

**PHARMACYCLICS, INC.**

**Up to 18,750,000 Shares of Common Stock**

Pharmacyclics, Inc., or Pharmacyclics, is distributing at no charge to the holders of our common stock, par value \$0.0001 per share, non-transferable subscription rights to purchase up to an aggregate of 18,750,000 shares of our common stock (subject to increase at the discretion of the Company by up to 3,750,000 additional shares ("Additional Shares") to cover oversubscriptions) at a subscription price of \$1.28 per share, for up to an aggregate purchase price of approximately \$24 million in cash and/or securities, as provided herein. Each stockholder will receive one subscription right for each share of our common stock owned on July 15, 2009 and each subscription right will entitle its holder to purchase 0.6808 shares of our common stock at the subscription price. We will not issue fractional shares, but rather will round up or down the aggregate number of shares you are entitled to receive to the nearest whole number.

The purpose of this rights offering is to raise equity capital in a cost-effective manner that gives all of our stockholders the opportunity to participate. The net proceeds will be used for general working capital purposes, including the repayment, to the extent then outstanding, of certain indebtedness of Pharmacyclics under an existing promissory note in favor of affiliates of Robert W. Duggan, our Chairman of the Board and Chief Executive Officer, and the beneficial owner of approximately 27% of Pharmacyclics' outstanding common stock. Mr. Duggan has indicated to us that he intends to exercise all of his rights, for a total exercise of 5,106,000 shares equaling approximately \$6.5 million, an amount sufficient to satisfy the indebtedness owed by Pharmacyclics to Mr. Duggan in its entirety. The reason Pharmacyclics decided to raise up to approximately \$24 million in cash and/or securities, as provided herein, in this rights offering was to ensure that even if no other stockholders participated in the rights offering, Mr. Duggan would be able to participate up to his proportionate 27% interest and Pharmacyclics would receive at least the necessary amount to satisfy the Company's indebtedness.

The subscription rights will be distributed and exercisable beginning on July 15, 2009, the record date of this rights offering. The subscription rights will expire and will have no value if they are not exercised prior to 5:00 p.m., New York City time, on July 31, 2009, the expected expiration date of this rights offering. We, in our sole discretion, may extend the period for exercising the subscription rights. We will extend the duration of the rights offering as required by applicable law, and may choose to extend the rights offering if we decide that changes in the market price of our common stock warrant an extension or if we decide that the degree of participation in this rights offering by holders of our common stock is less than the level we desire. You should carefully consider whether or not to exercise your subscription rights before the expiration date. We reserve the right to cancel the rights offering at any time before the expiration of the rights offering, for any reason.

There is no minimum number of shares that we must sell in order to complete the rights offering. If you exercise your rights in full, you may also exercise an oversubscription right to purchase additional shares of common stock that remain unsubscribed at the expiration of the rights offering, subject to the availability and allocation of shares among persons exercising this oversubscription right and certain other limitations as further described elsewhere in this prospectus. If an insufficient number of shares of Common Stock are available to fully satisfy all properly exercised oversubscription rights requests, the Company shall have the right, at its

discretion, to increase the number of shares available for issuance in the rights offering by up to an amount equal to 3,750,000 Additional Shares in order to satisfy additional properly exercised oversubscription rights requests. If Pharmacyclics does not elect to issue Additional Shares, or if the Additional Shares are not sufficient to satisfy all of the properly exercised oversubscription rights requests, then the available shares will be prorated among those who properly exercised oversubscription rights based on the number of shares each rights holder subscribed for under the basic subscription right.

Stockholders who do not participate in the rights offering will continue to own the same number of shares, but will own a smaller percentage of the total shares outstanding to the extent that other stockholders participate in the rights offering. Rights that are not exercised by the expiration date will expire and have no value.

We are distributing the rights and offering the underlying shares of common stock directly to you. We have not employed any brokers, dealers or underwriters in connection with the solicitation or exercise of rights in the rights offering and no commissions, fees or discounts will be paid in connection with the rights offering. Computershare Inc. is acting as the subscription agent and Georgeson Inc. is acting as the information agent for the rights offering. While certain of our directors, officers and other employees may solicit responses from you, those directors, officers and other employees will not receive any commissions or compensation for their services other than their normal compensation.

The subscription rights may not be sold or transferred except to affiliates of the recipient and by operation of law.

Shares of Pharmacyclics are traded on the NASDAQ Global Market under the trading symbol "PCYC."

	<u>Per Share</u>	<u>Aggregate</u>
Subscription Price	\$1.28	\$24,000,000
Estimated Expenses	\$0.02	\$448,339
Net Proceeds to Pharmacyclics	\$1.26	\$23,551,660

**INVESTING IN OUR COMMON STOCK INVOLVES SIGNIFICANT RISKS. SEE "RISK FACTORS" BEGINNING ON PAGE 14.**

Neither the Securities and Exchange Commission nor any state securities regulators have approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Our securities are not being offered in any jurisdiction where the offer is not permitted under applicable local laws.

The date of this prospectus is July 16, 2009.

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## ABOUT THIS PROSPECTUS

**You should rely only on the information contained in this prospectus or any free writing prospectus we may authorize to be delivered to you. We have not, and have not authorized anyone else, to provide you with different or additional information. We are not making an offer of securities in any state or other jurisdiction where the offer is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus regardless of its time of delivery, and you should not consider any information in this prospectus or in the documents incorporated by reference herein to be investment, legal or tax advice. We encourage you to consult your own counsel, accountant and other advisors for legal, tax, business, financial and related advice regarding an investment in our securities.**

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As used in this prospectus, “Pharmacyclics,” “Company,” “we,” “our” and “us” refer to Pharmacyclics, Inc., unless stated otherwise or the context requires otherwise. Unless otherwise indicated, all information in this Prospectus assumes no issuance of Additional Shares.

## **CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

Throughout this prospectus and the documents incorporated by reference in this prospectus we make “forward-looking statements,” as that term is defined in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Forward-looking statements include the words “may,” “would,” “could,” “likely,” “estimate,” “intend,” “plan,” “continue,” “believe,” “expect” or “anticipate” and similar words as well as our acquisition, development and expansion plans, objectives or expectations and our liquidity projections. These forward-looking statements generally relate to our plans, objectives, prospects and expectations for future operations and results and are based upon what we consider to be reasonable future estimates. Although we believe that our plans, objectives, prospects and expectations reflected in, or suggested by, such forward-looking statements are reasonable at the present time, we may not achieve or we may modify them from time to time. Furthermore, there is no assurance that any positive trends suggested or referred to in such statements will continue. You should read this prospectus thoroughly with the understanding that actual future results may be materially different from what we expect as well as the factors described in the “Risk Factors” section of this prospectus for information regarding risk factors that could affect our results. We do not plan to update forward-looking statements even though our situation or plans may change in the future, unless applicable law requires us to do so.

## PROSPECTUS SUMMARY

*The following summary provides an overview of certain information about Pharmacyclics and this offering and may not contain all the information that is important to you. This summary is qualified in its entirety by, and should be read together with, the information contained in other parts of this prospectus and the documents we incorporate by reference. You should read this entire prospectus and the documents that we incorporate by reference carefully before making a decision about whether to invest in our securities.*

### Pharmacyclics

We are a clinical-stage biopharmaceutical company focused on developing and commercializing innovative small-molecule drugs for the treatment of immune mediated disease and cancer. Our purpose is to create a profitable company by generating income from products we develop, license and commercialize, either with one or several potential collaborators/partners or alone as may best forward the economic interest of our stakeholders. We endeavor to create novel, patentable, differentiated products that have the potential to significantly improve the standard of care in the markets we serve.

Presently, we have four product candidates in clinical development and two product candidates in pre-clinical development. It is our business strategy to establish collaborations with large pharmaceutical and biotechnology companies for the purpose of generating present and future income in exchange for adding to their product pipelines. In addition, we strive to generate collaborations that allow us to retain valuable territorial rights and simultaneously fast forward the clinical development and commercialization of our products.

