other post-market information.

If we encounter delays or difficulties with contract manufacturers, packagers or distributors, market introduction and subsequent sales of our products could be delayed. In addition, we may need to seek alternative sources of supply. If so, we may incur additional costs or delays in product commercialization. If we change the source or location of supply or modify the manufacturing process, regulatory authorities will require us to demonstrate that the product produced by the new source or from the modified process is equivalent to the product used in any clinical trials that we had conducted.

We may not be able to enter into alternative supply arrangements at commercially acceptable rates, if at all. Moreover, the manufacturers utilized by us may not provide quantities of product sufficient to meet our specifications or our delivery, cost and other requirements.

We license patented technology and other proprietary rights from Sanofi- Synthelabo, including rights to pleconaril. If Sanofi-Synthelabo does not protect our rights under our license agreement with it, or if this license agreement is terminated, our business and results of operations would be harmed.

We have licensed from Sanofi-Synthelabo the exclusive United States and Canadian rights to antiviral agents for use in enterovirus and rhinovirus indications, which are the subject of two issued United States patents and two related Canadian patent applications owned by Sanofi-Synthelabo, including patent applications covering both pleconaril and technology used to manufacture pleconaril. We depend on Sanofi-Synthelabo to prosecute such patent applications and protect such patent rights. Failure by Sanofi- Synthelabo to prosecute such applications and protect such patent rights could harm our business. Under our license agreement, Sanofi-Synthelabo also has exclusive rights to market and sell products covered by these patents and patent applications in countries other than the United States and Canada, although we would receive royalties from Sanofi-Synthelabo on such sales. In connection with these rights, Sanofi-Synthelabo may require us to pay for clinical trials required for products to receive regulatory approval in the European Union if significant additional testing is required. If Sanofi- Synthelabo does not successfully market and sell products outside of the United States and Canada, our business and future results of operations may be harmed. If our license agreement with Sanofi-Synthelabo is terminated, our business and results of operations would be harmed.

We depend on collaborations with third parties, which may reduce our product revenues or restrict our ability to commercialize products.

We have entered into, and may in the future enter into, sales and marketing, distribution, manufacturing, development, licensing and other strategic arrangements with third parties. We are currently engaged in discussions relating to such arrangements. We cannot be sure that we will be able to enter into any such arrangements with third parties on terms acceptable to us or at all. Third party arrangements may require us to grant certain rights to third parties, including exclusive marketing rights to one or more products, or may have other terms that are burdensome to us, and may involve the acquisition of our equity securities.

Our ultimate success may depend upon the success of these third parties. We have obtained,

and intend to obtain in the future, licensed rights to certain proprietary technologies and compounds from other entities, individuals and research institutions, for which we may be obligated to pay license fees, make milestone payments and pay royalties. We may be unable to enter into collaborative licensing or other arrangements that we need to develop and commercialize our drug candidates. Moreover, we may not realize the contemplated benefits from such collaborative licensing or other arrangements. These arrangements may place responsibility on our collaborative partners for preclinical testing, human clinical trials, the preparation and submission of applications for regulatory approval, or for marketing, sales and distribution support for product commercialization. We cannot be certain that any of these parties will fulfill their obligations in a manner which maximizes our revenues. These arrangements may also require us to transfer certain material rights or issue our equity securities to corporate partners, licensees and others. Any license or sublicense of our commercial rights may reduce our product revenue. Moreover, we may not derive any revenues or profits from these arrangements. In addition, our current strategic arrangements may not continue and we may be unable to enter into future collaborations. Collaborators may also pursue alternative technologies or drug candidates, either on their own or in collaboration with others, that are in direct competition with us.

We depend on patents and proprietary rights, which may offer only limited protection against potential infringement. If we are unable to protect our patents and proprietary rights, our business, financial condition and results of operations will be harmed.

The pharmaceutical industry places considerable importance on obtaining patent and trade secret protection for new technologies, products and processes. Our success depends, in part, on our ability to develop and maintain a strong patent position for our products and technologies both in the United States and in other countries. Litigation or other legal proceedings may be necessary to defend against claims of infringement, to enforce our patents, or to protect our trade secrets, and could result in substantial cost to us and diversion of our efforts. We intend to file applications as appropriate for patents covering the composition of matter of our drug candidates, the proprietary processes for producing such compositions, and the uses of our drug candidates. We own six issued United States patents and have 12 pending United States patent applications. We also have filed international patent applications in order to pursue patent protection in major foreign countries.

We also rely on trade secrets, know-how and continuing technological advancements to protect our proprietary technology. We have entered into confidentiality agreements with our employees, consultants, advisors and collaborators. However, these parties may not honor these agreements and we may not be able to successfully protect our rights to unpatented trade secrets and know-how. Others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets and know-how.

Many of our scientific and management personnel were previously employed by competing companies. As a result, such companies may allege trade secret violations and similar claims against us.

To facilitate development of our proprietary technology base, we may need to obtain licenses to patents or other proprietary rights from other parties. If we are unable to obtain such licenses, our product development efforts may be delayed.

We may collaborate with universities and governmental research organizations which, as a result, may acquire certain rights to any inventions or technical information derived from such collaboration.

We may incur substantial costs in asserting any patent rights and in defending suits against us related to intellectual property rights. Such disputes could substantially delay our product development or commercialization activities. The United States Patent and Trademark Office or a private party could institute an interference proceeding relating to our patents or patent applications. An opposition or revocation proceeding could be instituted in the patent offices of foreign jurisdictions. An adverse decision in any such proceeding could result in the loss of our rights to a patent or invention.

Any of our future products, including pleconaril, may not be accepted by the market, which would harm our business and results of operations.

Even if approved by the FDA and other regulatory authorities, our product candidates may not achieve market acceptance and we may not receive revenues from these products as anticipated. The degree of market acceptance will depend upon a number of factors, including:

- . the receipt and timing of regulatory approvals;
- . the availability of third-party reimbursement; and
- . the establishment and demonstration in the medical community of the clinical safety, efficacy and cost-effectiveness of drug candidates, as well as their advantages over existing technologies and therapeutics.

We may not be able to successfully manufacture and market our products even if they perform successfully in clinical trials. Furthermore, physicians or the medical community in general may not accept and utilize any of our products.

We may not receive third party reimbursement for any of our future products, which may harm our results of operations.

Our future revenues, profitability and access to capital will be affected by the continuing efforts of governmental and private third-party payors to contain or reduce the costs of health care through various means. We expect a number of federal, state and foreign proposals to control the cost of drugs through governmental regulation. We are unsure of the form that any health care reform legislation may take or what actions federal, state, foreign, and private payors may take in response to the proposed reforms. Therefore, we cannot predict the effect of any implemented reform on our business.

Our ability to commercialize our products successfully will depend, in part, on the extent to which reimbursement for the cost of such products and related treatments will be available from government health administration authorities, such as Medicare and Medicaid in the United States, private health insurers and other organizations. Significant uncertainty exists as to the reimbursement status of newly approved health care products, particularly for indications for which there is no current effective treatment or for which medical care typically is not sought. Adequate third-party coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product research and development. If adequate coverage and reimbursement levels are not provided by government and third-party payors for use of our products, our products may fail to achieve market acceptance and our results of operations will be harmed.

We need substantial additional funding and may not have access to capital. If we are unable to raise capital when needed, we may need to delay, reduce or eliminate research and development programs or our commercialization efforts, which would harm our business.

We will need to raise substantial additional funds to continue our business activities. We have incurred losses from operations since inception and we expect to incur additional operating losses at an increasing rate over at least the next several years. We expect this increase to result from further research and development activities, further clinical trials, development of marketing and sales capabilities and milestone payments related to pleconaril and our other product candidates. We believe that we will require additional capital prior to early 2001. However, our actual capital requirements will depend upon numerous factors, including:

- . the development of commercialization activities and arrangements;
- . the progress of our research and development programs;
- . the progress of preclinical and clinical testing;
- . the time and cost involved in obtaining regulatory approvals;
- . the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

- . the effect of competing technological and market developments;
- . the effect of changes and developments in our existing collaborative, licensing and other relationships; and
- . the terms of any new collaborative, licensing and other arrangements that we may establish.

We may be unable to raise sufficient funds to complete our development, marketing and sales activities for pleconaril or any of our other product candidates. Potential funding sources include:

- . public and private securities offerings;
- . debt financing, such as bank loans; and
- . collaborative, licensing and other arrangements with third parties.

We may not be able to find sufficient debt or equity funding on acceptable terms. If we cannot, we may need to delay, reduce or eliminate research and development programs. The sale by us of additional equity securities or the expectation that we will sell additional equity securities may have an adverse effect on the price of our common stock. In addition, collaborative arrangements may require us to grant product development programs or licenses to third parties for products that we might otherwise seek to develop or commercialize ourselves.

We face intense competition, which could harm our business and results of operations.

There are many entities, both public and private, including well-known, large pharmaceutical companies, chemical companies, biotechnology companies and research institutions, engaged in developing pharmaceuticals for applications similar to those targeted by us. Developments by these or other entities may render our products under development non-competitive or obsolete. Many of these companies have substantially greater resources and experience than we have. Accordingly, our competitors may succeed in obtaining regulatory approval for products more rapidly and more effectively than we do. Competitors may succeed in developing products that are more effective and less costly than any that may be developed by us and also may prove to be more successful in the manufacture and marketing of products.

We may not be able to keep pace with technological changes in the biopharmaceutical industry, which may prevent us from commercializing our product candidates.

Our business is characterized by extensive research efforts and rapid technological progress. New developments in molecular biology, medicinal chemistry and other fields of biology and chemistry are expected to continue at a rapid pace in both industry and academia. Research and discoveries by others may render some or all of our programs or drug candidates non- competitive or obsolete.

Our business strategy is based, in part, upon the application of our technology platform to discover and develop pharmaceutical products for the treatment of infectious human diseases. This strategy is subject to the risks inherent in the development of new products using new and emerging technologies and approaches. There are no approved drugs on the market for the treatment of certain of the disease indications being targeted by us.

Unforeseen problems may develop with our technologies or applications. We may not be able to successfully address technological challenges that we encounter in our research and development programs and may not ultimately develop commercially feasible products.

We depend on key personnel and may not be able to retain these employees or recruit additional qualified personnel, which would harm our business.

Because of the specialized scientific nature of our business, we are highly dependent upon qualified scientific, technical and managerial personnel. There is intense competition for qualified personnel in the pharmaceutical field. Therefore, we may not be able to attract and retain the qualified personnel necessary for the development of our business. Furthermore, we have not entered into non-competition agreements with our

key employees. The loss of the services of existing personnel, as well as the failure to recruit additional key scientific, technical and managerial personnel in a timely manner would harm our research and development programs and our business. We do not maintain key man life insurance on any of our employees.

Our anticipated growth and expansion into new areas and activities will require additional expertise and the addition of new qualified personnel.

We may be subject to product liability claims, which may harm our business, financial condition and results of operations regardless of the outcome.

The administration of drugs to humans, whether in clinical trials or after marketing clearance is obtained, can result in product liability claims. Product liability claims can be expensive, difficult to defend and may result in large judgments or settlements against us. In addition, third party collaborators and licensees may not protect us from product liability claims. Although we maintain product liability insurance, claims could exceed the coverage obtained. A successful product liability claim in excess of our insurance coverage could harm our business, financial condition and results of operations. In addition, any successful claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable terms. Even if a claim is not successful, defending such a claim may be time-consuming and expensive.

The rights that have been and may in the future be granted to holders of our common or preferred stock may adversely affect the rights of other shareholders and may discourage a takeover.

Pursuant to our certificate of incorporation, our board of directors has the authority, without further action by the holders of our common stock, to issue 2,500,000 additional shares of preferred stock from time to time in such series and with such preferences and rights as it may designate, in addition to the 200,000 shares of series A junior participating preferred stock already designated. Such preferences and rights may be superior to those of the holders of our common stock. For example, the holders of preferred stock may be given a preference in payment upon our liquidation, or for the payment or accumulation of dividends before any distributions are made to the holders of our common stock.

On May 5, 1999, we completed the sale of 2,300,000 shares of series A convertible participating preferred stock to Perseus-Soros BioPharmaceutical Fund, L.P. This preferred stock is convertible into shares of common stock on a one-for-one basis (subject to adjustment) by Perseus-Soros at any time and by us under certain conditions. There is a 5% annual dividend associated with this preferred stock. We may choose to permanently defer payment of this dividend, in which case the dividend is added to the liquidation value and increases the conversion ratio of the preferred stock into common stock. Holders of the preferred stock have liquidation rights equal to their original investment, subject to adjustment. Such holders also have preemptive rights with respect to proposed private placements of our common stock or other equity securities for cash, other than issuances under our equity compensation or stock option plans and issuances pursuant to our stockholder rights plan, at a price below \$6.20 per share (with adjustment for any stock dividend, stock split or other subdivision of stock, or any combination or reclassification of stock).

In September 1998, our board of directors adopted a plan that grants each holder of our common stock the right to purchase shares of our series A junior participating preferred stock. This plan is designed to help insure that all our stockholders receive fair value for their shares of common stock in the event of a proposed takeover of ViroPharma, and to guard against the use of partial tender offers or other coercive tactics to gain control of ViroPharma without offering fair value to the holders of our common stock. The plan is likely to discourage a merger or tender offer involving our securities that is not approved by our board of directors by increasing the cost of effecting any such transaction and, accordingly, could have an adverse impact on holders of our stock who might want to vote in favor of such a merger or participate in such a tender offer.

While we have no present intention to authorize or issue any additional series of preferred stock, any such authorization or issuance, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could also have the effect of making it more difficult for a third party to acquire a majority

of our outstanding voting stock. The preferred stock may have other rights, including economic rights senior to those of our common stock, and, as a result, an issuance of additional preferred stock could adversely affect the market value of our common stock.

The exercise of outstanding registration rights held by holders of our common and preferred stock may have an adverse effect on the market price for our common stock and may impair our ability to raise additional funds.

As of September 1, 1999, holders of 1,860,454 shares of our common stock have both piggyback and demand registration rights. In addition, our founders have piggyback registration rights with respect to 877,750 shares of our common stock and the holders of shares of our series A convertible participating preferred stock that are convertible into 2,317,329 shares of our common stock and of warrants to purchase 595,000 shares of our common stock, have demand registration rights. Absent any contractual restrictions, the holders of demand registration rights can exercise such rights at any time. By exercising such registration rights, subject to some limitations, the holders of such rights could cause a significant number of shares of our common stock to be registered and sold in the public market. Such sales, or the perception that these sales could occur, may have an adverse effect on the market price for our common stock and could impair our ability to raise capital through an offering of equity securities. We have obtained waivers of all piggyback registration rights applicable to this offering.

Year 2000 issues could disrupt our business.