We were incorporated in the State of Delaware in April 1991. Our principal executive offices are located at 995 East Arques Avenue, Sunnyvale, California 94085. Our telephone number is (408) 774-0330. Our web site is <http://www.pharmacyclics.com>. Information contained on our web site does not constitute a part of this prospectus.

PHARMACYCLICS®,  (the pentadentate logo) and Xcytrin® are registered U.S. trademarks of Pharmacyclics, Inc. Other trademarks, trade names or service marks used herein are the property of their respective owners.

## The Rights Offering

Rights Granted	We will distribute to each stockholder of record on July 15, 2009 at no charge, one non-transferable subscription right for each share of our common stock then owned. The rights will be evidenced by non-transferable subscription rights certificates. If and to the extent that our stockholders exercise their right to purchase our common stock we will issue up to 18,750,000 shares and receive gross proceeds of up to approximately \$24 million in cash and/or securities, as provided herein, in the rights offering.
Subscription Rights	Each subscription right will entitle the holder to purchase 0.6808 shares of our common stock for \$1.28 per share, the subscription price, which shall be paid in cash or by the delivery to the Company by the holder of an equivalent amount of principal and accrued and unpaid interest of indebtedness owed by the Company to such holder, or a combination thereof. We will not issue fractional shares, but rather will round up or down the aggregate number of shares you are entitled to receive to the nearest whole number.
Aggregate Subscription Proceeds	The reason we decided to raise up to approximately \$24 million in cash and/or securities, as provided herein, in this rights offering was to ensure that even if no other stockholders participated in the rights offering, Mr. Duggan would be able to participate up to his proportionate 27% interest and Pharmacyclics would receive at least an amount sufficient to satisfy the \$6.4 million note payable to affiliates of Mr. Duggan.
Subscription Price	\$1.28 per share, which shall be paid in cash or by the delivery to the Company by the holder of an equivalent amount of principal and accrued and unpaid interest of indebtedness owed by the Company to such holder, or a combination thereof.
Record Date	July 15, 2009
Expiration Date	5:00 p.m., New York City time, on July 31, 2009, subject to extension or earlier termination
Oversubscription Rights	We do not expect that all of our stockholders will exercise all of their basic subscription rights. If you fully exercise your basic subscription right, the oversubscription right of each right entitles you to subscribe for additional shares of our common stock

unclaimed by other holders of rights in this offering at the same subscription price per share. If an insufficient number of shares of Common Stock are available to fully satisfy all properly exercised oversubscription rights requests, the Company shall have the right, at its discretion, to increase the number of shares available for issuance in the rights offering by up to an amount equal to 3,750,000 Additional Shares in order to satisfy additional properly exercised oversubscription rights requests. If Pharmacyclics does not elect to issue Additional Shares, or if the Additional Shares are not sufficient to satisfy all of the properly exercised oversubscription rights requests, then the available shares will be prorated among those who properly exercised oversubscription rights based on the number of shares each rights holder subscribed for under the basic subscription right. The subscription agent will return any excess payments in the form in which made, or if made in a combination of cash and indebtedness, in the form indicated, or if not indicated, Company indebtedness will be applied to payment first, followed by cash, by mail without interest or deduction promptly after the expiration of the subscription period.

Non-Transferability of Rights

The subscription rights are not transferable.

Amendment, Extension and Termination

We may extend the expiration date at any time after the record date. We may amend or modify the terms of the rights offering. We also reserve the right to terminate the rights offering at any time prior to the expiration date for any reason, in which event all funds received in connection with the rights offering will be returned without interest or deduction to those persons who exercised their subscription rights.

Fractional Shares

We will not issue fractional shares of our common stock.

Procedure for Exercising Rights

You may exercise your subscription rights by properly completing and executing your rights certificate and delivering it, together with the subscription price for each share of common stock for which you subscribe, to the subscription agent on or prior to the expiration date. If you use the mail, we recommend that you use insured, registered mail, return receipt requested. If you cannot deliver your rights certificate to the subscription agent on time, you may follow the guaranteed delivery procedures described under “The Rights Offering — Guaranteed Delivery Procedures”

beginning on page 53.

#### No Revocation

Once you submit the form of rights certificate to exercise any subscription rights, you may not revoke or change your exercise or request a refund of monies paid. All exercises of rights are irrevocable, even if you subsequently learn information about us that you consider to be unfavorable.

#### Payment Adjustments

If you send a payment that is insufficient to purchase the number of shares requested, or if the number of shares requested is not specified in the rights certificate, the payment received will be applied to exercise your subscription rights to the extent of the payment. If the payment exceeds the amount necessary for the full exercise of your subscription rights, including any oversubscription rights exercised and permitted, the excess will be returned to you as soon as practicable in the form in which made, or if made in a combination of cash and indebtedness, in the form indicated, or if not indicated, Company indebtedness will be applied to payment first, followed by cash. You will not receive interest or a deduction on any payments refunded to you under the rights offering.

#### How Rights Holders Can Exercise Rights Through Others

If you hold our common stock through a broker, custodian bank or other nominee, we will ask your broker, custodian bank or other nominee to notify you of the rights offering. If you wish to exercise your rights, you will need to have your broker, custodian bank or other nominee act for you. To indicate your decision, you should complete and return to your broker, custodian bank or other nominee the form entitled "Beneficial Owners Election Form." You should receive this form from your broker, custodian bank or other nominee with the other rights offering materials. You should contact your broker, custodian bank or other nominee if you believe you are entitled to participate in the rights offering but you have not received this form.

#### How Foreign Stockholders and Other Stockholders Can Exercise Rights

The subscription agent will not mail rights certificates to you if you are a stockholder whose address is outside the United States or if you have an Army Post Office or a Fleet Post Office address. Instead, we will have the subscription agent hold the subscription rights certificates for your account. To exercise your rights, you must notify the subscription agent prior to 11:00 a.m., New York City time, at least three business days prior to the expiration date, and

	<p>establish to the satisfaction of the subscription agent that it is permitted to exercise your subscription rights under applicable law. If you do not follow these procedures by such time, your rights will expire and will have no value.</p>
Material United States Federal Income Tax Consequences	<p>A holder will not recognize income or loss for United States Federal income tax purposes in connection with the receipt or exercise of subscription rights in the rights offering. For a detailed discussion, see “Material United States Federal Income Tax Consequences” beginning on page 58. You should consult your tax advisor as to the particular consequences to you of the rights offering.</p>
Issuance of Our Common Stock	<p>We will issue certificates representing shares purchased in the rights offering as soon as practicable after the expiration of the rights offering.</p>
Conditions	<p>See “The Rights Offering—Conditions to the Rights Offering.”</p>
No Recommendation to Rights Holders	<p>An investment in shares of our common stock must be made according to your evaluation of your own best interests and after considering all of the information herein, including the “Risk Factors” section of this prospectus. Neither we nor our Board of Directors are making any recommendation regarding whether you should exercise your subscription rights.</p>
Use of Proceeds	<p>The purpose of this rights offering is to raise equity capital in a cost-effective manner that gives all of our stockholders the opportunity to participate. The net proceeds available to Pharmacyclics from the rights offering will be approximately \$23.5 million (approximately \$28.3 million if all of the Additional Shares are issued) and will be used for general working capital purposes, including the repayment, to the extent then outstanding, of certain indebtedness of Pharmacyclics under an existing promissory note in favor of affiliates of Robert W. Duggan, our Chairman of the Board and Chief Executive Officer, and the beneficial owner of approximately 27% of Pharmacyclics’ outstanding common stock. The reason we decided to raise up to approximately \$24 million in cash and/or securities, as provided herein, in this rights offering was to ensure that even if no other stockholders participated in the rights offering, Mr. Duggan would be able to participate up to his proportionate 27% interest and Pharmacyclics would</p>

receive at least an amount sufficient to satisfy the \$6.4 million note payable to affiliates of Mr. Duggan.

Subscription Agent

Computershare Inc.

Information Agent

Georgeson Inc.

For additional information concerning the rights offering, see “The Rights Offering,” beginning on page 48.

Before investing in our common stock, you should carefully read and consider the information set forth in “Risk Factors” beginning on page 14 of this prospectus and all other information appearing elsewhere and incorporated by reference in this prospectus and any accompanying prospectus supplement.

## QUESTIONS AND ANSWERS ABOUT THE RIGHTS OFFERING

**Q: *What is a rights offering?***

**A:** A rights offering is an opportunity for you to purchase additional shares of common stock at a fixed price and in an amount at least proportional to your existing interest in Pharmacyclics, enabling you to maintain or possibly increase your current percentage ownership of Pharmacyclics.

**Q: *Why are we engaging in a rights offering, how did we decide on a maximum aggregate gross proceeds of approximately \$24 million in cash and/or securities, as provided herein, and how will we use the proceeds from the rights offering?***

**A:** The purpose of this rights offering is to raise equity capital in a cost-effective manner that gives all of our stockholders the opportunity to participate. The net proceeds will be used for general working capital purposes, including the repayment, to the extent then outstanding, of certain indebtedness of Pharmacyclics under an existing promissory note in favor of affiliates of Robert W. Duggan, our Chairman of the Board and Chief Executive Officer, and the beneficial owner of approximately 27% of Pharmacyclics' outstanding common stock. The reason we decided to raise up to approximately \$24 million in cash and/or securities, in this rights offering was to ensure that even if no other stockholders participated in the rights offering, Mr. Duggan would be able to participate up to his proportionate 27% interest and Pharmacyclics would receive at least an amount sufficient to satisfy the \$6.4 million note payable to affiliates of Mr. Duggan. See "Use of Proceeds."

**Q: *Am I required to subscribe in the rights offering?***

**A:** No.

**Q: *What is the basic subscription right?***

**A:** Each subscription right evidences a right to purchase 0.6808 shares of Pharmacyclics' common stock at a subscription price of \$1.28 per share, the subscription price, which shall be paid in cash or by the delivery to the Company by the holder of an equivalent amount of principal and accrued and unpaid interest of indebtedness owed by the Company to such holder, or a combination thereof.

**Q: *What is the oversubscription right?***

**A:** We do not expect all of our stockholders to exercise all of their basic subscription rights. The oversubscription right provides stockholders that exercise all of their basic subscription rights the opportunity to purchase the shares that are not purchased by other stockholders. If you fully exercise your basic subscription right, the oversubscription right of each right entitles you to subscribe for additional shares of our common stock unclaimed by other holders of rights in this offering at the same subscription price per share. If an insufficient number of shares of Common Stock are available to fully satisfy all properly exercised oversubscription rights requests, the Company shall have the right, at its discretion, to increase the number of shares available for issuance in the rights offering by up to an amount equal to 3,750,000 Additional Shares in order to satisfy additional properly exercised oversubscription rights requests. If Pharmacyclics does not elect to issue Additional Shares, or if the Additional

Shares are not sufficient to satisfy all of the properly exercised oversubscription rights requests, then the available shares will be prorated among those who properly exercised oversubscription rights based on the number of shares each rights holder subscribed for under the basic subscription right. The subscription agent will return any excess payments in the form in which made, or if made in a combination of cash and indebtedness, in the form indicated, or if not indicated, Company indebtedness will be applied to payment first, followed by cash, by mail without interest or deduction promptly after the expiration of the subscription period.

**Q: *How was the \$1.28 per share subscription price established?***

**A:** In determining the subscription price for this rights offering, a pricing committee of our board of directors has been established. In setting the subscription price, the pricing committee reviewed and considered a number of factors, including the amount of proceeds desired, our need for liquidity and equity capital, alternatives available to us for raising equity capital, the historic market price, moving averages and volume weighted moving averages of our common stock, the pricing of similar transactions, the liquidity and the historic volatility of the market price of our common stock, the historic trading volume of our common stock, our business prospects, our recent and anticipated operating results, the price at which our stockholders might be willing to participate in the rights offering, the desire to provide an opportunity to our stockholders to participate in the rights offering on a pro rata basis and general conditions in the securities market. The subscription price is not necessarily related to the book value of our assets, net worth, past operations, cash flows, losses, financial condition, or any other established criteria for valuing Pharmacyclics and may or may not be considered the fair value of our common stock to be offered in the rights offering. You should not assume or expect that, after the rights offering, our common shares will trade at or above the subscription price. The Company can give no assurance that our common shares will trade at or above the subscription price in any given time period.

**Q: *Who will receive subscription rights?***

**A:** Holders of our common stock will receive one non-transferable subscription right for each share of common stock owned as of July 15, 2009, the record date.

**Q: *How many shares may I purchase if I exercise my subscription rights?***

**A:** You will receive one non-transferable subscription right for each share of our common stock that you owned on July 15, 2009, the record date. Each subscription right evidences a right to purchase 0.6808 shares of our common stock at a subscription price of \$1.28 per share, the subscription price, which shall be paid in cash or by the delivery to the Company by the holder of an equivalent amount of principal and accrued and unpaid interest of indebtedness owed by the Company to such holder, or a combination thereof. You may exercise any number of your subscription rights.

**Q: *What happens if I choose not to exercise my subscription rights?***

**A:** If you choose not to exercise your subscription rights you will retain your current number of shares of common stock of Pharmacyclics. As a result, the percentage of the common stock of Pharmacyclics that you own will decrease and your voting rights and other rights will be diluted.

**Q: *Does Pharmacyclics need to achieve a certain participation level in order to complete the rights offering?***

**A:** No. We may choose to consummate, amend, extend or terminate the rights offering regardless of the number of shares actually purchased.

**Q: *Can Pharmacyclics terminate the rights offering?***

**A:** Yes. Our Board of Directors may decide to terminate the rights offering at any time prior to the expiration of the rights offering, for any reason. If we cancel the rights offering, any money or indebtedness received from subscribing stockholders will be refunded as soon as practicable, but no later than 10 business days from the announcement that the rights offering is terminated, without interest or a deduction on any payments refunded to you under the rights offering. See “The Rights Offering — Expiration of the Rights Offering and Extensions, Amendments and Termination.”

**Q: *May I transfer my subscription rights if I do not want to purchase any shares?***

**A:** No. Should you choose not to exercise your rights, you may not sell, give away or otherwise transfer your rights. However, rights will be transferable to affiliates of the recipient and by operation of law, for example, upon the death of the recipient.

**Q: *When will the rights offering expire?***

**A:** The subscription rights will expire and will have no value, if not exercised prior thereto, at 5:00 p.m., New York City time, on July 31, 2009, unless we decide to extend the rights offering expiration date until some later time or terminate it earlier. However, we will not extend the expiration date beyond 90 days from the date we distribute the rights. See “The Rights Offering — Expiration of the Rights Offering and Extensions, Amendments and Termination.” The subscription agent must actually receive all required documents and payments in cash and/or securities, as provide herein, before the expiration date. There is no maximum duration for the rights offering.

**Q: *How do I exercise my subscription rights?***

**A:** You may exercise your subscription rights by properly completing and executing your rights certificate and delivering it, together in full with the subscription price for each share of common stock you subscribe for, to the subscription agent on or prior to the expiration date. If you use the mail, we recommend that you use insured, registered mail, return receipt requested. If you cannot deliver your rights certificate to the subscription agent on time, you may follow the guaranteed delivery procedures described under “The Rights Offering — Guaranteed Delivery Procedures” beginning on page 53.

**Q: *What should I do if I want to participate in the rights offering but my shares are held in the name of my broker, custodian bank or other nominee?***

**A:** If you hold our common stock through a broker, custodian bank or other nominee, we will ask your broker, custodian bank or other nominee to notify you of the rights offering. If you wish to exercise your rights, you will need to have your broker, custodian bank or other nominee act for you. To indicate your decision, you should complete and return to your broker, custodian bank or other nominee the form entitled “Beneficial Owner

Election Form.” You should receive this form from your broker, custodian bank or other nominee with the other rights offering materials. You should contact your broker, custodian bank or other nominee if you believe you are entitled to participate in the rights offering but you have not received this form.