We have assessed our exposure to year 2000-related problems, focusing on four potential areas of exposure: internal information systems, scientific equipment, facility support systems and the readiness of significant third parties with whom we have material business relationships. We have substantially completed the implementation of all necessary upgrades and believe that the year 2000 issue will not pose significant operational problems for our internal information systems. After an inventory of our major pieces of scientific equipment and of our major facility support systems such as communications, security and building maintenance systems, we believe them to be year 2000-compliant. We are contacting our significant suppliers and service providers to determine if such parties are year 2000 compliant. To date, we have not been advised of material year 2000 issues by any of these parties. In addition, all contracts between us and third parties providing product development or manufacturing services to us require such third parties be in compliance with the laws, regulations and guidelines of the Federal Food, Drug, and Cosmetic Act (which requires appropriate steps to eliminate year 2000 computer risks). We cannot be certain that the systems of these third parties will be timely converted and any failure by these companies to do so may have an adverse impact on our business. We estimate that the remaining cost of the required upgrades and conversion will not have a significant impact on our results of operations.

The price of our common stock may be volatile.

The market prices of securities of small capitalization biotechnology companies, including ours, have historically been highly volatile. The market has from time to time experienced significant price and volume fluctuations unrelated to the operating performance of particular companies. The market price of our common stock may fluctuate significantly due to a variety of factors, including:

- . the results of preclinical testing and clinical trials by us or our competitors;
- . technological innovations or new therapeutic products;
- . governmental regulations;
- . developments in patent or other proprietary rights;
- . litigation;
- . public concern as to the safety of products developed by us or others;
- . comments by securities analysts; and
- . general market conditions in our industry.

In addition, if any of the risks described in these "Risk Factors" actually occurred, it could have a dramatic and adverse impact on the market price of our common stock.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in the sections entitled "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 constitute forward-looking statements. These statements involve known and unknown risks, uncertainties, and other factors that may cause our or our industry's results, levels of activity, performance, or achievements to be materially different from any future results, levels of activity, performance, or achievements expressed or implied by such forward-looking statements. Such factors include, among others, those listed under "Risk Factors" and elsewhere in this prospectus.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "intend," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," or "continue" or the negative of such terms or other comparable terminology.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance, or achievements. We do not assume responsibility for the accuracy and completeness of the forward-looking statements. We do not intend to update any of the forward-looking statements after the date of this prospectus to conform them to actual results.

## USE OF PROCEEDS

The net proceeds to us from this offering are estimated to be approximately \$63.1 million at an assumed public offering price of \$22.28 per share and after deducting underwriting discounts and estimated offering expenses. If the underwriters exercise their over-allotment option in full, the net proceeds to us are estimated to be approximately \$72.6 million.

We expect to use these proceeds for the following:

- . the further development and commercialization of pleconaril, including pre-marketing activities and hiring a specialty sales force;
- . the initiation of human clinical trials for hepatitis C and RSV disease product candidates;
- . ongoing research activities; and
- . general corporate purposes, which may include capital equipment expenditures.

The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development efforts, regulatory approvals, competition, marketing and sales activities and the market acceptance of any products introduced by us. Pending such uses, we intend to invest the net proceeds of this offering in short-term, investment grade, interest-bearing securities.

## PRICE RANGE OF COMMON STOCK

Our common stock is traded on the Nasdaq National Market under the symbol VPHM. We commenced trading on the Nasdaq National Market on November 19, 1996. The following table sets forth the high and low sale prices as quoted on the Nasdaq National Market since 1997.

	Common Stock Price	
	High	Low
Year Ended December 31, 1997		
First Quarter.....	\$13.75	\$ 9.00
Second Quarter.....	19.00	9.69
Third Quarter.....	22.63	14.00
Fourth Quarter.....	22.75	16.00
Year Ended December 31, 1998		
First Quarter.....	\$21.75	\$16.50
Second Quarter.....	26.13	19.63
Third Quarter.....	24.25	14.00
Fourth Quarter.....	20.00	7.88
Year Ended December 31, 1999		
First Quarter.....	\$13.00	\$ 5.00
Second Quarter.....	9.32	6.13
Third Quarter.....	29.44	7.65

There were approximately 182 record holders of our common stock as of September 1, 1999.

## DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain any future earnings to fund the development and growth of our business. Therefore, we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will be dependent on then existing conditions, including our financial condition, results of operations, contractual restrictions, capital requirements, business prospectus and other factors our board of directors deems relevant. In addition, our bank loan agreements restrict our ability to declare and pay cash dividends. We are obligated to pay any cash dividends paid to common stockholders to the holders of our series A convertible participating preferred stock on an as converted basis.

## CAPITALIZATION

The following table sets forth our capitalization as of June 30, 1999 on an actual basis and as adjusted to give effect to our sale of the 3,000,000 shares of our common stock offered by this prospectus at an assumed public offering price of \$22.28 per share, less the underwriting discounts and estimated offering expenses. This table should be read in conjunction with the section of this prospectus entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and notes thereto incorporated by reference into this prospectus.

	June 30, 1999	
	Actual	As Adjusted
	(unaudited)	
	(in thousands)	
Loans payable--non-current.....	\$ 1,782	\$ 1,782
Stockholders' equity:		
Preferred stock, par value \$.001 per share, 5,000,000 shares authorized;		
Series A convertible participating preferred stock; 2,300,000 shares designated; 2,300,000 shares issued and outstanding actual and as adjusted (liquidation value \$14,367,438).....	2	2
Series A junior participating preferred stock; 200,000 shares designated; no shares issued and outstanding actual and as adjusted.....	--	--
Common stock, par value \$.002 per share, 27,000,000 shares authorized; 11,572,654 shares issued and outstanding actual; and 14,572,654 shares issued and outstanding as adjusted.....	23	29
Additional paid-in capital.....	75,228	138,320
Deferred compensation.....	(121)	(121)
Unrealized gain on available for sale securities...	51	51
Deficit accumulated during the development stage...	(60,190)	(60,190)
Total stockholders' equity.....	14,993	78,091
Total capitalization.....	\$ 16,775	\$ 79,873

This table is based on the number of outstanding shares as of June 30, 1999 and does not include the following:

- . 581,092 options for shares of common stock available for issuance under our stock option plan;
- . 1,291,783 shares of common stock issuable upon the exercise of outstanding options at a weighted average exercise price of \$10.09 per share;
- . 2,317,329 shares of common stock issuable upon conversion of outstanding shares of series A convertible participating preferred stock, which are eligible for registration upon exercise of demand registration rights; and
- . 595,000 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$9.53 per share, which are eligible for registration upon exercise of demand registration rights.

As of September 1, 1999, there were 1,289,123 shares of common stock issuable upon the exercise of outstanding options at a weighted average exercise price of \$10.11 per share.

## DILUTION

Purchasers of the common stock offered by this prospectus will experience an immediate dilution in the net tangible book value of their common stock from the public offering price. The net tangible book value of our common stock as of June 30, 1999 was \$625,571 or \$0.05 per share. Net tangible book value per share of our common stock is equal to our net tangible assets (tangible assets less total liabilities) less our preferred stock liquidation value, divided by the number of shares of common stock issued and outstanding as of June 30, 1999. Dilution per share represents the difference between the public offering price per share of our common stock and the pro forma net tangible book value per share of our common stock after giving effect to this offering. After reflecting the assumed sale of 3,000,000 shares of common stock offered by us hereby at the assumed public offering price of \$22.28 per share, less underwriting discounts and estimated offering expenses, our pro forma net tangible book value per share of our common stock as of June 30, 1999 would have been \$63,723,571 or \$4.37 per share. The change represents an immediate increase in net tangible book value per share of our common stock of \$4.32 per share to existing stockholders and an immediate dilution of \$17.91 per share to new investors purchasing the shares of common stock in this offering. The following table illustrates this per share dilution:

Assumed public offering price.....	\$22.28
Net tangible book value per share of our common stock before the offering.....	\$0.05
Increase per share attributable to new investors in the offering.....	4.32
	-----
Pro forma net tangible book value per share of our common stock after this offering.....	4.37
	-----
Dilution per share to new investors.....	\$17.91
	=====

This table is based on the number of outstanding shares of common stock as of June 30, 1999 and does not include the following:

- . 581,092 options for shares of common stock available for issuance under our stock option plan;
- . 1,291,783 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of \$10.09 per share;
- . 2,317,329 shares of common stock issuable upon conversion of outstanding shares of series A convertible participating preferred stock, which are eligible for registration upon exercise of demand registration rights; and
- . 595,000 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$9.53 per share, which are eligible for registration upon exercise of demand registration rights.

As of September 1, 1999, there were 1,289,123 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of \$10.11 per share.

If the underwriters' over-allotment option is exercised in full, the pro forma net tangible book value per share of our common stock as of June 30, 1999 after giving effect to the assumed sale of 3,450,000 shares of common stock offered by us hereby at the assumed public offering price of \$22.28 per share, less underwriting discounts and estimated offering expenses, would have been \$73,248,271 or \$4.88 per share, representing an immediate dilution of \$17.40 per share to new investors purchasing the shares of common stock in this offering and an immediate increase in net tangible book value per share of our common stock of \$4.83 per share to existing stockholders.

## SELECTED FINANCIAL DATA

The following selected financial data with respect to the period from December 5, 1994 (inception) through December 31, 1994 and for each of the years in the four-year period ended December 31, 1998, have been derived from our audited financial statements. The data provided as of and for the six months ended June 30, 1998 and 1999 is unaudited, but in the opinion of management contains all adjustments, consisting only of normal recurring accruals, which are necessary for a fair statement of the results of such periods. The information set forth below is not necessarily indicative of the results of future operations and should be read in conjunction with the financial statements and notes thereto that are incorporated by reference into this prospectus and the section of this prospectus entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Period from December 5, 1994 (inception) through December 31, 1994					Six Months Ended June 30,	
	Year Ended December 31,					1998	1999
	1995	1996	1997	1998	1998	1999	
	(in thousands, except per share data)					(unaudited)	
Statement of Operations Data:							
License fee and milestone revenue.....	\$ --	\$ --	\$ 1,000	\$ 1,500	\$ 1,500	\$ 750	\$ --
Grant revenue.....	--	91	436	--	--	--	--
Total revenues.....	--	91	1,436	1,500	1,500	750	--
Operating expenses:							
Research and development.....	76	2,931	6,695	10,929	25,130	9,637	10,095
General and administrative.....	243	1,091	1,421	3,341	4,376	1,879	2,394
Total operating expenses.....	319	4,022	8,116	14,270	29,506	11,516	12,489
Loss from operations..	(319)	(3,931)	(6,680)	(12,770)	(28,006)	(10,766)	(12,489)
Interest income, net....	--	76	285	1,320	1,604	704	720
Net loss.....	(319)	(3,855)	(6,395)	(11,450)	(26,402)	(10,062)	(11,769)
Beneficial conversion feature of preferred stock.....	--	--	--	--	--	--	4,140
Accretion of redemption value attributable to mandatorily redeemable convertible preferred stock.....	--	19	1,597	--	--	--	--
Net loss allocable to common stockholders....	\$(319)	\$ (3,874)	\$ (7,992)	\$ (11,450)	\$ (26,402)	\$ (10,062)	\$ (15,909)
Net loss per share allocable to common stockholders:							
Basic.....	\$ (4.67)	\$ (3.89)	\$ (1.13)	\$ (2.30)	\$ (.88)	\$ (1.38)	
Diluted.....	\$ (3.52)	\$ (3.44)	\$ (1.13)	\$ (2.30)	\$ (.88)	\$ (1.38)	
Shares used in computing net loss per share allocable to common stockholders:							
Basic.....	829	2,053	10,093	11,486	11,479	11,564	
Diluted.....	1,099	2,324	10,093	11,486	11,479	11,564	

	As of December 31,					As of June 30,
	1994	1995	1996	1997	1998	1999
	(in thousands)					(unaudited)
Balance Sheet Data:						
Cash, cash equivalents and short-term investments.....	\$ 23	\$ 4,713	\$ 22,548	\$ 43,369	\$ 20,012	\$ 20,583
Other current assets....	2	104	197	495	474	320
Total current assets..	25	4,817	22,745	43,864	20,486	20,903
Equipment and leasehold improvements, net.....	--	--	672	1,085	2,477	2,654
Other assets.....	--	57	36	1,327	694	675
Total assets.....	\$ 25	\$ 4,874	\$ 23,453	\$ 46,276	\$ 23,657	\$ 24,232
Accounts payable, accrued expenses and other current liabilities.....						
Loans payable--current..	\$ 268	\$ 1,547	\$ 2,743	\$ 6,555	\$ 8,796	\$ 7,257
Total current liabilities.....	268	1,547	2,743	6,655	8,996	7,457
Loans payable--non-current.....	--	--	--	417	1,822	1,782
Capital leases--non-current.....	--	--	105	53	3	--
Total liabilities.....	268	1,547	2,848	7,125	10,821	9,239
Mandatorily redeemable convertible preferred stock.....						
Preferred stock.....	60	7,417	--	--	--	--
Common stock.....	--	--	--	--	--	2
Additional paid-in capital.....	2	2	18	23	23	23
Notes receivable on common stock.....	80	104	31,759	61,323	61,374	75,228
Deferred compensation...	(2)	--	--	--	--	--
Unrealized gains on securities available for sale.....	(64)	(49)	(661)	(452)	(248)	(121)
Deficit accumulated during the development stage.....	--	27	58	276	108	51
Total stockholders' equity.....	(319)	(4,174)	(10,569)	(22,019)	(48,421)	(60,190)
Total liabilities and stockholders' equity.....	(303)	(4,090)	20,605	39,151	12,836	14,993
Total liabilities and stockholders' equity.....	\$ 25	\$ 4,874	\$ 23,453	\$ 46,276	\$ 23,657	\$ 24,232

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

### Overview

Since inception, we have devoted substantially all of our resources to our research and product development programs. We have generated no revenues from product sales and have been dependent upon funding primarily from equity financing. We do not expect any revenues from product sales for at least the next fifteen months, if at all. We have not been profitable since inception and we have incurred a cumulative net loss of \$60,190,365 through June 30, 1999. Losses have resulted principally from costs incurred in research and development activities and general and administrative expenses. We expect to incur additional operating losses over at least the next several years. We expect such losses to increase over historical levels, primarily due to expected increases in our research and development expenses, further clinical trials of our most advanced product candidate, pleconaril (including any significant additional studies for approval in the European Union, if any are required), and milestone payments that may be payable under the terms of our agreement with Sanofi-Synthelabo for pleconaril. Also, we expect to incur expenses related to our marketing and market research activities for pleconaril, our development of a marketing and sales staff and further research and development related to other product candidates. Our ability to achieve profitability is dependent on a number of factors, including our ability to develop and obtain regulatory approvals for our product candidates, successfully commercialize those product candidates (which may include entering into collaborative agreements for product development and commercialization), and secure contract manufacturing and distribution and logistics services.

### Liquidity and Capital Resources

We began operations in December 1994. We are a development stage pharmaceutical company and to date have not generated revenues from product sales. The cash flows used in operations are primarily for research and development activities and supporting general and administrative expenses. Through June 30, 1999, we have used approximately \$51.3 million in operating activities. We invest our cash in short-term investments. Through June 30, 1999, we have used approximately \$16.5 million in investing activities, including \$12.3 million in short-term investments and \$3.7 million in equipment purchases and new construction. Through June 30, 1999, we have financed our operations primarily through public offerings of common stock, private placements of preferred stock, two bank loans, equipment lease lines and a milestone advance totaling approximately \$76.1 million. At June 30, 1999, we had cash and cash equivalents and short-term investments aggregating approximately \$20.6 million.

We lease our corporate and research and development facilities under an operating lease expiring in 2008. We also have the right to expand the facility and, under certain circumstances, to purchase the facility. We have financed substantially all of our equipment under two bank loans and two master lease agreements. The first bank loan, which we entered into in February 1997, is for \$600,000, is payable in equal monthly installments over 72 months and has a 9.06% interest rate. The second bank loan, which we entered into in December 1998, is for \$500,000, is payable in equal monthly installments over 60 months and has a 7.25% interest rate. We are required to repay amounts outstanding under the two master lease agreements within periods ranging from 36 to 48 months. As of September 1, 1999, aggregate outstanding borrowings under these bank loans and lease agreements were approximately \$884,000.

Under our agreement with Sanofi-Synthelabo, we are required to make milestone payments upon the achievement of certain development milestones and, until the expiration of the last patent on pleconaril or any related drug, royalty payments on any sales in the United States and Canada of products developed under the agreement. The development milestones include regulatory submissions of New Drug Applications and regulatory approvals in various jurisdictions. If we successfully complete ongoing Phase III clinical trials with pleconaril for the treatment of viral meningitis, and if we file a New Drug Application for pleconaril for the

treatment of viral meningitis, upon such filing we will be required to pay Sanofi-Synthelabo \$900,000. However, we may not be able to achieve these milestones.

We entered into an Addendum to our Development Agreement with SELOC France in 1998. Under this Addendum, SELOC France has manufactured three validation batches of pleconaril drug substance. SELOC France also is assisting us in preparing the pleconaril drug master file and is preparing certain documentation that will be required with our New Drug Applications for pleconaril. We estimate that \$700,000 will be payable under the Addendum in 1999.

On October 9, 1997, we received \$1.0 million from Boehringer Ingelheim Pharmaceuticals, Inc. as an advance on a future milestone in connection with a Collaborative Research Agreement. The Boehringer Agreement expired in August 1998. The advance was made in the form of a loan that bears interest at 8.5% and is evidenced by a convertible promissory note. If amounts due under the note are not paid by August 15, 2000, Boehringer Ingelheim may convert the then-outstanding principal balance and accrued interest into shares of our common stock based on the last sale price of the common stock on the date immediately prior to the date Boehringer Ingelheim notifies us of its intention to convert the promissory note.

We are currently expanding our research and development capabilities at our facility. We expect that we will invest approximately \$900,000 for this expansion over the next nine months. In addition, we have exercised our right to expand our current facility by 22,500 square feet. We will incur no material capital expenditures in connection with this expansion. We expect that rent expense in future years will increase approximately \$268,000 per annum, commencing in mid-2000.

We have incurred losses from operations since inception. We expect to incur additional operating losses over at least the next several years. We expect to incur such losses at an increasing rate over at least the next several years, primarily due to expected increases in our research and development expenses, further clinical trials and clinical development of our most advanced product candidate, pleconaril (including any significant additional studies for approval in the European Union, if any are required), and milestone payments that may be payable under the terms of our agreement with Sanofi-Synthelabo for pleconaril. Also, we expect to incur expenses for pleconaril marketing and market research activities, our development of a marketing and sales staff and further research and development related to other product candidates.

On May 5, 1999, we completed the sale of 2,300,000 shares of series A convertible participating preferred stock to Perseus-Soros BioPharmaceutical Fund, L.P. Our net proceeds from this sale were approximately \$13.3 million, including a cost of \$450,000 which was paid and recorded in September 1999. In addition, we issued Perseus-Soros warrants to purchase 595,000 shares of our common stock at \$9.53 per share. These warrants expire on May 5, 2004. The preferred stock is convertible into shares of common stock on a one-for-one basis (subject to adjustment) by Perseus-Soros at any time and by us under certain conditions. There is a 5% annual dividend associated with this preferred stock. We may choose to permanently defer payment of this dividend, in which case the dividend is added to the liquidation value and increases the conversion ratio of the preferred stock into common stock. Holders of the preferred stock have voting rights equivalent to those of the common stockholders. Such holders also have preemptive rights with respect to proposed private placements of our common stock or other equity securities for cash, other than issuances under our equity compensation or stock option plans and issuances pursuant to our stockholder rights plan, at a price below \$6.20 per share (with adjustment for any stock dividend, stock split or other subdivision of stock, or any combination or reclassification of stock). In addition, holders of the preferred stock have liquidation rights equal to their original investment, subject to adjustment. As a result of the difference in the price paid per share for the preferred stock and the fair market value per share of our common stock on the date of sale to Perseus-Soros, we have reflected the amount of the beneficial conversion feature of the preferred stock in our net loss allocable to common stockholders for the six months ended June 30, 1999. The fair market value per share of our common stock was determined using the closing price of our stock as quoted on Nasdaq on the date of our sale of this stock to Perseus-Soros. The beneficial conversion feature of the preferred stock aggregated \$4,140,000 and is included in the net loss allocable to common stockholders for the six months ended June 30, 1999.

We expect that we will need to raise additional funds to continue our business activities and to further expand our facilities. We may need additional financing to complete all clinical studies and to develop our marketing and sales staffs for pleconaril. We expect that we will need additional financing for the development and required testing of our hepatitis C and RSV disease compounds, and for any other product candidates. To obtain this financing, we intend to access the public or private equity markets or enter into additional arrangements with corporate collaborators. If we raise additional capital by issuing equity securities, the terms and prices for these financings may be much more favorable to the new investors than the terms obtained by our existing stockholders. These financings also may dilute the ownership of existing stockholders. Collaborative arrangements may require us to grant product development programs or licenses to third parties for products that we might otherwise seek to develop or commercialize ourselves. Additional financing, however, may not be available on acceptable terms from any source. If sufficient additional financing is not available, we may need to delay, reduce or eliminate current research and development programs or other aspects of our business. We expect that the proceeds from this offering along with current resources will fund our operations through early 2001.

## **Results of Operations**

### **Six-months ended June 30, 1999 and 1998**

We earned no revenues for the six-month period ended June 30, 1999. We earned milestone revenue of \$750,000 for the six-month period ended June 30, 1998. Our research and development expenses increased to \$10,094,585 for the six-month period ended June 30, 1999 from \$9,636,927 for the six-month period ended June 30, 1998. Research and development expenses for both periods were primarily incurred for clinical trials of pleconaril and to advance product candidates for the treatment of hepatitis C and RSV disease. General and administrative expenses were \$2,394,332 in the six-month period ended June 30, 1999 compared to \$1,878,645 for the same period of 1998. The increase in 1999 is related to the medical education program that we are conducting in preparation for the potential marketing of pleconaril. The net loss increased to \$11,769,403 for the six-month period ended June 30, 1999 from \$10,062,208 for the six-month period ended June 30, 1998.

### **Years ended December 31, 1998 and 1997**

We earned and received two milestone payments for \$1,500,000 from Boehringer Ingelheim for each of the years ended December 31, 1998 and 1997. Net interest income increased to \$1,603,916 for the year ended December 31, 1998 from \$1,320,174 for the year ended December 31, 1997, principally due to larger invested balances provided by the proceeds of a follow-on public offering in July 1997.

Research and development expenses increased to \$25,130,232 for the year ended December 31, 1998 from \$10,928,976 for the year ended December 31, 1997. The increase was principally due to the cost of ongoing multiple clinical trials, including the manufacture of bulk drug substance for stability and validation batches, related to pleconaril conducted during the year ended December 31, 1998. Also, we had more scientists conducting discovery research in the year ended December 31, 1998 compared to the year ended December 31, 1997 to advance product candidates for our hepatitis C and RSV disease programs. In addition, we incurred increased expenses for preclinical activities for our hepatitis C and RSV disease research programs in the year ended December 31, 1998 versus the year ended December 31, 1997. We recorded \$1,200,000 as a reduction to research and development expenses in the year ended December 31, 1998 for an adjustment to a milestone payable to Sanofi-Synthelabo and the reimbursement that we received from Sanofi-Synthelabo for a license fee that we had previously paid to them. Such amounts were originally recorded as research and development expenses in prior periods.

General and administrative expenses increased to \$4,375,800 for the year ended December 31, 1998 from \$3,341,081 for the year ended December 31, 1997. The increase is principally due to increased pleconaril marketing and market research expenses, salary expenses and facilities costs related to our move to our current facilities in March 1998.

The net loss increased to \$26,402,116 for the year ended December 31, 1998 from \$11,449,883 for the year ended December 31, 1997.

## Years ended December 31, 1997 and 1996

We earned and received two milestone payments aggregating \$1,500,000 in 1997 from Boehringer Ingelheim. We received a non-refundable technology access fee of \$1,000,000 from Boehringer Ingelheim and earned \$436,081 of grant revenue for the year ended December 31, 1996. Net interest income increased to \$1,320,174 for the year ended December 31, 1997 from \$285,142 for the year ended December 31, 1996, principally due to larger invested balances provided by the proceeds of our public offerings in November 1996 and in July 1997.

Research and development expenses increased to \$10,928,976 for the year ended December 31, 1997 from \$6,694,703 for the year ended December 31, 1996. The increase was principally due to the cost of multiple clinical trials related to pleconaril and advancing product candidates for our hepatitis C, RSV disease and influenza programs.

General and administrative expenses increased to \$3,341,081 for the year ended December 31, 1997 from \$1,421,524 for the year ended December 31, 1996. The increase was principally due to increased salary expenses, costs of being a public company for a full fiscal year, facilities costs, and increased costs associated with the pursuit of corporate collaborations.

The net loss increased to \$11,449,883 for the year ended December 31, 1997 from \$6,395,004 for the year ended December 31, 1996.

### **Year 2000 Impact**

Many currently installed computer systems are not capable of distinguishing 21st century dates from 20th century dates. As a result, beginning on January 1, 2000, computer systems and software used by many companies and organizations in a wide variety of industries including technology, transportation, utilities, finance and telecommunications will produce erroneous results or fail unless they have been modified or upgraded to process date information correctly. There is significant uncertainty concerning the scope and magnitude of problems associated with the century change. We recognize the need to ensure that our operations will not be harmed by year 2000 software failures. We are assessing the potential overall impact of the impending century change on our business, financial condition and operating results.

We have assessed our exposure to year 2000-related problems, focusing on four potential areas of exposure: internal information systems, scientific equipment, facility support systems and the readiness of significant third parties with whom we have material business relationships. We have substantially completed the implementation of all necessary upgrades and believe that the year 2000 issue will not pose significant operational problems for our internal information systems. After an inventory of our major pieces of scientific equipment and of our major facility support systems such as communications, security and building maintenance systems, we believe them to be year 2000-compliant.

We are contacting our significant suppliers and service providers to determine if such parties are year 2000 compliant. To date, we have not been advised of material year 2000 issues by any of these parties. In addition, all contracts between us and third parties providing product development or manufacturing services to us require such third parties be in compliance with the laws, regulations and guidelines of the Federal Food, Drug, and Cosmetic Act, which require appropriate steps to eliminate year 2000 computer risks.

The failure of third party suppliers and service providers, particularly contract research organizations engaged by us to monitor clinical trials, to be year 2000 compliant could adversely affect our operations. If such third parties are not year 2000 compliant, or are unable to fix problems that they encounter related to the year 2000 issue in a timely manner, our business or operation could be disrupted. If systems used by our contact research organizations are not year 2000 compliant, and the data collected by the contact research organizations on our behalf is corrupted or not available, we will have to recreate such data from the source documents, either by ourselves or by engaging others to perform the task on our behalf. If we are required to recreate such data, significant delays in reporting the results of our clinical trials could result.

To date, we have not expended material amounts on the year 2000 issue. We believe that the costs, if any, of addressing year 2000 issues presented by our internal systems will not have a material adverse impact on our financial position or results of operations. We also face the risks that the year 2000 issue poses to industry generally, such as the risk that communications, transportation or utility service will be interrupted.

# BUSINESS

## Overview

We are a pharmaceutical company dedicated to the commercialization, development and discovery of new antiviral medicines. We have focused our current product development and discovery activities on a number of RNA virus diseases, including:

- . viral respiratory infection, or VRI;
- . viral meningitis;
- . hepatitis C; and
- . respiratory syncytial virus diseases, or RSV diseases.

In September 1999, we commenced our Phase III clinical program with our lead product candidate, pleconaril, for the treatment of VRI, a severe form of the common cold. We are also conducting a Phase III clinical program with pleconaril for the treatment of viral meningitis. Approximately 1,700 patients have been treated with pleconaril in clinical studies completed to date. Based on our analysis of the data from these studies, pleconaril demonstrated a clinical benefit to patients and exhibited an adverse event profile similar to that of placebo.

## Market Overview

Viruses are intracellular parasites that require a living host cell within which to reproduce. Infection by viruses, and their ensuing replication, can lead to disease. Viral epidemics, pandemics, acute outbreaks and chronic viral diseases continue to cause an enormous amount of human suffering and death. There are three fundamental classes of viruses:

- . DNA viruses, which use DNA as their genetic material and replicate their DNA in a manner similar to human cells;
- . retroviruses, which reproduce by first converting their RNA into DNA in infected cells, then converting this DNA back into RNA; and
- . RNA viruses, which have the unique ability to directly reproduce their RNA to create new RNA virus offspring through a process known as RNA replication. This ability to directly replicate RNA distinguishes RNA viruses from DNA viruses, retroviruses and human cells.

DNA viruses cause diseases such as herpes, hepatitis B and papillomas (warts). The retrovirus HIV, or human immunodeficiency virus, causes AIDS. RNA viruses, however, are responsible for the majority of human viral diseases, causing a multitude of illnesses ranging from acute and chronic ailments to fatal infections. The following is a list of selected diseases caused by RNA viruses:

RNA Virus Diseases		
Bronchiolitis	Hemorrhagic fevers	Rhinovirus common cold
Bronchitis	Hepatitis A, D and E	RSV diseases
Dengue fever	Hepatitis C	Rubella
Diarrhea diseases	Influenza	Tick fevers
Ebola fever	Measles	Viral meningitis
Encephalitis	Myocarditis	Viral pharyngitis
Hand-foot-and-mouth disease	Neonatal enteroviral disease	Viral respiratory infection
Hantavirus pulmonary syndrome	Otitis media	Yellow fever
Hemorrhagic conjunctivitis	Rabies	

We have focused our current product development and discovery activities on the italicized diseases.

Despite efforts by the scientific and medical communities to develop pharmaceuticals and vaccines to treat and prevent RNA virus diseases, medicines are either inadequate or currently unavailable for the majority of RNA virus diseases. In fact, even though RNA viruses cause the majority of human viral diseases, these diseases have few available treatment options.