**Q: *What should I do if I want to participate in the rights offering, but I am a stockholder with a foreign address or a stockholder with an Army Post Office or Fleet Post Office address?***

**A:** The subscription agent will not mail rights certificates to you if you are a stockholder whose address is outside the United States or if you have an Army Post Office or a Fleet Post Office address. To exercise your rights, you must notify the subscription agent prior to 11:00 a.m., New York City time, at least three business days prior to the expiration date, and establish to the satisfaction of the subscription agent that it is permitted to exercise your subscription rights under applicable law. If you do not follow these procedures by such time, your rights will expire and will have no value.

**Q: *Will I be charged a sales commission or a fee if I exercise my subscription rights?***

**A:** We will not charge a brokerage commission or a fee to rights holders for exercising their subscription rights. However, if you exercise your subscription rights through a broker, dealer or nominee, you will be responsible for any fees charged by your broker, dealer or nominee.

**Q: *Has the Board of Directors made a recommendation regarding the rights offering?***

**A:** Neither the Company, nor our Board of Directors is making any recommendation as to whether or not you should exercise your subscription rights. You are urged to make your decision based on your own assessment of the rights offering, after considering all of the information herein, including the “Risk Factors” section of this prospectus, and of your best interests.

**Q: *May stockholders in all states participate in the rights offering?***

**A:** Although we intend to distribute the rights to all stockholders, we reserve the right in some states to require stockholders, if they wish to participate, to state and agree upon exercise of their respective rights that they are acquiring the shares for investment purposes only, and that they have no present intention to resell or transfer any shares acquired. Our securities are not being offered in any jurisdiction where the offer is not permitted under applicable local laws.

**Q: *Is the exercise of my subscription rights risky?***

**A:** The exercise of your subscription rights involves significant risks. Exercising your rights means buying additional shares of our common stock and should be considered as carefully as you would consider any other equity investment. Among other things, you should carefully consider the risks described under the heading “Risk Factors,” beginning on page 14.

**Q: *How many shares of our common stock will be outstanding after the rights offering?***

**A:** The number of shares of our common stock that will be outstanding after the rights offering will depend on the number of shares that are purchased in the rights offering. If we sell all of the shares being offered, then we will issue approximately 18,750,000 shares of common stock. In that case, we will have approximately 46,289,378 shares of common stock outstanding after the rights offering. This would represent an increase of approximately 68% in the number of outstanding shares of common stock. Our largest stockholder, Robert W. Duggan, has indicated to us that he intends to exercise all of his rights, for a total exercise of 5,106,000 shares. If no rights holders, other than Mr. Duggan, were to exercise their rights in the rights offering, we will have approximately 32,645,378 shares of common stock outstanding after the rights offering.

**Q: *What will be the proceeds of the rights offering?***

**A:** If we sell all the shares being offered, we will receive gross proceeds of approximately \$24 million in cash and/or securities, as provided herein. We are offering shares in the rights offering with no minimum purchase requirement. As a result, there is no assurance we will be able to sell all or any of the shares being offered, and it is not likely that all of our stockholders will participate in the rights offering. If no rights holders, other than Mr. Duggan, were to exercise their rights in the rights offering, we will receive gross proceeds equal to the necessary amount to repay the loan made to us by Mr. Duggan.

**Q: *After I exercise my rights, can I change my mind and cancel my purchase?***

**A:** No. Once you exercise and send in your subscription rights certificate and payment in cash and/or securities, as provided herein, you cannot revoke the exercise of your subscription rights, even if you later learn information about Pharmacyclics that you consider to be unfavorable and even if the market price of our common stock falls below the \$1.28 per share subscription price. You should not exercise your subscription rights unless you are certain that you wish to purchase additional shares of our common stock at a price of \$1.28 per share. See “The Rights Offering — No Revocation or Change.”

**Q: *What are the material United States Federal income tax consequences of exercising my subscription rights?***

**A:** A holder will not recognize income or loss for United States Federal income tax purposes in connection with the receipt or exercise of subscription rights in the rights offering. For a detailed discussion, see “Material United States Federal Income Tax Consequences.” You should consult your tax advisor as to the particular consequences to you of the rights offering.

**Q: *If the rights offering is not completed, for any reason, will my subscription payment be refunded to me?***

**A:** Yes. If the rights offering is not completed, for any reason, any money or indebtedness received from subscribing stockholders will be refunded in the form which paid as soon as practicable, without interest or deduction.

**Q: *If I exercise my subscription rights, when will I receive shares of common stock I purchased in the rights offering?***

**A:** We will deliver certificates representing the shares of our common stock purchased in the rights offering as soon as practicable after the expiration of the rights offering and after all pro rata allocations and adjustments have been completed. We will not be able to calculate the number of shares to be issued to each exercising holder until 5:00 p.m., New York City time, on the third business day after the expiration date of the rights offering, which is the latest time by which subscription rights certificates may be delivered to the subscription agent under the guaranteed delivery procedures described under “The Rights Offering — Guaranteed Delivery Procedures.”

**Q: *To whom should I send my forms and payment?***

**A:** If your shares are held in the name of a broker, dealer or other nominee, then you should send your subscription documents, rights certificate and payment in cash and/or securities, as provided herein, to that record holder. If you are the record holder, then you should send your subscription documents, rights certificate and payment in cash and/or securities, as provided herein, by first class mail or courier service to Computershare Inc., the subscription agent. The address for delivery to the subscription agent is as follows:

***By Mail:***

*Computershare  
c/o Voluntary Corporate Actions -  
Pharmacyclics Rights Offering  
Suite V  
P.O. Box 43011  
Providence, RI 02941-3011*

***By Overnight Delivery:***

*Computershare  
c/o Voluntary Corporate Actions -  
Pharmacyclics Rights Offering  
250 Royall Street  
Suite V  
Canton, MA 02021*

Your delivery to a different address or other than by the methods set forth above will not constitute valid delivery.

**Q: *What if I have other questions?***

**A:** If you have other questions about the rights offering, please contact our information agent, Georgeson Inc., 199 Water Street, New York, New York 10038 by telephone at (212) 806-6859 (call collect) or 800-279-5722 (toll-free) or by email at [pharmacyclics@georgeson.com](mailto:pharmacyclics@georgeson.com).

**Q: *Are there any conditions to my right to exercise my subscription rights?***

**A:** Yes. We may terminate the rights offering, in whole or in part, if at any time before completion of the rights offering there is any judgment, order, decree, injunction, statute, law or regulation entered, enacted, amended or held to be applicable to the rights offering that in the sole judgment of our board of directors would or might make the rights offering or its completion, whether in whole or in part, illegal or otherwise restrict or prohibit completion of the rights offering. See “The Rights Offering—Conditions to the Rights Offering.”

**Q:** *Have any stockholders indicated they will exercise their rights?*

**A:** Yes. Our largest stockholder, Robert W. Duggan has indicated to us that he intends to exercise all of his rights, but has not made any formal commitment to do so, for a total exercise of 5,106,000 shares equaling approximately \$6.5 million, an amount sufficient to satisfy the indebtedness owed by Pharmacyclics to Mr. Duggan in its entirety (he currently holds approximately 27% of the outstanding shares of the Company's common stock).