Antiviral pharmaceuticals that are currently available to treat RNA virus diseases are limited. There are at least 87 distinct RNA virus species or groups that infect humans and cause significant disease. However, there are approved antiviral pharmaceuticals available to treat diseases caused by only four of these virus groups. Of these,

- . zanamivir is used to treat influenza due to influenza A and B viruses;
- . amantadine and rimantadine are used to treat influenza A virus infections;
- . ribavirin is used to treat serious respiratory disease caused by RSV; and
- . interferon, alone or in combination with ribavirin, is used to treat hepatitis C.

In addition to these pharmaceutical products, several biological products, including interferons and immunoglobulins, are used to treat or prevent some RNA virus diseases.

Vaccines are designed to prevent disease by eliciting a protective antiviral immune response in vaccinated individuals. This response involves the production by the body of specific antibodies and white blood cells, both of which attempt to destroy the virus and virus-infected cells. Vaccines do not exist for most RNA virus diseases. Moreover, the effectiveness of those that are available is limited by one or more reasons, including the following:

- . many viruses constantly and rapidly change their outer surface, thereby rendering existing vaccines obsolete;
- . many individuals at greatest risk for serious disease, including the young, the elderly and the immunocompromised, respond poorly to vaccines; and
- . existing vaccines may not be readily available and, even when available, may not be widely used.

We believe that the significance and prevalence of RNA virus diseases and the limited availability and effectiveness of current antiviral pharmaceuticals and vaccines, have created a compelling need for new pharmaceuticals to treat these diseases. Given this large, unmet market need, we have focused our product development and discovery research on antiviral pharmaceuticals designed to treat diseases caused by RNA viruses.

## Product Pipeline

We are focusing our current product discovery and development activities on a number of RNA virus diseases affecting children and adults, including VRI, viral meningitis, hepatitis C and RSV diseases. The following chart sets forth these target disease indications and the status of our product candidates:

Disease Indication	Product Candidate	Development Status
Viral respiratory infection	Pleconaril	First Phase III trial in adolescents/adults ongoing Two Phase II trials in adolescents/adults completed Phase II trial in adolescents/adults with asthma completed Phase II challenge study completed
Viral meningitis	Pleconaril	Phase III trial in children ongoing Phase III trial in adolescents/adults ongoing Phase II/III trial in children completed Phase II/III trial in adolescents/adults completed Phase II trial completed
High risk picornavirus diseases	Pleconaril	Open label compassionate use ongoing
Hepatitis C	VP 50406 series	Preclinical development
RSV diseases	VP 14637 series	Preclinical development

### Pleconaril

We are currently developing our most advanced product candidate, pleconaril, for the treatment of common diseases caused by picornaviruses. Picornaviruses are a large, very prevalent group of RNA viruses that are responsible for a significant portion of human disease caused by RNA viruses. Picornaviruses, particularly enteroviruses and rhinoviruses, are the predominant cause of VRI, viral meningitis, myocarditis, encephalitis, common cold, bronchitis, otitis media and neonatal enteroviral disease, as well as viral exacerbations in individuals with asthma and chronic obstructive pulmonary disease. Immunocompromised patients, including transplant patients and patients receiving chemotherapy, also are extremely susceptible to severe disease caused by picornavirus infections.

Pleconaril is a proprietary, orally-administered small molecule inhibitor of picornaviruses that was discovered by scientists currently with ViroPharma. Pleconaril has been demonstrated to inhibit picornavirus replication in vitro by a novel, virus-specific mode of action. Pleconaril works by inhibiting the function of the viral protein coat, also known as the viral capsid, which is essential for virus infectivity and transmission. Preclinical studies have shown that pleconaril integrates within the picornavirus capsid at a specific site that is common to a majority of picornaviruses and disrupts several stages of the virus infection cycle. As a result of these studies and our clinical trials completed to date, we believe that pleconaril will be effective against a broad spectrum of diseases caused by picornaviruses.

We have developed liquid, solid, suspension and intranasal formulations of pleconaril. The liquid formulation has been used in all of our trials completed to date and is being used in our ongoing trials for viral meningitis. The solid formulation is being used in our ongoing VRI trial. We expect to market the liquid formulation of pleconaril for the treatment of viral meningitis and the solid formulation of pleconaril for the treatment of VRI. We may use the suspension and the intranasal formulations as line extensions to expand pleconaril's market opportunity.

We believe that there are significant market opportunities for pleconaril based upon the following information that we have derived from market research:

- . there are over 76 million physician visits in the United States annually for diseases either caused by or leaving patients at an increased susceptibility to picornaviruses;
- . each year in the United States there are more than 34 million physician visits for VRI;
- . each year in the United States there are more than 500,000 cases of viral meningitis; and
- . currently, there are no antiviral treatments for any diseases caused by picornaviruses.

Pleconaril for the Treatment of VRI. In September 1999, we commenced the first of two planned Phase III studies of pleconaril for the treatment of respiratory illness caused predominantly by picornaviruses, which is often referred to as viral respiratory infection, or VRI. VRI is a severe form of the common cold characterized by sore throat, runny nose, cough, body aches and weakness. The Centers for Disease Control and Prevention estimates that each year there are more than 60 million cases of the common cold in the United States that require medical attention or result in restricted activity. The National Institutes for Health, quoting data issued by the Centers for Disease Control and Prevention, reports that common colds caused 24 million days of restricted activity and 20 million days of missed school in 1994. Based on our market research, we believe that there are more than 34 million physician visits annually in the United States for VRI.

Currently, there are no antiviral pharmaceuticals for the treatment of VRI. However, physicians often prescribe antibiotics to patients with VRI. In fact, there are 18 million to 20 million antibiotic prescriptions written annually in the United States for patients suffering from the symptoms of VRI. Other than to prevent secondary bacterial infections, antibiotics are ineffective in treating viral diseases, including VRI. Therefore, many people afflicted with this illness seek relief from prescription and over-the-counter cough and cold remedies, analgesics and antipyretics. However, these medicines are only able to reduce the symptoms of VRI, and do not treat the underlying disease.

In July 1999, we reported our preliminary analysis of data from our Phase II clinical program for pleconaril for the treatment of VRI. The program enrolled 1,501 patients in three double-blinded, placebo-controlled trials for VRI. The largest of the three studies enrolled 1,024 otherwise healthy adolescent and adult patients who received either 400 milligrams of pleconaril or placebo two times or three times daily. Based on our analysis of the data from this study, randomized patients who received 400 milligrams of pleconaril three times daily experienced a clinical benefit and a statistically significant reduction in their disease when compared to placebo. Specifically, these patients reported:

- . a 3.5 day reduction in the median time to complete elimination of disease symptoms from 14 days to 10.5 days ( $p = 0.009$ );
- . a 3.5 day reduction in the median time to patient overall wellness from 14 days to 10.5 days ( $p = 0.002$ );
- . a 1.5 day reduction in median time to elimination of nasal congestion ( $p = 0.030$ );
- . a 1.5 day reduction in median time to elimination of runny nose ( $p = 0.035$ );
- . a one day reduction in median time to elimination of sore throat ( $p = 0.008$ ); and
- . no overall differences in adverse event profiles relative to placebo- treated patients.

We designed our Phase III clinical program with pleconaril for the treatment of VRI based on the results of this study and data obtained from our two smaller studies. We expect this clinical program to include two Phase III double-blinded placebo-controlled clinical trials. In September 1999, we initiated our first Phase III clinical trial for VRI using 400 milligrams of pleconaril three times daily in otherwise healthy adolescent and adult patients.

Pleconaril for the Treatment of Viral Meningitis. In July 1998, we commenced our Phase III clinical program with pleconaril for the treatment of viral meningitis in both adults and children between the ages of eight and 14 years. If we successfully complete our two Phase III clinical trials that are ongoing and receive FDA approval in a timely manner, we expect to commence commercial sale of pleconaril for the treatment of viral meningitis in late 2000.

Meningitis is an infection of the central nervous system predominantly caused by enteroviruses, and is characterized by the abrupt onset of severe headache, stiffness of the neck or back, fever, muscle pain, nausea, vomiting and malaise. The disease generally requires emergency medical care and occasionally progresses to serious neurologic effects, particularly among infants. Based on our market research, we believe that there are more than 500,000 cases of viral meningitis annually in the United States. There are currently no antiviral pharmaceuticals for the treatment of viral meningitis.

We reported our preliminary analysis of data from our Phase II/III clinical program for viral meningitis in adolescents and adults in January 1999 and in pediatric patients in November 1998.

The results for 130 adult patients treated with 200 milligrams of pleconaril or placebo three times daily were as follows:

- . a two day reduction in the median duration of headache for pleconaril- treated patients with confirmed enteroviral meningitis from nine to seven days ( $p = 0.04$ );
- . a one day reduction in the median duration of headache in all randomized patients from nine to eight days ( $p = 0.03$ );
- . a two day reduction in the median time for patients to return to work ( $p = 0.045$ );
- . a clinical benefit within 24 hours after initiation of therapy; and
- . no overall differences in adverse event profiles relative to placebo- treated patients.

The results for 144 pediatric patients treated with 2.5 milligrams/kilogram of pleconaril or placebo three times daily were as follows:

- . a one day reduction in disease duration when measured by the elimination of major meningitis symptoms ( $p = 0.033$ );
- . a three day reduction in disease duration when measured by a caregiver's assessment of the patient's illness ( $p = 0.048$ ); and
- . no overall differences in adverse event profiles relative to placebo- treated patients.

While our analysis of the data from this pediatric study demonstrated a statistically significant reduction in disease duration when measured by headache in children between the ages of eight and 14 years, the data did not show a statistically significant reduction in the duration of headache for all children treated in this study. We believe that this result was due to the difficulty in assessing headache severity in children between the ages of four and seven years. The results for 76 children between the ages of eight and 14 years who received 2.5 milligrams/kilogram of pleconaril or placebo three times daily were as follows:

- . a one day reduction in disease duration when measured by headache ( $p = 0.029$ );
- . a three day reduction in disease duration when measured by the elimination of major meningitis symptoms ( $p = 0.045$ ); and
- . no overall differences in adverse event profiles relative to placebo- treated patients.

We designed our Phase III clinical program for pleconaril for the treatment of viral meningitis based on these studies. This clinical program, which commenced in July 1998, includes one Phase III double-blinded

placebo-controlled clinical trial using 200 milligrams of pleconaril three times daily in otherwise healthy adolescent and adult patients, and one Phase III double-blinded placebo-controlled clinical trial using 2.5 milligrams/kilogram of pleconaril three times daily in otherwise healthy children between the ages of eight and 14 years. In addition, we are conducting a non-drug, natural history study of viral meningitis in children between the ages of four and seven years to further understand the disease in this population.

**Pleconaril for the Treatment of High Risk Patients.** Since August 1996, we have made pleconaril available on an open label basis for patients with life-threatening or seriously disabling diseases caused by picornaviruses. As of September 3, 1999, a total of 96 patients have been treated for a variety of life-threatening illnesses, including chronic meningoencephalitis in patients with immune deficiency, myocarditis, neonatal enteroviral disease, poliomyelitis syndromes, enterovirus infections after bone marrow transplantation, rhinovirus pneumonia, encephalitis, post-polio syndrome, chronic fatigue, enteroviral infection in patients with immune deficiency and enteroviral gastroenteritis in patients with immune deficiency. A majority of these high risk patients receiving a short course of pleconaril treatment have experienced a sustained clinical benefit and clearance of the virus. Although data from the compassionate use of pleconaril in these patients will be included in our New Drug Application for viral meningitis, these data are typically not sufficient to support an independent label indication.

**Commercialization of Pleconaril.** We have an exclusive license to market and sell pleconaril for all enterovirus and rhinovirus indications in the United States and Canada. We plan to leverage the infrastructure of partners for the manufacturing and distribution of pleconaril. We currently use SELOC France to manufacture bulk drug substance and Patheon, Inc. to manufacture drug product, and we expect to select a third party distribution and logistics partner in late 1999. We have not yet committed to a commercial supply agreement with any third party. Our marketing plans for pleconaril include a focused medical education program involving peer-to-peer presentations at appropriate medical meetings. In addition, we have an extensive medical and scientific publications plan in place, with approximately 42 publications expected prior to the launch of pleconaril for the treatment of viral meningitis and more than 100 publications expected prior to the launch of pleconaril for the treatment of VRI. Within four months after we file our New Drug Application for pleconaril for the treatment of viral meningitis, we intend to have in place a specialty sales force of approximately 50 to 70 sales representatives to market pleconaril for the treatment of viral meningitis to emergency medicine, infectious disease and pediatric infectious disease physicians, within four months after we file our New Drug Application for this indication. In order to penetrate the VRI marketplace, we intend to identify a strategic partner to help us target primary care physicians. In addition, we intend to add personnel to our sales force to target other physician groups.

#### **VP50406 Series for the Treatment of Hepatitis C**

We currently are conducting preclinical toxicology studies on product candidate VP50406 for the treatment of hepatitis C due to the hepatitis C virus, commonly known as HCV. VP50406 is a proprietary, orally bioavailable small molecule that has been demonstrated to inhibit RNA replication of HCV in vitro. This compound is the lead compound in a chemical series discovered and developed by ViroPharma. We intend to initiate human clinical studies with VP50406 for the treatment of hepatitis C in early 2000.

HCV is recognized as a major cause of chronic hepatitis worldwide. Approximately 85% of persons infected with HCV develop chronic hepatitis, of which 20% progress to liver cirrhosis. Chronic HCV infection can also lead to the development of hepatocellular carcinoma and liver failure. According to the Centers for Disease Control and Prevention, there currently are nearly four million people infected with HCV in the United States and 150,000 individuals are newly infected with HCV annually in the United States. The World Health Organization estimates that an additional 8.9 million individuals are infected with HCV in Europe and a total of 170 million people are infected worldwide. The Centers for Disease Control and Prevention estimates that hepatitis C currently is responsible for approximately 8,000 to 10,000 deaths in the United States annually. This number is projected to triple over the next decade.

There currently is no vaccine for HCV. Several interferon products, and interferon in combination with ribavirin, are currently approved for use in the United States for treatment of hepatitis C. These treatments are effective in 10% to 40% of patients. However, considerable side-effects are often associated with the use of interferon in the treatment of hepatitis C. As a result, nearly 20% of patients using this drug discontinue therapy before completing a standard 48-week regimen. Thus, while interferon products are often used to treat hepatitis C, their effectiveness is limited. We estimate that the current market for interferon and interferon in combination with ribavirin for the treatment of hepatitis C is over \$1.0 billion worldwide.

### **VP14637 Series for the Treatment of RSV Diseases**

We currently are conducting preclinical toxicology studies on product candidate VP14637 for the treatment of diseases caused by respiratory syncytial virus, or RSV. VP14637 is a proprietary, small molecule that has been demonstrated to inhibit RSV replication in vitro. This compound is the lead compound in a chemical series discovered and developed by ViroPharma. We intend to initiate human clinical studies with VP14637 for the treatment of RSV diseases in early to mid-2000.