## RISK FACTORS

*An investment in our securities involves a high degree of risk. Anyone who is making an investment decision regarding our securities should carefully consider the following risk factors, as well as the other information contained or incorporated by reference in this report. The risks and uncertainties described below are those that we currently believe may materially affect our Company or your investment. Other risks and uncertainties that we do not presently consider to be material, or of which we are not presently aware, may become important factors that adversely affect our security holders or us in the future. If any of the risks discussed below actually materialize, then our business, financial condition, operating results, cash flows and future prospects, or your investment in our securities, could be materially and adversely affected, resulting in a loss of all or part of your investment.*

### **Risks Relating to Pharmacyclics**

***We will need substantial additional financing and we may have difficulty raising needed capital in the future.***

We have expended and will continue to expend substantial funds to complete the research, development and clinical testing of our products. We are unable to entirely fund these efforts with our current financial resources. Currently, we are actively seeking partnership collaborations to help fund the development of our product candidates. On April 16, 2009, we entered into a partnership with Les Laboratoires Servier (“Servier”). On May 11, 2009, Pharmacyclics received the upfront payment of \$10.45 million. Pharmacyclics will also receive an additional guaranteed \$4 million for research collaboration over a 24 month period, paid in equal increments every 6 months with the initial payment due October 1, 2009. We may also raise additional funds through the public or private sale of equity securities, bank debt, collaborations or otherwise. Such additional financing may occur concurrently with this rights offering, or thereafter.

If we are unable to secure additional funds, whether through additional partnership collaborations or sale of our securities, we will have to delay, reduce the scope of or discontinue one or more of our product development programs. Under such circumstances, if the company would not be able to raise additional capital, we believe we can adjust our operational expenses, the clinical trial and product development schedule in such a manner to have sufficient funds until at least June 30, 2010.

Our actual capital requirements will depend on many factors, including:

- our ability to establish new partnership collaboration arrangements and the timing of such arrangements;
- continued progress of our research and development programs;
- our ability to establish and maintain collaborative arrangements with third parties;
- progress with preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory approval;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

- the amount and timing of capital equipment purchases; and
- competing technological and market developments.

In addition, our ability to raise additional capital may be dependent upon our stock being quoted on the NASDAQ Capital Market. In the past, our stock price has fallen below the \$1.00 minimum bid price requirement for continued listing set forth in NASDAQ Marketplace Rule 4450(a)(5). While we have since regained compliance with Marketplace Rule 4450(a)(5), we cannot assure you that our stock price will continue to remain above the required minimum bid price. If we do not remain in compliance with the \$1.00 minimum bid price requirement or any other NASDAQ listing requirement, our stock may be delisted by NASDAQ.

We also expect to raise any necessary additional funds through the public or private sale of equity securities, bank debt financings, collaborative arrangements with corporate partners or other sources that may be highly dilutive or otherwise disadvantageous, to existing stockholders or subject us to restrictive covenants. In addition, in the event that additional funds are obtained through arrangements with collaborative partners or other sources, such arrangements may require us to relinquish rights to some of our technologies, product candidates or products under development that we would otherwise seek to develop or commercialize ourselves. Additional funds may not be available on acceptable terms, if at all. Our failure to raise capital when needed and on acceptable terms would require us to reduce our operating expenses, delay or reduce the scope of or eliminate one or more of our research or development programs and would limit our ability to respond to competitive pressures or unanticipated requirements and to continue operations. Any one of the foregoing would have a material adverse effect on our business, financial condition and results of operations.

***Failure to obtain product approvals or comply with ongoing governmental regulations could adversely affect our business.***

The manufacture and marketing of our products and our research and development activities are subject to extensive regulation for safety, efficacy and quality by numerous government authorities in the United States and abroad. Before receiving FDA approval to market a product, we will have to demonstrate to the satisfaction of the FDA that the product is safe and effective for the patient population and for the diseases that will be treated. Clinical trials, and the manufacturing and marketing of products, are subject to the rigorous testing and approval process of the FDA and equivalent foreign regulatory authorities. The Federal Food, Drug and Cosmetic Act and other federal, state and foreign statutes and regulations govern and influence the testing, manufacture, labeling, advertising, distribution and promotion of drugs and medical devices. As a result, clinical trials and regulatory approval can take a number of years to accomplish and require the expenditure of substantial resources. Data obtained from clinical trials are susceptible to varying interpretations that could delay, limit or prevent regulatory approvals.

In addition, we may encounter delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. We may encounter similar delays in foreign countries. We may be unable to obtain requisite approvals from the FDA and foreign regulatory authorities and even if obtained, such approvals may not be received on a timely basis, or they may not cover the clinical uses that we specify.

Furthermore, regulatory approval may entail ongoing requirements for post-marketing studies. The manufacture and marketing of drugs are subject to continuing FDA and foreign

regulatory review and later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions, including withdrawal of the product from the market. Any of the following events, if they were to occur, could delay or preclude us from further developing, marketing or realizing full commercial use of our products, which in turn would have a material adverse effect on our business, financial condition and results of operations:

- failure to obtain and thereafter maintain requisite governmental approvals;
- failure to obtain approvals for specific indications of our products under development;  
or
- identification of serious and unanticipated adverse side effects in our products under development.

Any regulatory approval that we receive for a product candidate may be subject to limitations on the indicated uses for which the product may be marketed. In addition, if the FDA and/or foreign regulatory agencies approve any of our product candidates, the labeling, packaging, adverse event reporting, storage, advertising and promotion of the product will be subject to extensive regulatory requirements. We and the manufacturers of our product candidates must also comply with the applicable FDA Good Manufacturing Practice (“GMP”) regulations, which include quality control and quality assurance requirements as well as the corresponding maintenance of records and documentation. Manufacturing facilities are subject to ongoing periodic inspection by the FDA and corresponding state agencies, including unannounced inspections, and must be licensed before they can be used in commercial manufacturing of our products. We or our present or future suppliers may be unable to comply with the applicable GMP regulations and other FDA regulatory requirements. Failure of our suppliers to follow current GMP Practice or other regulatory requirements may lead to significant delays in the availability of products for commercial or clinical use and could subject us to fines, injunctions and civil penalties.

***All of our product candidates are in development, and we cannot be certain that any of our products under development will be commercialized.***

To be profitable, we must successfully research, develop, obtain regulatory approval for, manufacture, introduce, market and distribute our products under development. The time frame necessary to achieve these goals for any individual product is long and uncertain. Before we can sell any of our products under development, we must demonstrate to the satisfaction of the FDA and regulatory authorities in foreign markets through the submission of preclinical (animal) studies and clinical (human) trials that each product is safe and effective for human use for each targeted disease. We have conducted and plan to continue to conduct extensive and costly clinical trials to assess the safety and effectiveness of our potential products. We cannot be certain that we will be permitted to begin or continue our planned clinical trials for our potential products, or if permitted, that our potential products will prove to be safe and produce their intended effects.

The completion rate of our clinical trials depends upon, among other factors, the rate of patient enrollment, the adequacy of patient follow-up and the completion of required clinical evaluations. Many factors affect patient enrollment, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, competing clinical trials and new drugs or procedures used for the conditions we are investigating. Other companies are conducting clinical trials and have announced plans for future trials that are seeking or are likely

to seek patients with the same diseases that we are studying. We may fail to obtain adequate levels of patient enrollment in our clinical trials. Delays in planned patient enrollment may result in increased costs, delays or termination of clinical trials, which could have a material adverse effect on us. Many factors can affect the adequacy of patient follow-up and completion of required clinical evaluations, including failure of patients to return for scheduled visits or failure of clinical sites to complete necessary documentation. Delays in or failure to obtain required clinical follow-up and completion of clinical evaluations could also have a material adverse effect on the timing and outcome of our clinical trials and product approvals.

Additionally, clinical trials require substantial administration and monitoring. We may fail to effectively oversee and monitor the various trials we have underway at any particular time which would result in increased costs or delays of our clinical trials.

Data already obtained from preclinical studies and clinical trials of our products under development do not necessarily predict the results that will be obtained from later preclinical studies and clinical trials. Moreover, data from clinical trials we are conducting are susceptible to varying interpretations that could delay, limit or prevent regulatory approval. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. The failure to adequately demonstrate the safety and effectiveness of a product under development could limit or prevent regulatory approval of the potential product and would materially harm our business. Our clinical trials may not demonstrate the sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approval or may not result in marketable products.