RSV is a major viral respiratory tract pathogen that often causes pneumonia and bronchiolitis. Infants and young children with underlying conditions such as prematurity, congenital heart disease, bronchopulmonary dysplasia and various congenital or acquired immunodeficiency syndromes (such as asthma or immunodeficiency resulting from bone marrow transplants) are at greatest risk of serious RSV morbidity and mortality. RSV is also a major cause of morbidity and mortality in the elderly. Certain patient groups are particularly at risk for suffering from serious and life-threatening complications arising from RSV infections. These groups include:

	Estimated 1995 U.S. Population
	-----
Bone marrow transplant patients.....	47,000
Chronic obstructed pulmonary disease patients (including bronchitis and emphysema).....	16,500,000
Asthmatic patients.....	14,800,000

There currently are no vaccines available for the prevention of RSV disease. Two immunoglobulin products, one an intravenous human plasma-derived immune globulin preparation and the other an injectable humanized monoclonal antibody (palivizumab), currently are approved for prophylactic use in certain high risk infants with RSV infections. The only pharmaceutical drug approved for treatment of RSV disease is ribavirin. Ribavirin is administered by aerosol to minimize the drug's adverse effects and is generally reserved for treatment of only the most serious cases of RSV pneumonia and bronchiolitis.

### **Discovery Research**

Based on our experienced RNA virologists and our focus on RNA viral diseases, we believe that ViroPharma is a leader in RNA virology and RNA antiviral drug discovery and development. As a result of our focus on, and expertise in, RNA virus replication, our unique molecular target selection and assay development technologies, and our development and possession of proprietary chemical inhibitors and specialized chemical library, we believe that we are well positioned to develop effective antiviral pharmaceuticals for RNA virus diseases.

### **The RNA Virus Replication Process**

Important to the successful discovery and development of antiviral pharmaceuticals is the ability to analyze the virus in a laboratory setting and to dissect the molecular and biochemical events critical to virus replication. The manipulation of RNA viruses and, in particular, the virus' RNA genome, requires special techniques and skills. Historically, technical limitations have hampered investigation of RNA virus replication. Consequently, the scientific community's understanding of the molecular events of RNA virus replication is incomplete. However, significant recent advancements in biological and molecular technologies related to the manipulation of RNA and RNA viruses have enabled us to pursue the discovery and development of effective treatments for RNA virus diseases.

We believe that the process of viral RNA uncoating and replication represents an attractive target for the therapeutic intervention in disease caused by RNA viruses. For RNA viruses to cause disease, they must replicate. RNA virus replication is depicted in the following diagram:

**[GRAPHICS HERE]**

Inhibiting RNA virus replication can prevent, limit or stop disease. In addition to thwarting disease, the direct inhibition of viral RNA uncoating and replication should reduce generation of drug-resistant virus offspring and decrease virus transmission from infected individuals to healthy persons. RNA replication is a complicated process involving several viral proteins that must act together in a coordinated fashion. Due to the nature of this process, changes or mutations in these proteins are not readily tolerated. Consequently, viral proteins required for RNA replication are not only specific to the virus, they are among the least variable proteins of the virus. This is in contrast to the highly variable viral surface proteins generally involved in immune responses to virus infections. This invariability of the viral proteins responsible for viral RNA replication represents an important attribute in their selection as molecular targets for antiviral product discovery and development.

### **The ViroPharma Approach**

While the RNA uncoating and replication process is common among all RNA viruses, the detailed molecular and biochemical mechanisms involved currently are not fully understood. However, we have used our experience in RNA virology, RNA virus uncoating and RNA replication, along with recent advances in biological, molecular and informatics technologies, to gain an understanding of several aspects of the RNA virus uncoating and replication process. Scientists now with ViroPharma have elucidated fundamental processes involved in virus uncoating and have used this knowledge to design compounds to inhibit these processes. These scientists have also succeeded in discovering essential virus enzyme activities that are critical to RNA replication. They have further characterized RNA virus replication activities and have used the resulting information to develop novel drug screening assays. Our assays are optimized for high sensitivity and specificity and are validated for reproducibility. These assays are automated using state-of-the-art robotics technologies to facilitate

the high throughput screening of large chemical libraries. Using our novel assays, we have discovered proprietary small molecule compounds that inhibit the targeted virus-specific activities.

Once active compounds are identified, we advance such compounds to clinical product candidates through a process of chemical optimization. This process involves the rapid generation of an expanded chemical analog series based on the initial active compounds and utilizes an array of technologies including computer-assisted pharmacophore modeling and drug design techniques, two-dimensional and three-dimensional structure and substructure chemical database searches and conventional medicinal chemistry, combinatorial chemistry and automated high capacity chemical synthetic methods. We then evaluate analog series in various biochemical and biological assays that assess compound selectivity, potency, safety and bioavailability. Importantly, we chemically optimize active compounds for these four key parameters in parallel, not sequentially. We believe that our combination of chemical and biological technologies and our parallel compound optimization process allows us to accelerate product discovery and development. The generation of large numbers of specific chemical analogs by our scientists also enables us to rapidly expand our valuable chemical library in a manner that is biased toward inhibitors of enzymes and activities essential to RNA virus replication. We believe that this library provides a significant advantage in our efforts to discover novel inhibitors for additional RNA virus diseases.

## **Manufacturing**

We currently do not have commercial manufacturing capabilities, and do not intend to develop such capabilities for any product in the near future. Our commercialization plans are to leverage the infrastructure of partners for the manufacturing and distribution of pleconaril and our other product candidates. Pleconaril drug substance is prepared from readily available materials using reliable processes. Both pleconaril and the technology used to manufacture it are proprietary and covered by the patents licensed to us by Sanofi- Synthelabo. In April 1997, we entered into a Development Agreement with SELOC France for the manufacture of pleconaril bulk drug substance and the development of a process for its commercial-scale production. In March 1998, we entered into an Addendum to the Development Agreement with SELOC France for the manufacture of validation batches of pleconaril bulk drug substance and the preparation of certain documentation that will be required in connection with our New Drug Applications for pleconaril. We have entered into agreements with Patheon, Inc. for the manufacture of liquid and solid formulations of pleconaril drug product from bulk drug substance.

We have developed liquid, solid, suspension and intranasal formulations of pleconaril. We have used a liquid formulation of pleconaril in all of our trials completed to date and the liquid formulation is being used in our ongoing trials for viral meningitis. We are using a solid formulation in our ongoing trial for pleconaril in the treatment of VRI. We expect to market the liquid formulation of pleconaril for the treatment of viral meningitis and the solid formulation of pleconaril for the treatment of VRI. We may use the suspension and intranasal formulations as line extensions to expand pleconaril's market opportunity.

We anticipate that our current supply of pleconaril drug substance and drug product, together with the bulk drug substance and drug product that we will receive from our suppliers, will be sufficient to complete our formulation development activities and our ongoing clinical trials.

We have established quality control guidelines, which require that third party manufacturers under contract produce the drug product in accordance with the FDA's current Good Manufacturing Practices requirements. We maintain confidentiality agreements with potential and existing manufacturers in order to protect our proprietary rights related to pleconaril.

For the preparation of other compounds, we intend to contract with third- party manufacturers for preclinical research, manufacture of drug substances for clinical development and manufacture of drug products for commercial sale.

## **Marketing and Sales**

We are continuing our market research on the multiple disease indications for which we are developing pleconaril. Our marketing plans focus on medical education, including the use of thought leaders in peer-to-peer presentations at appropriate medical meetings. In addition, we have an extensive medical and scientific publications plan in place, with approximately 42 publications expected prior to the launch of pleconaril for the treatment of viral meningitis and more than 100 publications expected prior to the launch of pleconaril for the treatment of VRI.

We currently do not have a sales staff. However, within four months after we file our New Drug Application for pleconaril for the treatment of viral meningitis, we intend to have in place a specialty sales force of approximately 50 to 70 sales representatives to market pleconaril for the treatment of viral meningitis to emergency medicine, infectious disease and pediatric infectious disease physicians. To penetrate the VRI marketplace, we intend to identify a strategic partner to help us market pleconaril for the treatment of VRI to primary care physicians. We also intend to add to our internal sales organization to market to other specialty physician groups.

## **Sanofi-Synthelabo License**

Pleconaril was discovered by scientists currently with ViroPharma while they were with Sterling Winthrop, Inc., now Sanofi-Synthelabo S.A. In December 1995, we entered into an agreement with Sanofi-Synthelabo under which we received exclusive rights under patents owned by Sanofi-Synthelabo to develop and market all products relating to pleconaril and related compounds for use in enterovirus and rhinovirus disease indications in the United States and Canada, as well as a right of first refusal for any other indications in the United States and Canada. Our rights include rights to use all of Sanofi-Synthelabo's patents, know-how and trademarks relating to pleconaril for those indications in the United States and Canada. We have the right to sublicense our rights under the agreement subject to Sanofi-Synthelabo's consent, which consent is not to be unreasonably withheld. Pleconaril, which is currently in clinical trials, is covered by one of the licensed United States patents, which expires in 2012, and one of the licensed Canadian patent applications. We will be dependent on Sanofi-Synthelabo to prosecute such patent applications and may be dependent on Sanofi-Synthelabo to protect such patent rights.

Under our agreement with Sanofi-Synthelabo, we are required to make milestone payments to Sanofi-Synthelabo upon the achievement of certain development milestones and, until the expiration of the last patent on pleconaril or any related drug, royalty payments on any sales of products developed under the agreement in the United States and Canada. We would receive royalties from Sanofi-Synthelabo on sales of products by Sanofi-Synthelabo outside the United States and Canada. We believe that the royalty rates payable by both Sanofi-Synthelabo and us are comparable to the rates generally payable by other companies under similar arrangements. The milestone events include regulatory submissions of new drug applications and regulatory approvals in various jurisdictions. These milestones, however, may never be attained. Sanofi-Synthelabo must reimburse certain of the milestone fees previously paid by us upon submission of pleconaril for regulatory approval in Japan. Also, if foreign regulatory authorities require significant additional testing of pleconaril for use in the European Union, we will be required to conduct such studies at our own expense.

Our agreement with Sanofi-Synthelabo terminates on the later of expiration of the last patent licensed to us under the agreement or ten years following our first sale of a product containing a compound licensed to us under the agreement in the United States or Canada, or earlier under certain circumstances. In addition, Sanofi-Synthelabo has the right to terminate the agreement if we are subject to a change of control that would materially and adversely affect the development, manufacturing and marketing of the products under the agreement. The term automatically renews for successive five-year terms unless six months' prior written notice of termination is given by either party. We also have the right to manufacture, or contract with third parties to manufacture, any drug product derived from the pleconaril drug substance.

## Patents and Proprietary Technology

We believe that patent protection and trade secret protection are important to our business and that our future will depend, in part, on our ability to maintain our technology licenses, maintain trade secret protection, obtain patents and operate without infringing the proprietary rights of others both in the United States and abroad. We currently have received two issued United States patents covering compounds and methods for treating hepatitis C, one issued United States patent covering methods for treating pestivirus disease (a disease caused by viruses related to HCV) and three issued United States patents for compounds or methods for treating influenza. We have three pending United States patent applications covering compounds and methods for treating RSV diseases and influenza, as well as eight United States patent applications covering methods for treating hepatitis C and related virus diseases, as well as pestivirus diseases. We have one pending United States patent application covering technology and methods for identifying inhibitors of HCV. We also have filed patent applications under the Patent Cooperation Treaty, or PCT. These patent applications cover compounds and methods for treating hepatitis C and related virus diseases, pestivirus diseases, RSV diseases and influenza and technology, compositions and methods for identifying inhibitors of HCV. We intend to seek patent protection on these inventions in countries having significant market potential around the world on the basis of our PCT filings.

As patent applications in the United States are maintained in secrecy until patents issue and as publication of discoveries in the scientific or patent literature often lags behind the actual discoveries, we cannot be certain that we or our licensors were the first to make the inventions covered by each of these pending patent applications or that we or our licensors were the first to file patent applications for such inventions. Furthermore, the patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions, and, therefore, the breadth of claims allowed in biotechnology and pharmaceutical patents or their enforceability cannot be predicted. We cannot be sure that any patents will issue from any of these patent applications or, should any patents issue, that we will be provided with adequate protection against potentially competitive products. Furthermore, we cannot be sure that should patents issue, they will be of commercial value to us, or that private parties, including competitors, will not successfully challenge these patents or circumvent our patent position in the United States or abroad. In the absence of adequate patent protection, our business may be adversely affected by competitors who develop comparable technology or products.

Pursuant to the terms of the Uruguay Round Agreements Act, patents filed on or after June 8, 1995 have a term of twenty years from the date of filing, irrespective of the period of time it may take for the patent to ultimately issue. This may shorten the period of patent protection afforded to our products as patent applications in the biopharmaceutical sector often take considerable time to issue. Under the Drug Price Competition and Patent Term Restoration Act of 1984, a sponsor may obtain marketing exclusivity for a period of time following Food and Drug Administration approval of certain drug applications, regardless of patent status, if the drug is a new chemical entity or if new clinical studies were used to support the marketing application for the drug. Pursuant to the FDA Modernization Act of 1997, this period of exclusivity can be extended if the applicant performs certain studies in pediatric patients. This marketing exclusivity prevents a third party from obtaining FDA approval for a similar or identical drug under an Abbreviated New Drug Application or a "505(b)(2)" New Drug Application.

The Drug Price Competition and Patent Term Restoration Act of 1984 also allows a patent owner to obtain an extension of applicable patent terms for a period equal to one-half the period of time elapsed between the filing of an Investigational New Drug Application and the filing of the corresponding New Drug Application plus the period of time between the filing of the New Drug Application and FDA approval, with a five year maximum patent extension. We cannot be sure that we will be able to take advantage of either the patent term extension or marketing exclusivity provisions of this law.

In order to protect the confidentiality of our technology, including trade secrets and know-how and other proprietary technical and business information, we require all of our employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the use or disclosure of confidential information. The agreements also oblige our employees, consultants, advisors and collaborators to assign to us

ideas, developments, discoveries and inventions made by such persons in connection with their work with us. We cannot be sure that these agreements will maintain confidentiality, will prevent disclosure, or will protect our proprietary information or intellectual property, or that others will not independently develop substantially equivalent proprietary information or intellectual property.

The pharmaceutical industry is highly competitive and patents have been applied for by, and issued to, other parties relating to products competitive with those being developed by us. Therefore, our product candidates may give rise to claims that they infringe the patents or proprietary rights of other parties existing now and in the future. Furthermore, to the extent that we, or our consultants or research collaborators, use intellectual property owned by others in work performed for us, disputes may also arise as to the rights in such intellectual property or in related or resulting know-how and inventions. An adverse claim could subject us to significant liabilities to such other parties and/or require disputed rights to be licensed from such other parties. A license required under any such patents or proprietary rights may not be available to us, or may not be available on acceptable terms. If we do not obtain such licenses, we may encounter delays in product market introductions, or may find that we are prevented from the development, manufacture or sale of products requiring such licenses. In addition, we could incur substantial costs in defending ourselves in legal proceedings instituted before the United States Patent and Trademark Office or in a suit brought against us by a private party based on such patents or proprietary rights, or in a suit by us asserting our patent or proprietary rights against another party, even if the outcome is not adverse to us.

## **Government Regulation**

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements on the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval and promotion of our products. All of our products will require regulatory approval before commercialization. In particular, therapeutic products for human use are subject to rigorous preclinical and clinical testing and other requirements of the Federal Food, Drug, and Cosmetic Act, implemented by the FDA, as well as similar statutory and regulatory requirements of foreign countries. Obtaining these marketing approvals and subsequently complying with ongoing statutory and regulatory requirements is costly and time consuming. Any failure by us or our collaborators, licensors or licensees to obtain, or any delay in obtaining, regulatory approval or in complying with other requirements, could adversely affect the commercialization of products then being developed by us and our ability to receive product or royalty revenues.

The steps required before a new drug product may be distributed commercially in the United States generally include:

- . conducting appropriate preclinical laboratory evaluations of the product's chemistry, formulation and stability, and animal studies to assess the potential safety and efficacy of the product;
- . submitting the results of these evaluations and tests to the FDA, along with manufacturing information and analytical data, in an Investigational New Drug Application, or IND;
- . making the Investigational New Drug Application effective after the resolution of any safety or regulatory concerns of FDA;
- . obtaining approval of Institutional Review Boards, or IRBs, to introduce the drug into humans in clinical studies;
- . conducting adequate and well-controlled human clinical trials that establish the safety and efficacy of the drug product candidate for the intended use, typically in the following three sequential, or slightly overlapping stages:
  - . Phase I: The drug is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution and excretion;

. Phase II: The drug is studied in patients to identify possible adverse effects and safety risks, to determine dose tolerance and the optimal dosage, and to collect initial efficacy data;

. Phase III: The drug is studied in an expanded patient population at multiple clinical study sites, to confirm efficacy and safety at the optimized dose, by measuring a primary endpoint established at the outset of the study;

. submitting the results of preliminary research, preclinical studies, and clinical studies as well as chemistry, manufacturing and control information on the drug to the FDA in a New Drug Application, or NDA; and

. obtaining FDA approval of the New Drug Application prior to any commercial sale or shipment of the drug product.

This process can take a number of years and often requires substantial financial resources. The results of preclinical studies and initial clinical trials are not necessarily predictive of the results from large-scale clinical trials, and clinical trials may be subject to additional costs, delays or modifications due to a number of factors, including the difficulty in obtaining enough patients, clinical investigators, drug supply, or financial support. The FDA has issued regulations intended to accelerate the approval process for the development, evaluation and marketing of new therapeutic products intended to treat life-threatening or severely debilitating diseases, especially where no alternative therapies exist. If applicable, this procedure may shorten the traditional product development process in the United States. Similarly, products that represent a substantial improvement over existing therapies may be eligible for priority review with a target lapsed approval time of six months. Nonetheless, approval may be denied or delayed by FDA or additional trials may be required. FDA also may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the agency has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Upon approval, a drug product may be marketed only in those dosage forms and for those indications approved in the New Drug Application, although information may be distributed about off-label indications in certain circumstances.

In addition to obtaining FDA approval for each indication to be treated with each product, each domestic drug product manufacturing establishment must register with the FDA, list its drug products with the FDA, comply with current Good Manufacturing Practices and permit and pass inspections by the FDA. Moreover, the submission of applications for approval may require additional time to complete manufacturing stability studies. Foreign establishments manufacturing drug products for distribution in the United States also must list their products with the FDA and comply with current Good Manufacturing Practices. They also are subject to periodic inspection by the FDA or by local authorities under agreement with the FDA.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to extensive continuing regulation by the FDA, including record-keeping requirements and a requirement to report adverse experiences with the drug. In addition to continued compliance with standard regulatory requirements, the FDA also may require post-marketing testing and surveillance to monitor the safety and efficacy of the marketed product. Adverse experiences with the product must be reported to the FDA. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product are discovered following approval.

The Federal Food, Drug, and Cosmetic Act also mandates that drug products be manufactured consistent with current Good Manufacturing Practices. In complying with the FDA's regulations on current Good Manufacturing Practices, manufacturers must continue to spend time, money and effort in production, recordkeeping, quality control, and auditing to ensure that the marketed product meets applicable specifications and other requirements. The FDA periodically inspects drug product manufacturing facilities to ensure compliance with current Good Manufacturing Practices. Failure to comply subjects the manufacturer to possible FDA action, such as warning letters, suspension of manufacturing, seizure of the product, voluntary recall of a

product or injunctive action, as well as possible civil penalties. We currently rely on, and intend to continue to rely on, third parties to manufacture our compounds and products. Such third parties will be required to comply with current Good Manufacturing Practices.

Even after FDA approval has been obtained, and often as a condition to expedited approval, further studies, including post-marketing studies, may be required. Results of post-marketing studies may limit or expand the further marketing of the products. If we propose any modifications to the product, including changes in indication, manufacturing process, manufacturing facility or labeling, a New Drug Application supplement may be required to be submitted to the FDA.

Products manufactured in the United States for distribution abroad will be subject to FDA regulations regarding export, as well as to the requirements of the country to which they are shipped. These latter requirements are likely to cover the conduct of clinical trials, the submission of marketing applications, and all aspects of product manufacture and marketing. Such requirements can vary significantly from country to country. As part of our strategic relationships our collaborators may be responsible for the foreign regulatory approval process of our products, although we may be legally liable for noncompliance.

We are also subject to various federal, state and local laws, rules, regulations and policies relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research work. Although we believe that our safety procedures for handling and disposing of such materials comply with current federal, state and local laws, rules, regulations and policies, the risk of accidental injury or contamination from these materials cannot be entirely eliminated.

The extent of government regulation which might result from future legislation or administrative action cannot be accurately predicted. In this regard, although the Food and Drug Administration Modernization Act of 1997 modified and created requirements and standards under the Federal Food, Drug, and Cosmetic Act with the intent of facilitating product development and marketing, the FDA is still in the process of developing regulations implementing the Food and Drug Administration Modernization Act of 1997. Consequently, the actual effect of these developments on our business is uncertain and unpredictable.

Moreover, we anticipate that Congress, state legislatures and the private sector will continue to review and assess controls on health care spending. Any such proposed or actual changes could cause us or our collaborators to limit or eliminate spending on development projects and may otherwise impact us. We cannot predict the likelihood, nature, or extent of adverse governmental regulation that might result from future legislative or administrative action, either in the United States or abroad. Additionally, in both domestic and foreign markets, sales of our proposed products will depend, in part, upon the availability of reimbursement from third-party payors, such as government health administration authorities, managed care providers, private health insurers and other organizations. Significant uncertainty often exists as to the reimbursement status of newly approved health care products. In addition, third-party payors are increasingly challenging the price and cost effectiveness of medical products and services. There can be no assurance that our proposed products will be considered cost-effective or that adequate third-party reimbursement will be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product research and development.

## **Competition**

The pharmaceutical and biopharmaceutical industries are intensely competitive and are characterized by rapid technological progress. Certain pharmaceutical and biopharmaceutical companies and academic and research organizations currently engage in, or have engaged in, efforts related to the discovery and development of new antiviral medicines. Significant levels of research in chemistry and biotechnology occur in universities and other nonprofit research institutions. These entities have become increasingly active in seeking patent protection and licensing revenues for their research results. They also compete with us in recruiting skilled scientific talent.

Antiviral therapeutics for certain RNA virus diseases are currently available. For example,

- . zanamivir is used to treat influenza due to influenza A and B viruses;
- . amantadine and rimantadine are used to treat influenza A virus infections;
- . ribavirin is used to treat serious respiratory disease caused by RSV; and
- . interferon, alone or in combination with ribavirin, is used to treat hepatitis C.

In addition, several immunoglobulin products are used to treat or prevent some RNA virus diseases. We believe, however, that based on the characteristics of existing treatments, there is a clear need for new agents with superior therapeutic efficacy to treat these viral diseases.

In addition to approved products, other companies are developing treatments for RNA virus diseases, including compounds in clinical development for influenza and rhinovirus infections. Moreover, there are compounds in preclinical studies for RSV, influenza, rhinovirus and HCV infections. Our ability to compete successfully will be based on our ability to create and maintain scientifically advanced technology, develop proprietary products, attract and retain scientific personnel, obtain patent or other protection for our products, obtain required regulatory approvals and manufacture and successfully market our products either alone or through outside parties. Some of our competitors have substantially greater financial, research and development, manufacturing, marketing and human resources and greater experience in product discovery, development, clinical trial management, FDA regulatory review, manufacturing and marketing than we do.

### **Human Resources**

As of September 1, 1999, we had 91 full-time employees, including 18 persons with Ph.D. or M.D. degrees. Sixty-four of our employees are engaged in research and development activities at our laboratory facility in Exton, Pennsylvania. A significant number of our management and professional employees have had prior experience with pharmaceutical, biotechnology or medical products companies. None of our employees is covered by collective bargaining agreements. We believe that our relations with our employees are good.

### **Legal Proceedings**

We are currently not a party to any legal proceedings.

### **Facilities**

Our corporate facilities located in Exton, Pennsylvania currently occupy approximately 48,400 square feet. We are expanding by 22,500 square feet and may expand to a total of 86,500 square feet. The lease, which will expire in 2008, has two 5-year renewal options, monthly base rent and additional provisions for allocation of direct expense charges for utilities, maintenance, insurance and property taxes.

## MANAGEMENT

### Directors, Executive Officers and Other Key Employees

The following is a list of our directors and executive officers, including their ages, as of September 1, 1999:

Name	Age	Position
Claude H. Nash.....	56	Chief Executive Officer, President and Chairman of the Board of Directors
Marc S. Collett, Ph.D.....	48	Vice President, Discovery Research
Guy D. Diana, Ph.D.....	64	Vice President, Chemistry Research
Thomas F. Doyle.....	39	Vice President, General Counsel and Secretary
Johanna A. Griffin, Ph.D.....	55	Vice President, Business Development
Michael Kelly.....	34	Executive Director, Marketing
Mark A. McKinlay, Ph.D.....	48	Vice President, Research & Development
Vincent J. Milano.....	36	Vice President, Chief Financial Officer and Treasurer
Frank Baldino, Jr., Ph.D.....	46	Director
Robert J. Glaser.....	47	Director
Ann H. Lamont.....	42	Director
Jeremy M. Levin, D.Phil., M.B., B. Chir..	46	Director
Howard Pien.....	41	Director
David J. Williams.....	49	Director

Claude H. Nash, a co-founder of ViroPharma, has served as Chairman of the Board of Directors of ViroPharma since February 1997, and as Chief Executive Officer, President and director since our commencement of operations in December 1994. From 1983 until 1994, Dr. Nash served as Vice President, Infectious Disease and Tumor Biology at Schering-Plough Corporation, a pharmaceutical company. Dr. Nash received his Ph.D. from Colorado State University.

Marc S. Collett, Ph.D., a co-founder of ViroPharma, has served as Vice President, Discovery Research of ViroPharma since our commencement of operations in December 1994. From 1993 until 1994, he served as Senior Director, Viral Therapeutics at PathoGenesis Corporation, a biotechnology company. Prior to joining PathoGenesis Corporation, Dr. Collett served as Director, Virology & Antibody Engineering and Director, Biochemical Virology at MedImmune, Inc., a biotechnology company, where he was employed from 1988 to 1993. Dr. Collett received his Ph.D. from the University of Michigan.

Guy D. Diana, Ph.D., a co-founder of ViroPharma, has served as Vice President, Chemistry Research of ViroPharma since June 1995. From our commencement of operations in December 1994 until June 1995, Dr. Diana served as Executive Director, Chemistry Research of ViroPharma. Prior to joining ViroPharma, Dr. Diana worked at Sterling Winthrop Incorporated, a pharmaceutical company, for 33 years, most recently as a Senior Fellow in Medicinal Chemistry, where he led the team that discovered pleconaril. Dr. Diana received his Ph.D. from Rice University.

Thomas F. Doyle has served as Vice President, General Counsel of ViroPharma since November 1997, as Secretary since February 1997 and as Executive Director, Counsel since joining ViroPharma in November 1996. From 1990 until 1996, Mr. Doyle was a corporate attorney with the law firm of Pepper, Hamilton LLP. Mr. Doyle received his J.D. from Temple University School of Law. Prior to attending Temple University, Mr. Doyle was a certified public accountant. Mr. Doyle received his B.S. in accounting from Mt. St. Mary's College.

Johanna A. Griffin, Ph.D., a co-founder of ViroPharma, has served as Vice President, Business Development since June 1995 and, from December 1994 until June 1995, Dr. Griffin served as Executive Director, Business Development. From 1990 until 1994, Dr. Griffin served as Director of Molecular Biology at Boehringer Ingelheim Pharmaceuticals, Inc., a pharmaceutical company. Dr. Griffin received her Ph.D. from the University of Alabama at Birmingham.

Michael Kelly has served as Executive Director, Marketing since joining ViroPharma in April 1997. From 1991 until 1997, Mr. Kelly held various positions at TAP Pharmaceuticals, a pharmaceutical company, the latest being Manager of Hospital Account Executives within the Mid-Atlantic Region. Mr. Kelly received his B.S. in Marketing from the Trenton State College and his M.B.A. from Rider College.

Mark A. McKinlay, Ph.D., a co-founder of ViroPharma, has served as Vice President, Research & Development since our commencement of operations in December 1994, and served as Secretary from December 1994 until February 1997. From 1989 through 1994, Dr. McKinlay served in several positions, including Senior Director, at Sterling Winthrop Pharmaceuticals Research Division, a division of Sterling Winthrop Incorporated, a pharmaceutical company. Dr. McKinlay received his Ph.D. from Rensselaer Polytechnic Institute.

Vincent J. Milano has served as Vice President, Chief Financial Officer since November 1997, as Vice President, Finance & Administration of ViroPharma since February 1997, as Treasurer since July 1996, and as Executive Director, Finance & Administration from April 1996 until February 1997. From 1985 until 1996, Mr. Milano was with KPMG Peat Marwick LLP, independent certified public accountants, where he was Senior Manager since 1991. Mr. Milano is a Certified Public Accountant. Mr. Milano received his B.S. in accounting from Rider College.

Frank Baldino, Jr., Ph.D., has served as a Director of ViroPharma since June 1995. Since 1987, he has served as President, Chief Executive Officer and director of Cephalon, Inc., an integrated specialty biopharmaceutical company committed to the discovery, development and marketing of products to treat neurological disorders and cancer. Dr. Baldino is also a director of First Consulting Group, Inc. and Pharmacoepia, Inc.

Robert J. Glaser has served as a Director of ViroPharma since August 1997. Mr. Glaser is currently President of the McKesson HBOC Pharmaceutical Services division of McKesson HBOC. He was President and Chief Operating Officer of Ostex International from 1996-1997. Mr. Glaser was Senior Vice President of Marketing for Merck U.S. Human Health from 1994-1996, Vice President of Marketing from 1993-1994 and Vice President of Merck's Vaccine Division from 1991-1993.