***We have a history of operating losses and we expect to continue to have losses in the future.***

We have incurred significant operating losses since our inception in 1991 and, as of March 31, 2009, had an accumulated deficit of approximately \$357.5 million. We expect to continue to incur substantial additional operating losses until such time, if ever, as the commercialization of our products generates sufficient revenues to cover our expenses. All of our product candidates are in the early stages of development and the commercialization of those products will not occur, if at all, for at least the next several years. Our achieving profitability depends upon our ability, alone or with others, to successfully complete the development of our product candidates, and to obtain required regulatory approvals and to successfully manufacture and market our proposed product. While we have most recently generated \$10.45 million in cash from product licensing, we have to date not generated significant revenue from either the licensing or commercial sale of our products.

***Acceptance of our products in the marketplace is uncertain, and failure to achieve market acceptance will harm our business.***

Even if approved for marketing, our products may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

- the receipt of regulatory approvals for the indications that we are studying, and the acceptance by physicians and patients of the clinical benefits that our products may offer;
- the establishment and demonstration in the medical community of the safety, clinical efficacy and cost-effectiveness of our products and their potential advantages over existing therapeutic products;

- marketing and distribution support;
- the introduction, market penetration and pricing strategies of competing and future products; and
- coverage and reimbursement policies of governmental and other third- party payors such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, payors or the medical community in general may be unwilling to accept, purchase, utilize or recommend any of our products.

***We may fail to adequately protect or enforce our intellectual property rights or secure rights to third-party patents.***

Our success depends in part upon our ability to protect and defend our proprietary technology and product candidates through patents and trade secret protection. We, therefore, aggressively pursue, prosecute, protect and defend patent applications, issued patents, trade secrets, and licensed patent and trade secret rights covering certain aspects of our technology. The evaluation of the patentability of United States and foreign patent applications can take years to complete and can involve considerable expense.

We have a number of patents and patent applications related to our compounds but we cannot be certain that issued patents will be enforceable or provide adequate protection or that pending patent applications will issue as patents. Even if patents are issued and maintained, these patents may not be of adequate scope to benefit us, or may be held invalid and unenforceable against third parties.

We face risks and uncertainties related to our intellectual property rights. For example:

- we may be unable to obtain or maintain patent or other intellectual property protection for any products or processes that we may develop;
- third parties may obtain patents covering the manufacture, use or sale of these products, which may prevent us from commercializing any of our products under development globally or in certain regions; and
- any future patents that we may obtain may not prevent other companies from competing with us by designing their products or conducting their activities so as to avoid the coverage of our patents.

The actual protection afforded by a patent varies depending on the product candidate and country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patents under existing and future laws. Our ability to maintain or enhance our proprietary position for our product candidates will depend on our success in obtaining effective claims and enforcing those claims once granted. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar products. Due to the extensive amount of time required for the development, testing and regulatory review of a potential product, it is possible that, before any of our products can be

commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. Although we take steps to protect our proprietary rights and information, including the use of confidentiality and other agreements with our employees and consultants, and in our academic and commercial relationships, these steps may be inadequate, these agreements may be violated, or there may be no adequate remedy available for a violation. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology. We may be unable to meaningfully protect our rights in unpatented proprietary technology.

***We rely heavily on third parties for product and clinical development of our products.***

We currently depend heavily and will depend heavily in the future on third parties for support in product development and clinical development of our products. The termination of a significant number of our existing collaborative arrangements, or our inability to establish and maintain collaborative arrangements could have a material adverse effect on our ability to complete clinical development of our products. Given our limited resources, it may be necessary to establish partnerships with other pharmaceutical companies that have greater financial and technical resources in order to successfully develop and commercialize our products. Although we recently entered into a global strategic alliance with Servier, the leading French independent pharmaceutical company related to the research, development, and commercialization of Pharmacyclics' PCI-24781, an orally active, novel, small molecule inhibitor of Pan HDAC enzymes, that is currently in Phase I/II clinical trials in the United States and being developed for the treatment of solid tumors and hematologic malignancies, there is no assurance that any additional partnerships can be obtained, and if obtained, may require us to relinquish product rights that could affect the financial success of these products.

We rely on contract clinical research organizations, or CROs, for various aspects of our clinical development activities including clinical trial monitoring, data collection, safety monitoring and data management. As a result, we have had and continue to have less control over the conduct of clinical trials, the timing and completion of the trials, the required reporting of adverse events and the management of data developed through the trial than would be the case if we were relying entirely upon our own staff. Although we rely on CROs to conduct some of our clinical trials, we are responsible for confirming that each of our clinical trials is conducted in accordance with the investigational plan and protocol. Moreover, the FDA and foreign regulatory agencies require us to comply with regulations and standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements.

Outside parties may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct our trials. We may experience unexpected cost increases that are beyond our control. Any failure of such CROs to successfully accomplish clinical trial monitoring, data collection, safety monitoring and data management and the other services they provide for us in a timely manner and in compliance with regulatory requirements could have a material adverse effect on our ability to

complete clinical development of our products and obtain regulatory approval. Problems with the timeliness or quality of the work of a CRO may lead us to seek to terminate the relationship and use an alternate service provider. However, making such changes may be costly and may delay our trials, and contractual restrictions may make such a change difficult or impossible. Additionally, it may be difficult to find a replacement organization that can conduct our trials in an acceptable manner and at an acceptable cost.

***We lack the resources, capability and experience necessary to manufacture pharmaceuticals and thus rely heavily upon contract manufacturers.***

We have no manufacturing facilities and we currently rely on third parties for manufacturing and storage activities related to all of our products in development. Our manufacturing strategy presents the following risks:

- delays in scale-up to quantities needed for multiple clinical trials, or failure to manufacture such quantities to our specifications, or deliver such quantities on the dates we require, could cause delay or suspension of clinical trials, regulatory submissions and commercialization of our products in development;
- there is no guarantee that the supply of clinical materials can be maintained during the clinical development of our product candidates;
- our current and future manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding regulatory agencies for compliance with strictly enforced current Good Manufacturing Practice and similar foreign standards. Failure to pass these inspections could have a material adverse effect on our ability to produce our products to support our operations;
- if we need to change to other commercial manufacturing contractors, there is no guarantee that we will be able to locate a suitable replacement contractor. The FDA and comparable foreign regulators must approve material manufactured by these contractors prior to our use. This would require new testing and compliance inspections. The new manufacturers would have to practice substantially equivalent processes for the production of our products;
- our current manufacturers might not be able to fulfill our commercial needs, which would require us to seek new manufacturing arrangements and may result in substantial delays in meeting market demand; and
- any disruption of the ability of our manufacturing contractors to supply necessary quantities of our products could have a material adverse effect on our ability to support our operations.

Any of these factors could delay clinical trials or commercialization of our products under development and entail higher costs.

***We lack marketing, distribution and sales experience.***

We have no experience marketing, selling or distributing products and currently lack the internal capability to do so. If any of our product candidates are approved by the FDA, we will need a sales force with technical expertise prior to the commercialization of any of our product candidates. We have no experience in developing, training or managing a sales force. We will

incur substantial additional expenses in developing, training and managing such an organization. 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 direct marketing and sales efforts may be unsuccessful. In addition, we compete with many other companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts may be unable to compete successfully against those of such other companies. We will need to enter into co-promotion or other licensing arrangements with larger pharmaceutical or biotechnology firms in order to increase the commercial success of our products. To the extent we enter into co-promotion or other licensing agreements, our product revenues are likely to be lower than if we directly marketed and sold our products, and some or all of the revenues we receive will depend upon the efforts of third parties, which may not be successful and may not be within our control. If we are unable to enter into co-promotion or other licensing agreements on acceptable terms or at all, we may not be able to successfully commercialize our existing and future product candidates. If we are not successful in commercializing our existing and future product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant losses.

***If we lose or are unable to hire and retain qualified personnel, then we may not be able to develop our products or processes and obtain the required regulatory approvals.***

We are highly dependent on qualified scientific and management personnel. We will need to expand and effectively manage our managerial, operational, financial, development and other resources in order to successfully pursue our research, development and commercialization efforts for our existing and future product candidates. Our success depends on our continued ability to attract, retain and motivate highly qualified management and personnel with pre-clinical and clinical experience. We will need to hire additional personnel as we continue to expand our research and development and partnering activities.

We face intense competition from other companies and research and academic institutions for qualified personnel. We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco, California area. In September 2008, four members of our Board of Directors resigned and were replaced by four new members. At the same time of this change in our Board, our CEO and CFO resigned their positions and were replaced with Robert W. Duggan as CEO, Glenn C. Rice as President and COO and Rainer (Ramses) Erdtmann as Vice President of Finance and Administration. We are highly dependent on these officers, and in fact Mr. Duggan has provided significant financing to the Company. If Mr. Duggan were to terminate his position with the Company, or we were to lose an additional executive officer, any of our senior scientists, a manager of one of our programs, or a significant number of any of our staff or are unable to hire and retain qualified personnel, then our ability to develop and commercialize our products and processes, raise additional capital or implement our business strategy may be adversely affected or prevented and our business may be harmed as a result.

***Our business is subject to risks associated with international operations and collaborations.***

The laws of foreign countries do not protect our intellectual property rights to the same extent as do the laws of the United States. In countries where we do not have and/or have not applied for patents on our products, we will be unable to prevent others from developing or selling similar products. In addition, in jurisdictions outside the United States where we acquire

patent rights, we may be unable to prevent unlicensed parties from selling or importing products or technologies derived elsewhere using our patented technology.

Until we or our licensees obtain the required regulatory approvals for pharmaceuticals in any specific foreign country, we or our licensees will be unable to sell these products in that country. International regulatory authorities have imposed numerous and varying regulatory requirements and the approval procedures can involve additional testing. Approval by one regulatory authority does not ensure approval by any other regulatory authority.

***We may be subject to damages resulting from claims that our employees or we have wrongfully used or disclosed alleged trade secrets of their former employers.***

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or prevent our ability to commercialize certain potential drugs, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

***We may need to implement additional finance and accounting systems, procedures and controls to satisfy reporting requirements.***

As a public reporting company, we are required to comply with the Sarbanes-Oxley Act of 2002, including Section 404, and the related rules and regulations of the Securities and Exchange Commission, including expanded disclosures and accelerated reporting requirements and more complex accounting rules. Compliance with Section 404 and other requirements will increase our costs and require additional management resources. We may need to continue to implement additional finance and accounting systems, procedures and controls to satisfy reporting requirements. While we have been able to complete an unqualified assessment as to the adequacy of our internal control over financial reporting for our fiscal year ending June 30, 2008, there is no assurance that future assessments of the adequacy of our internal control over financial reporting will be unqualified. If we are unable to obtain future unqualified reports as to the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our internal control over financial reporting, which could adversely affect our stock price.

***Our corporate compliance program cannot guarantee that we are in compliance with all potentially applicable regulations.***

The development, manufacturing, pricing, sales, coverage and reimbursement of our products, together with our general operations, are subject to extensive regulation by federal, state and other authorities within the United States and numerous entities outside of the United States. While we have developed and instituted a corporate compliance program based on what we believe are the current best practices, we cannot provide any assurance that governmental authorities will find that our business practices comply with current or future administrative or judicial interpretations of potentially applicable laws and regulations. If we fail to comply with any of these laws and regulations, we could be subject to a range of regulatory actions, including suspension or termination of clinical trials, the failure to approve a product candidate,

restrictions on our products or manufacturing processes, withdrawal of products from the market, significant fines, or other sanctions or litigation.

***Our facility in California is located near an earthquake fault, and an earthquake or other types of natural disasters or resource shortages could disrupt our operations and adversely affect results.***

Important documents and records, such as hard copies of our laboratory books and records for our drug candidates and compounds, are located in our corporate headquarters at a single location in Sunnyvale, California, which is near active earthquake zones. We do not have a formal business continuity or disaster recovery plan, and could therefore experience a significant business interruption in the event of a natural disaster, such as an earthquake, drought or flood, or localized extended outages of critical utilities or transportation systems. In addition, California from time to time has experienced shortages of water, electric power and natural gas. Future shortages and conservation measures could disrupt our operations and cause expense, thus adversely affecting our business and financial results.

***Anti-takeover provisions in our charter documents and Delaware law could prevent or delay a change in control.***

Our certificate of incorporation and bylaws may discourage, delay or prevent a merger or acquisition that a stockholder may consider favorable. In addition, provisions of the Delaware General Corporation Law also restrict certain business combinations with interested stockholders. These provisions are intended to encourage potential acquirers to negotiate with us and allow our board of directors the opportunity to consider alternative proposals in the interest of maximizing stockholder value. However, these prohibitions may also discourage acquisition proposals or delay or prevent a change in control, which could harm our stock price.

## **Risks Related to Our Industry**

***We face rapid technological change and intense competition.***

The pharmaceutical industry is subject to rapid and substantial technological change. Therapies designed by other companies to treat the conditions that are the focus of our products are currently in clinical trials. Developments by others may render our products under development or technologies noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Many of these entities have significantly greater research and development capabilities than we do, as well as substantially more marketing, sales, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors' financial, marketing, manufacturing and other resources. In addition, we may experience competition from companies that have acquired or may acquire technology from universities and other research institutions. As these companies develop their technologies, they may develop proprietary positions that compete with our products. We are engaged in the development of novel therapeutic technologies. Our resources are limited and we may experience technical challenges inherent in such novel technologies.

Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have

an entirely different approach or means of accomplishing similar therapeutic effects than our products. Our competitors may develop products that are safer, more effective or less costly than our products and, therefore, present a serious competitive threat to our product offerings. Our competitors may price their products below ours, may receive better coverage and/or reimbursement or may have products that are more cost effective than ours.

The widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our products even if commercialized. The diseases for which we are developing our therapeutic products can also be treated, in the case of cancer, by surgery, radiation, biologics and chemotherapy. These treatments are widely accepted in the medical community and have a long history of use. The established use of these competitive products may limit the potential for our products to receive widespread acceptance if commercialized.

***The price of our common stock may be volatile.***

The market prices for securities of biotechnology companies, including ours, have historically been highly volatile. Our stock, like that of many other companies, has from time to time experienced significant price and volume fluctuations sometimes unrelated to operating performance. For example, during the period beginning July 1, 2005 and ending July 15, 2009, the sales price for one share of our common stock reached a high of \$9.64 per share and a low of \$0.55 per share. The market price of our common stock may fluctuate significantly due to a variety of factors, including:

- the progress and results of our preclinical testing, clinical trials, product development and partnering activities;
- quarterly fluctuations in our financial results;
- the development of technological innovations or new therapeutic products by us, our competitors or others;
- changes in governmental regulation;
- developments in patent or other proprietary rights by us, our competitors or others;
- developments and/or announcements by us, our competitors or others;
- litigation;
- public concern as to the safety of products developed by us, our competitors or others;
- departure of key personnel;
- ability to manufacture our products to commercial standards;
- changes in the structure of healthcare payment systems and the coverage and reimbursement policies of governmental and other third-party payors;
- our ability to successfully commercialize our products if they are approved;
- comments by securities analysts; and

- general market conditions in our industry.

In addition, if any of the risks described in this section entitled “Risk Factors” actually occur, there could be a dramatic and material adverse impact on the market price of our common stock.

***If our products are not accepted by the market or if users of our products are unable to obtain adequate coverage of and reimbursement for our products from government and other third-party payors, our revenues and profitability will suffer.***

Our ability to commercialize our products successfully will depend in significant part on the extent to which appropriate coverage of and reimbursement for our products and related treatments are obtained from governmental authorities, private health insurers and other organizations, such as HMOs. Third-party payors are increasingly challenging the prices charged for medical products and services. We cannot provide any assurances that third-party payors will consider our products cost-effective or provide coverage of and reimbursement for our products, in whole or in part.