Ann H. Lamont, a co-founder of ViroPharma, has served as a Director of ViroPharma since June 1995. Since 1986, Ms. Lamont has served as general partner and managing member of certain limited partnerships affiliated with Oak Investment Partners, a venture capital organization whose affiliates are principal stockholders in ViroPharma. Ms. Lamont also serves on the Board of Directors of BMJ Medical Management, Inc.

Jeremy M. Levin, D. Phil., M.B., B.Chir., has served as a director of ViroPharma since May 1999. Since 1999, Dr. Levin has served as a Managing Director of Perseus Capital, LLC, an entity related to Perseus-Soros BioPharmaceutical Fund, L.P. which is a principal stockholder of ViroPharma. Dr. Levin has served as Chairman, Physiome Sciences, Inc. since 1994 and was Chairman, President and Chief Executive Officer of Cadus Pharmaceutical Corporation from 1992 to 1998.

Howard Pien has served as a Director of ViroPharma since August 1998. Mr. Pien is President, Pharmaceuticals, SmithKline Beecham, and has overall responsibility for the commercial operations of SmithKline Beecham's global pharmaceutical business. Since joining SmithKline Beecham in 1991, Mr. Pien has held key positions in SmithKline Beecham's pharmaceutical business in the United States, the United Kingdom, China and Korea.

David J. Williams has served as a Director of ViroPharma since November 1997. Mr. Williams has been President and Chief Operating Officer of Pasteur Merieux Connaught USA since 1988. Mr. Williams also serves on the Board of Directors of Blue Cross of Northeastern Pennsylvania.

## PRINCIPAL STOCKHOLDERS

The following table sets forth certain information regarding the beneficial ownership of our common stock as of September 1, 1999, and as adjusted to reflect the sale of common stock offered hereby for (i) each stockholder who is known by us to own beneficially more than 5% of our common stock, (ii) each director and executive officer, and (iii) all of our directors and executive officers as a group. Except as otherwise indicated, we believe, based on information furnished by the persons named in this table that such persons have voting and investment power with respect to all shares of common stock beneficially owned by them, subject to community property laws, where applicable.

Beneficial Owner -----	Number of Shares Beneficially Owned -----	Percentage of Shares Beneficially Owned(1)	
		Prior to Offering -----	After Offering -----
<b>5% Stockholders</b> -----			
Perseus-Soros BioPharmaceutical Fund, L.P. (2).....	2,912,329	20.10%	16.65%
Oak Investment Partners VI, Limited Partnership (3).....	1,090,746	9.41	7.48
<b>Directors and Executive Officers</b> -----			
Ann H. Lamont (3).....	1,090,746	9.41	7.48
Claude H. Nash (4).....	489,859	4.22	3.35
Marc S. Collett (5).....	238,175	2.05	1.63
Mark A. McKinlay (6).....	168,585	1.45	1.15
Johanna A. Griffin (7).....	124,739	1.07	0.85
Guy D. Diana (8).....	97,190	*	*
Frank Baldino, Jr. (9).....	62,333	*	*
Vincent J. Milano (10).....	41,240	*	*
Robert J. Glaser (11).....	26,833	*	*
Thomas F. Doyle (12).....	25,814	*	*
Michael Kelly (13).....	16,333	*	*
David J. Williams (14).....	6,667	*	*
Howard Pien (15).....	6,667	*	*
Jeremy M. Levin (2).....	--	--	--
All directors and executive officers as a group (14 persons) (16).....	2,420,754	20.35	16.25

\* Less than one percent.

(1) Percentage of beneficial ownership is based on 11,576,824 shares of common stock were outstanding as of September 1, 1999. Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission and generally includes voting or investment power with respect to securities. Shares of common stock issued upon conversion of preferred stock or subject to options or warrants currently convertible or exercisable, or convertible or exercisable within 60 days after the date of this table, are deemed outstanding for purposes of computing the percentage ownership of the person holding the preferred stock, option or warrant but are not deemed outstanding for purposes of computing the percentage ownership of any other person. Except as indicated in the footnotes to this table and pursuant to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock beneficially owned.

(2) Includes 2,300,000 shares of series A convertible participating preferred stock purchased by Perseus-Soros BioPharmaceutical Fund, L.P. on May 5, 1999, which are convertible into 2,317,329 shares of common stock, and a warrant to purchase 595,000 shares of common stock. The series A convertible participating preferred stock has a 5% annual dividend that we have elected to permanently defer payment of, which dividend has been added to the liquidation value of such stock and has increased the conversion ratio of such stock into common stock. Dr. Levin, a director of ViroPharma, serves as a managing director of Perseus Capital, LLC, an entity related to Perseus-Soros BioPharmaceutical Fund, L.P. Dr. Levin has advised us that he does not have voting or investment power over the shares of common stock held by Perseus-Soros BioPharmaceutical Fund L.P. The address of Perseus-Soros BioPharmaceutical Fund L.P. is c/o Perseus Capital LLC, The Army and Navy Club Building, 1627 I Street, N.W., Suite 610, Washington, D.C. 20006.

(footnotes continue on next page)

- (3) As reflected in a Schedule 13G of Oak Management Corp. dated February 16, 1999, as adjusted by filings with the Securities and Exchange Commission of which we are aware. Includes 1,077,139 shares of common stock owned by Oak Investment Partners VI, Limited Partnership and 13,607 shares of common stock owned by Ms. Lamont. Ms. Lamont is a managing member of Oak Associates VI, LLC, the general partner of Oak Investment Partners VI Limited Partnership. Ms. Lamont shares voting and investment power with respect to the limited partnership with the other managing members of Oak Associates VI, LLC. Ms. Lamont disclaims beneficial ownership of shares in which she has no pecuniary interest. Oak has advised us that on September 17, 1999, it distributed 500,000 shares of our common stock to its general and limited partners. The address of Oak Investment Partners VI, Limited Partnership, is One Gorham Island, Westport, CT 06880.
- (4) Includes 600 shares of common stock held by Mr. Nash as custodian for two minor children, and 42,638 shares of common stock issuable upon the exercise of options.
- (5) Includes 1,000 shares of common stock held by Dr. Collett as custodian for a minor child, and 51,823 shares of common stock issuable upon the exercise of options.
- (6) Includes 61,385 shares of common stock issuable upon the exercise of options.
- (7) Includes 27,822 shares of common stock issuable upon the exercise of options.
- (8) Includes 19,572 shares of common stock issuable upon the exercise of options.
- (9) Includes 13,333 shares of common stock issuable upon the exercise of options.
- (10) Includes 22,116 shares of common stock issuable upon the exercise of options.
- (11) Includes 13,333 shares of common stock issuable upon the exercise of options.
- (12) Includes 24,100 shares of common stock issuable upon the exercise of options.
- (13) Includes 16,333 shares of common stock issuable upon the exercise of options.
- (14) Includes 6,667 shares of common stock issuable upon the exercise of options.
- (15) Includes 6,667 shares of common stock issuable upon the exercise of options.
- (16) Includes 305,789 shares of common stock issuable upon the exercise of options, and 595,000 shares of common stock issuable upon the exercise of the warrants issued to Perseus-Soros BioPharmaceutical Fund, L.P.

## DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 32,000,000 shares, including 27,000,000 shares of common stock, par value \$0.002 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share.

### Common Stock

As of September 1, 1999 there were 11,576,824 shares of common stock outstanding held of record by 182 stockholders.

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Elections of directors are determined by a plurality of the votes cast and the board of directors is divided into three classes, as nearly equal in number as possible. Our certificate of incorporation may be amended as permitted by law. Except as otherwise required by law, all other matters are determined by a majority of the votes cast. Holders of our common stock are entitled to receive ratably such dividends, if any, as may be declared by the board of directors out of funds legally available therefor, subject to any preferential dividend rights of outstanding preferred stock. Upon our liquidation, dissolution or winding up, subject to any preferential liquidation rights of outstanding preferred stock, the holders of our common stock are entitled to receive ratably our net assets available after the payment of all debts and other liabilities. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The outstanding shares of our common stock are fully paid and nonassessable. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock which we may designate and issue in the future.

### Preferred Stock

As of September 1, 1999, there were 2,300,000 shares of series A convertible participating preferred stock outstanding. There were also rights to purchase Series A junior participating preferred stock in connection with our Stockholder Rights Plan discussed below.

On May 5, 1999, we completed the sale of 2,300,000 shares of series A convertible participating preferred stock to Perseus-Soros BioPharmaceutical Fund, L.P. Our net proceeds from this sale were approximately \$13.3 million, including a cost of \$450,000 which was paid and recorded in September 1999. In addition, as discussed below, we issued Perseus-Soros warrants to purchase 595,000 shares of our common stock at \$9.53 per share. These warrants expire on May 5, 2004. The series A convertible participating preferred stock is convertible into shares of common stock on a one-for-one basis (subject to adjustment) by its holder at any time and by us under certain conditions. As of September 1, 1999, these shares were convertible into 2,317,329 shares of our common stock. There is a 5% annual dividend associated with the series A convertible participating preferred stock. We may choose to permanently defer payment of this dividend, in which case the dividend is added to the liquidation value and increases the conversion ratio of the series A convertible participating preferred stock into common stock. Holders of the series A convertible participating preferred stock have voting rights equivalent to those of the holders of our common stock. Such holders also have preemptive rights with respect to proposed private placements of our common stock or other equity securities for cash, other than issuances under our equity compensation or stock option plans and issuances pursuant to our stockholder rights plan, at a price below \$6.20 per share (with adjustment for any stock dividend, stock split or other subdivision of stock, or any combination or reclassification of stock). In addition, holders of the series A convertible participating preferred stock have liquidation rights equal to their original investment, subject to adjustment. As a result of the difference in the price paid per share for the series A convertible participating preferred stock and the fair market value per share of our common stock on the date of our sale of this stock to Perseus-Soros, we have reflected the amount of the beneficial conversion feature of this preferred stock in our net loss allocable to common stockholders for the six months ended June 30, 1999. The fair market value per share of our common stock was determined using the closing price of our stock as quoted on Nasdaq on the date of our sale of this stock to Perseus-Soros. The beneficial conversion feature of the series A convertible participating preferred stock aggregated \$4,140,000 and is included in the net loss allocable to common stockholders for the six months ended June 30, 1999.

As of September 1, 1999, pursuant to our certificate of incorporation, our board of directors has the authority, without further action by the holders of our common stock, to issue 2,500,000 additional shares of preferred stock from time to time in such series and with such preferences and rights as it may designate, in addition to the 200,000 shares of series A junior participating preferred stock already designated. These preferences and rights may be superior to those of the holders of our common stock. For example, the holders of preferred stock may be given a preference in payment upon our liquidation, or for the payment or accumulation of dividends before any distributions are made to the holders of common stock. We have no plans, agreements or understandings for the issuance of any shares of any additional series of preferred stock.

## **Warrants**

Pursuant to a common stock purchase warrant agreement dated May 5, 1999, we issued a warrant to purchase 595,000 shares of common stock to Perseus-Soros BioPharmaceutical Fund, LP in connection with the sale to Perseus of the series A convertible participating preferred stock described above. The warrant is exercisable at a price of \$9.53 per share and expires on May 5, 2004. The number of shares of common stock purchasable under the warrant and the exercise price of the warrant are subject to adjustment in the event of certain recapitalizations, reorganizations, stock splits and combinations.

## **Indemnification and Limitation of Liability**

Our certificate of incorporation provides that our directors shall not be personally liable to us or our stockholders for monetary damages for a breach of fiduciary duty as a director, except for liability (i) for any breach of such person's duty of loyalty to us or our stockholders, (ii) for acts or omissions not in good faith or involving intentional misconduct or a knowing violation of law, (iii) for the payment of unlawful dividends and certain other actions prohibited by Delaware corporate law, and (iv) for any transaction resulting in receipt by such person of an improper personal benefit. In addition, our by-laws provide for the indemnification, to the full extent authorized by law, of any person made, or threatened to be made, a party to an action or proceeding, whether criminal, civil, administrative or investigative, by reason of the fact that such person is or was one of our directors, officers or employees, or serves or served any other enterprise as a director, officer or employee at our request.

We have obtained a directors' and officers' liability insurance policy which provides directors and officers with insurance coverage for losses arising from claims based on breaches of duty, negligence, error and other wrongful acts. At present, there is no pending litigation or proceeding and we are not aware of any threatened litigation or proceedings, involving any director, officer, employee or agent where indemnification will be required or permitted under our certificate of incorporation or by-laws.

## **Anti-Takeover Effects of Provisions of Charter Documents and Delaware Law**

Our certificate of incorporation and by-laws include several provisions that may have the effect of deterring hostile takeovers or delaying or preventing changes in our control or management. First, our board of directors is divided into three classes, nearly equal in number. Under Delaware law, directors of a corporation with a classified board may be removed only for cause unless the corporation's certificate of incorporation provides otherwise. Our certificate of incorporation does not provide otherwise. Each class of directors will serve for a term of three years and until their successors have been elected and qualified. Accordingly, our officers and directors and related stockholders who hold a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election and may exert considerable influence over our management and policies and all matters requiring stockholder approval, including fundamental transactions.

In addition, our board of directors has the ability to establish the rights of, and to issue, substantial amounts of preferred stock without the need for stockholder approval, which preferred stock may be used to create voting impediments. These and other provisions of the certificate of incorporation and by-laws and the Delaware law could discourage potential acquisition proposals and could delay or prevent a change in our control or management.

## **Stockholder Rights Plan**

On September 10, 1998, our board of directors adopted a stockholder rights plan and in connection with that plan designated 200,000 shares of Series A junior participating preferred stock. Under this plan, a preferred share purchase right was issued as a dividend on each outstanding share of our common stock as of September 17, 1998. This preferred share purchase right entitles its holder to purchase from us a unit consisting of 1/100th of a share of our series A junior participating preferred stock at an exercise price of \$125 per unit, subject to adjustment. Each unit carries voting and dividend rights that are intended to produce the equivalent of one share of common stock. These rights expire on September 10, 2008.

The preferred share purchase rights granted under the stockholder rights plan will be exercisable and will trade separately from our common stock only if a person or group acquires beneficial ownership of 20% or more of our common stock or commences a tender or exchange offer that would result in such a person or group owning 20% or more of our common stock. Only when one or more of these events occur will stockholders receive certificates for the rights granted under the stockholder rights plan.

If any person actually acquires 20% or more of our common stock--other than through a tender or exchange offer for our common stock at a price and on terms that provide fair value to all stockholders--or if a holder of 20% or more of our common stock engages in certain "self-dealing" transactions or engages in a merger or other business combination in which we survive and our common stock remains outstanding, the other holders of our common stock will be able to exercise their preferred share purchase rights and receive shares of our common stock having a value equal to double the exercise price of the right. Additionally, if we are involved in certain other mergers where our shares are exchanged or certain major sales of our assets occur, the holders of our common stock will be able to exercise their preferred share purchase rights and receive shares of the acquiring company having a value equal to double the exercise price of the right. In either case, the holders of the rights may, in lieu of exercise, surrender the rights in exchange for one-half of the amount of securities otherwise purchasable. Upon the occurrence of any of these events, the preferred share purchase rights will no longer be exercisable into series A junior participating preferred stock.

We will be entitled to redeem the preferred share purchase rights at \$.01 per right at any time until the 10th day following a public announcement that a person has acquired a 20% ownership position in our common stock. In our discretion, we may extend the period during which we can redeem these rights.

## **Registration Rights**

As of September 1, 1999, holders of 1,860,454 shares of our common stock have both piggyback and demand registration rights. In addition, our founders have piggyback registration rights with respect to 877,750 shares of our common stock and the holders of shares of our series A convertible participating preferred stock that are convertible into 2,317,329 shares of our common stock, and the holders of warrants to purchase 595,000 shares of our common stock, have demand registration rights. Absent any contractual restrictions, the holders of demand registration rights can exercise such rights at any time. By exercising such registration rights, subject to some limitations, the holders of such rights could cause a significant number of shares of our common stock to be registered and sold in the public market. Such sales, or the perception that these sales could occur, may have an adverse effect on the market price for our common stock and could impair our ability to raise capital through an offering of equity securities. We are seeking waivers of all such piggyback registration rights applicable to this offering.

## **Stock Option Plan**

We adopted a stock option plan in September 1995. We authorized a total of 1,200,000 shares of our common stock for issuance under our 1995 stock option plan. Our board of directors amended and restated our 1995 stock option plan in March 1998 and our stockholders approved the amended and restated plan in May 1998. A total of 2,000,000 shares of our common stock have been authorized for issuance under our stock option

plan, including 1,200,000 shares authorized under the original plan and 800,000 additional shares authorized since the amended and restated plan was adopted.

The stock option plan provides for grants of stock options to our employees and directors and to our consultants and advisors who perform valuable services for us. The stock option plan is intended to further the growth and success of ViroPharma and its subsidiaries by enabling our employees, directors, consultants and advisors to acquire shares of our common stock, thereby increasing their personal interest in our growth and success. The stock option plan also is intended to provide a means of rewarding outstanding performance by such persons to ViroPharma and its subsidiaries.

The stock option plan may be administered by our board of directors or a committee consisting of at least two of our non-employee directors. In accordance with the provisions of our stock option plan, the board of directors or the committee has the authority to determine the persons to whom stock options will be granted, the number of shares to be covered by each stock option, and the exercise price per share. The board of directors or the committee also has the authority to prescribe, amend and rescind rules and regulations relating to our stock option plan, to determine the conditions that must be satisfied in order for a stock option to vest and become exercisable, to accelerate the vesting or exercise date of any stock option, and to interpret our stock option plan or any agreement entered into with respect to a stock option under the plan.

The exercise price for shares of our common stock subject to an option under our stock option plan may, at the discretion of the board of directors or the committee, be paid in cash, in shares of our common stock valued at fair market value on the exercise date, or in a combination of cash and shares of our common stock.

If we are subject to a change of control in which our stock option plan is not continued by our successor, or in which equivalent, substituted options to acquire common stock of our successor are not provided to persons holding options issued under our stock option plan, the stock option plan will terminate and all unvested options held by employees we have employed for at least two years prior to the change of control, or by directors who have served on our board of directors for at least two years prior to the change of control, will become fully and immediately vested and exercisable. As to unvested options held by our other employees and directors, 50% will become immediately vested and exercisable, and the remainder will lapse and be forfeited.

If we are subject to a change of control in which our stock option plan is continued by our successor, or in which equivalent, substituted options to acquire common stock of our successor are provided to persons holding options issued under our stock option plan, options held by our executive officers and directors who are not offered substantially equivalent employment with our successor or a related employer, or whose employment is terminated within six months after the change of control, will become fully and immediately vested and exercisable, while options held by our employees and directors who are offered substantially equivalent employment with our successor or a related employer will not be subject to accelerated vesting.

In addition, in the event of a merger, consolidation or tax-free reorganization or sale of substantially all of our assets, our board of directors has the authority to distribute to each person holding options issued under our stock option plan, cash and other property in an amount equal to and in the same form as the person would have received from our successor if that person had owned the shares subject to the option at the time of the change of control, provided that the exercise price the person would have paid to purchase such shares will be deducted from the amount paid to the person.

The board of directors may suspend, amend or terminate our stock option plan, subject to any required approval by our stockholders.

### **Transfer Agent and Registrar**

The transfer agent and registrar for the shares of common stock being offered is StockTrans, Inc.

## UNDERWRITERS

Under the terms and subject to the conditions contained in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. Incorporated and U.S. Bancorp Piper Jaffray Inc. are acting as representatives, have severally agreed to purchase, and ViroPharma has agreed to sell to them, severally, the number of shares indicated below:

Name ----	Number of Shares -----
Morgan Stanley & Co. Incorporated.....	
U.S. Bancorp Piper Jaffray Inc. ....	
Total.....	---
	===

The underwriters are offering the shares of common stock subject to their acceptance of the shares from ViroPharma and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of \$ a share under the public offering price. Any underwriter may allow, and such dealers may reallow, a concession not in excess of \$ a share to other underwriters or to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

ViroPharma has granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to an aggregate of 450,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table. If the underwriters' option is exercised in full, the total price to the public would be \$ , the total underwriters' discounts and commissions would be \$ and total proceeds to ViroPharma would be \$ .

Each of ViroPharma and the directors, executive officers and certain other stockholders of ViroPharma has agreed that, without the prior written consent of Morgan Stanley & Co. Incorporated on behalf of the underwriters, it will not, during the period ending 90 days after the date of this prospectus:

. offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or

. enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock.

whether any transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise.

The restrictions described in this paragraph do not apply to:

- . the sale of shares to the underwriters;
- . the issuance by ViroPharma of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;
- . the issuance by ViroPharma of additional options under its existing stock option plan, provided that such options are not exercisable during such 90-day period;
- . transactions by any person other than ViroPharma relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares; or
- . transfers by any person other than ViroPharma by gift, will or intestacy, or to affiliates or immediate family members, provided that the transferee agrees to be bound by such restrictions.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may over-allot in connection with the offering, creating a short position in the common stock for their own account. In addition, to cover over-allotments or to stabilize the price of the common stock, the underwriters may bid for, and purchase, shares of common stock in the open market. Finally, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the common stock in the offering, if the syndicate repurchases previously distributed common stock in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the common stock above independent market levels. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

The underwriters and dealers may engage in passive market making transactions in the common stock in accordance with Rule 103 of Regulation M promulgated by the Securities and Exchange Commission. In general, a passive market maker may not bid for, or purchase, the common stock at a price that exceeds the highest independent bid. In addition, the net daily purchases made by any passive market maker generally may not exceed 30% of its average daily trading volume in the common stock during a specified two-month prior period, or 200 shares, whichever is greater. A passive market maker must identify passive market making bids as such or maintain the market price of the common stock above independent market levels. Underwriters and dealers are not required to engage in passive market making and may end passive market making activities at any time.

From time to time, Morgan Stanley & Co. Incorporated has provided, and continues to provide, investment banking services to ViroPharma.

ViroPharma and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

## **LEGAL MATTERS**

The validity of the shares of common stock offered hereby will be passed upon for ViroPharma by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania. Certain legal matters will be passed upon for the underwriters by Ropes & Gray, Boston, Massachusetts.

## **EXPERTS**

The financial statements of ViroPharma Incorporated as of December 31, 1997 and 1998 and for each of the years in the three-year period ended December 31, 1998 and for the period from December 5, 1994

(inception) to December 31, 1998 have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent certified public accountants, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

## ADDITIONAL INFORMATION

A registration statement on Form S-3 with respect to the shares offered hereby (together with any amendments, exhibits and schedules thereto) has been filed with the Securities and Exchange Commission under the Securities Act. This prospectus does not contain all of the information contained in such registration statement on Form S-3, certain portions of which have been omitted pursuant to the rules and regulations of the Securities and Exchange Commission. For further information with respect to ViroPharma and the shares offered hereby, reference is made to the registration statement on Form S-3. Statements contained in this prospectus regarding the contents of any contract or any other documents are not necessarily complete and, in each instance, reference is hereby made to the copy of such contract or document filed as an exhibit to the registration statement on Form S-3. The registration statement may be inspected without charge at the Securities and Exchange Commission's principal office in Washington D.C., and copies of all of any part thereof may be obtained from the Public Reference section, Securities and Exchange Commission, Washington D.C., 20549, upon payment of prescribed fees.

We also file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any reports, statements or other information we file at the Securities and Exchange Commission public reference rooms located at Judiciary Plaza, 450 Fifth Street, N.W., Washington, D.C. 20549, Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, IL 60661 and 7 World Trade Center, Suite 1300, New York, NY 10048.

Please call the Securities and Exchange Commission at 1-800-SEC-0330 for further information on the public reference rooms. Our filings are also available to the public from commercial document retrieval services and at the web site maintained by the Securities and Exchange Commission at <http://www.sec.gov>.

The Securities and Exchange Commission allows us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the Securities and Exchange Commission. The information incorporated by reference is deemed to be part of this prospectus, except for any information superseded by information in this prospectus. This prospectus incorporates by reference the documents set forth below that we have previously filed with the Securities and Exchange Commission. These documents contain important information about us, our business and our finances.

The documents that we are incorporating by reference are:

1. Our Quarterly Report on Form 10-Q for the quarter ended June 30, 1999;
2. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 1999;
3. Our Annual Report on Form 10-K for the year ended December 31, 1998;
4. The description of our common stock contained in the Registration Statement on Form 8-A filed with the Securities and Exchange Commission on November 8, 1996; and
5. The description of rights to purchase preferred shares contained in the Registration Statement on Form 8-A filed with the Securities and Exchange Commission on September 21, 1998.

Any documents which we file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus but before the end of any offering of securities made under this prospectus will also be considered to be incorporated by reference.

If you request, either orally or in writing, we will provide you with a copy of any or all documents which are incorporated by reference. We will provide such documents to you free of charge, but will not include any exhibits, unless those exhibits are incorporated by reference into the document. You should address written requests for documents to Thomas F. Doyle, Vice President and General Counsel, ViroPharma Incorporated, 405 Eagleview Boulevard, Exton, PA 19341, (610) 458-7300.

We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in our 10-Q, 8-K and 10-K reports to the Securities and Exchange Commission. Also note that we provide a cautionary discussion of risks and uncertainties relevant to our business in the "Risk Factors" section of this prospectus. These are factors that we think could cause our actual results to differ materially from expected results. Other factors besides those listed here could also adversely affect us. This discussion is provided as permitted by the Private Securities Litigation Reform Act of 1995.

## Part II

### Information Not Required In Prospectus

#### Item 14. Other Expenses of Issuance and Distribution

The following table shows the estimated expenses of the issuance and distribution of the securities offered hereby:

Securities and Exchange Commission registration fee.....	\$ 24,487
Nasdaq National Market listing fee.....	\$ 17,500
National Association of Securities Dealers filing fee.....	\$ 9,308
Printing and engraving fees and expenses.....	\$100,000
Accounting fees and expenses.....	\$ 75,000
Legal fees and expenses.....	\$125,000
Miscellaneous.....	\$ 48,705
	-----
Total.....	\$400,000
	=====

All of the amounts shown are estimates except for the Securities and Exchange Commission registration fee, the Nasdaq National Market listing fee and the National Association of Securities Dealers filing fee.

#### Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law ("Section 145") permits a corporation 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, by reason of the fact that he is or was a director, officer or agent of the corporation or another enterprise if serving at the request of the corporation. Depending on the character of the proceeding, a corporation may indemnify against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding if the person indemnified acted in good faith and, in respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. In the case of an action by or in the right of the corporation, no indemnification may be made with respect to 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 that, despite the adjudication of liability, such person is fairly and reasonably entitled to indemnity for such expenses which the court shall deem proper. Section 145 further provides that to the extent a director, officer, employee or agent of a corporation has been successful in the defense of any action, suit or proceeding referred to above, or in the defense of any claim, issue or matter therein, he shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by him in connection therewith.

The Certificate of Incorporation of ViroPharma limits the personal liability of directors to ViroPharma or any of its stockholders for monetary damages for breach of fiduciary duty as a director, provided, however, that this limitation does not apply to any liability of a director (i) for any breach of the director's duty of loyalty to ViroPharma or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of Title 8 of the General Corporation Law of Delaware, or (iv) for any transaction from which the director derived an improper personal benefit.

Section 6.4 of ViroPharma's By-laws provides for the indemnification, to the full extent authorized by law, of any person made, or threatened to be made, a party to an action or proceeding, whether criminal, civil, administrative or investigative, by reason of the fact that such person, his testator or intestate, is or was a director,

officer or employee of ViroPharma or any predecessor of ViroPharma, or serves or served any other enterprise as a director, officer or employee at the request of ViroPharma or any predecessor of ViroPharma.

## Item 16. List of Exhibits

The exhibits filed as part of this registration statement are as follows:

Exhibit	Description
1.1**	Form of Underwriting Agreement.
5.1***	Opinion of Morgan, Lewis & Bockius LLP regarding legality of securities being registered.
23.1*	Consent of KPMG LLP.
23.2***	Consent of Morgan, Lewis & Bockius LLP (included in its Opinion filed as Exhibit 5.1 hereto).
24.1***	Powers of Attorney (included on signature page).

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\* Filed herewith. \*\* To be filed by amendment.

\*\*\* Previously filed.

## 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;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided, however, that paragraph (1)(i) and 1(ii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the Registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

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

The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement shall be

deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

The Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 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 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 of 1933 and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Amendment No. 1 to the registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in Exton, Pennsylvania on October 1, 1999.

### Viropharma Incorporated

*/s/ Claude H. Nash*  
By: \_\_\_\_\_  
*Claude H. Nash, Ph.D.*  
*President, Chief Executive*  
*Officer*

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 1 to the registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature -----	Title -----	Date ----
<i>/s/ Claude H. Nash</i> _____ Claude H. Nash, Ph.D.	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	October 1, 1999
<i>/s/ Vincent J. Milano</i> _____ Vincent J. Milano	Vice President, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	October 1, 1999
* _____ Frank Baldino, Jr., Ph.D.	Director	October 1, 1999
* _____ Robert J. Glaser	Director	October 1, 1999

Signature -----	Title -----	Date -----
* ----- Ann H. Lamont	Director	October 1, 1999
* ----- Jeremy M. Levin, D. Phil., M.B., B. Chir.	Director	October 1, 1999
* ----- Howard Pien	Director	October 1, 1999
* ----- David J. Williams	Director	October 1, 1999
*/s/ Vincent J. Milano ----- Vincent J. Milano as Attorney-in-fact		October 1, 1999

## Exhibit Index

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\* Filed herewith. \*\* To be filed by amendment.

\*\*\* Previously filed.

**Exhibit 23.1**

**Accountants' Consent**

The Board of Directors  
ViroPharma Incorporated:

We consent to the use of our report incorporated herein by reference and to the reference to our firm under the heading "Experts" in the prospectus.

**KPMG LLP**

*Princeton, New Jersey*

*/s/KPMG LLP*

*September 30, 1999*

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**End of Filing**

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