Uncertainty exists as to the coverage and reimbursement status of newly approved medical products and services and newly approved indications for existing products. Third-party payors may conclude that our products are less safe, less clinically effective, or less cost-effective than existing products, and third-party payors may not approve our products for coverage and reimbursement. If we are unable to obtain adequate coverage of and reimbursement for our products from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them. Such reduction or limitation in use of our products could cause our sales to suffer. Even if third-party payors make reimbursement available, payment levels may not be sufficient to make the sale of our products profitable.

Also, the trend towards managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of medical services and products, may result in inadequate coverage of and reimbursement for our products. Many third-party payors, including in particular HMOs, are pursuing various ways to reduce pharmaceutical costs, including, for instance, the use of formularies. The market for our products depends on access to such formularies, which are lists of medications for which third-party payors provide reimbursement. These formularies are increasingly restricted, and pharmaceutical companies face significant competition in their efforts to place their products on formularies of HMOs and other third-party payors. This increased competition has led to a downward pricing pressure in the industry. The cost containment measures that third-party payors are instituting could have a material adverse effect on our ability to operate profitably.

***Current health care laws and regulations and future legislative or regulatory changes to the healthcare system may affect our ability to sell our products profitably.***

In the United States, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners, and the availability of capital. Federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system and, in particular, that are intended to contain or reduce the costs of medical products and services. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or

MMA, could significantly influence the manner in which pharmaceutical products are prescribed and purchased and will impact reimbursement for our products, which could result in a reduction in demand for our products. The MMA established a new reimbursement methodology for certain drugs furnished in hospital outpatient departments and physicians' offices which is based on the average sales price, or ASP, of the product. Application of the ASP reimbursement methodology has resulted in a decrease in the reimbursement levels for certain oncology drugs furnished in hospital outpatient departments and physicians' offices. As implemented in a recent rule establishing an MMA- mandated competitive bidding program, or CAP, physicians who administer drugs in their offices are offered an option to acquire injectable and infused drugs currently covered under the Medicare Part B benefit from vendors who are selected in a competitive bidding process. Winning vendors are selected based on criteria that include their bid price. These new reimbursement measures, effective beginning July 1, 2006, could negatively impact our ability to sell our products. The MMA also established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries are able to obtain prescription drug coverage from private sector providers. These private sector providers are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. We cannot predict whether our products will be placed on the formularies of the private sector providers participating in the Part D program in the future, and if our products are not placed on such formularies, this could negatively impact our ability to sell our products. It remains difficult to predict the full impact that the prescription drug program, and the MMA generally, will have on us and our industry. The expanded access to prescription medications afforded by Medicare coverage of prescription drugs may increase the volume of pharmaceutical sales. However, this potential sales volume increase may be offset by increased downward pricing pressures resulting from the enhanced purchasing power of private sector providers who will negotiate drug pricing on behalf of Medicare beneficiaries under Part D.

There also have been and likely will continue to be legislative and regulatory proposals at the state and federal levels that could bring about significant changes to the Medicaid drug rebate program and other federal pharmaceutical pricing programs in which we plan to participate for our products. Given these and other recent federal and state government initiatives directed at lowering the total cost of health care, federal and state lawmakers will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid programs. We cannot predict the impact on our business of any legislation or regulations that may be adopted in the future. Any cost containment measures and other healthcare system reforms that are adopted could have a material adverse effect on our ability to operate profitably.

***We may need to change our business practices to comply with health care fraud and abuse regulations, and our failure to comply with such laws could adversely affect our business, financial condition and results of operations.***

Our operations will be directly, or indirectly through our customers, subject to various state and federal fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing or arranging for a good or service, for which payment may be made under a federal healthcare program such as the Medicare and Medicaid programs. Several courts have interpreted the statute's intent requirement to mean

that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The Anti-Kickback Statute is broad and prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Recognizing that the Anti-Kickback Statute is broad and may technically prohibit many innocuous or beneficial arrangements, Congress authorized the Department of Health and Human Services, Office of Inspector General (“OIG”) to issue a series of regulations, known as the “safe harbors.” These safe harbors set forth provisions that, if all their applicable requirements are met, will assure healthcare providers and other parties that they will not be prosecuted under the Anti-Kickback Statute. The failure of a transaction or arrangement to fit precisely within one or more safe harbors does not necessarily mean that it is illegal or that prosecution will be pursued. However, conduct and business arrangements that do not fully satisfy each applicable safe harbor may result in increased scrutiny by government enforcement authorities such as the OIG. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other federal healthcare programs. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal False Claims Act prohibits persons from knowingly filing or causing to be filed a false claim to, or the knowing use of false statements to obtain payment from, the federal government. Suits filed under the False Claims Act, known as “qui tam” actions, can be brought by any individual on behalf of the government and such individuals, sometimes known as “relators” or, more commonly, as “whistleblowers,” may share in any amounts paid by the entity to the government in fines or settlement. The frequency of filing of qui tam actions has increased significantly in recent years, causing greater numbers of healthcare companies to have to defend a False Claim action. When an entity is determined to have violated the federal False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties of between \$5,500 to \$11,000 for each separate false claim. Various states have also enacted laws modeled after the federal False Claims Act.

In addition to the laws described above, the Health Insurance Portability and Accountability Act of 1996 created two new federal crimes: healthcare fraud and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private payors. A violation of this statute is a felony and may result in fines, imprisonment or exclusion from government sponsored programs. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. A violation of this statute is a felony and may result in fines or imprisonment.

If our operations are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare programs, and the curtailment or restructuring of our operations.

***Our business exposes us to product liability claims.***

The testing, manufacture, marketing and sale of our products involve an inherent risk that product liability claims will be asserted against us. We face the risk that the use of our products in human clinical trials will result in adverse effects. If we complete clinical testing for

our products and receive regulatory approval to market our products, we will mark our products with warnings that identify the known potential adverse effects and the patients who should not receive our product. We cannot ensure that physicians and patients will comply with these warnings. In addition, unexpected adverse effects may occur even with use of our products that receive approval for commercial sale. Although we are insured against such risks in connection with clinical trials, our present product liability insurance may be inadequate. A successful product liability claim in excess of our insurance coverage could have a material adverse effect on our business, financial condition and results of operations. Any successful product liability claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our pharmaceutical products. A product liability claim or recall would have a material adverse effect on our reputation, business, financial condition and results of operations.

***Our business involves environmental risks.***

In connection with our research and development activities and our manufacture of materials and products, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with the applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the controlled use of hazardous materials, including but not limited to certain hazardous chemicals and radioactive materials. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of contamination or injury from these materials. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

**Risks Related to the Rights Offering**

***The Subscription Price Determined for this Offering Is Not an Indication of Our Value.***

In determining the subscription price for this rights offering, a pricing committee of our board of directors has been established. In setting the subscription price, the pricing committee reviewed and considered a number of factors, including the amount of proceeds desired, our need for liquidity and equity capital, alternatives available to us for raising equity capital, the historic market price, moving averages and volume weighted moving averages of our common stock, the pricing of similar transactions, the liquidity and the historic volatility of the market price of our common stock, the historic trading volume of our common stock, our business prospects, our recent and anticipated operating results, the price at which our stockholders might be willing to participate in the rights offering, the desire to provide an opportunity to our stockholders to participate in the rights offering on a pro rata basis and general conditions in the securities market. The subscription price is not necessarily related to the book value of our assets, net worth, past operations, cash flows, losses, financial condition, or any other established criteria for valuing Pharmacyclics and may or may not be considered the fair value of our common stock to be offered in the rights offering. As of July 15, 2009, the day immediately prior to the

filing of this prospectus, the closing price of our common stock was \$1.26. You should not consider the subscription price as an indication of the value of Pharmacyclics or our common stock.

***The Market Price of Our Common Stock May Decline.***

We cannot assure you that the market price of our common stock will not either increase or decline before the subscription rights expire. If you exercise your subscription rights and the market price of the common stock falls below the subscription price, then you will have committed to buy shares of common stock in the rights offering at a price that is higher than the market price. Moreover, we cannot assure you that you will ever be able to sell shares of common stock that you purchased in the rights offering at a price equal to or greater than the subscription price. Until certificates are delivered upon expiration of the rights offering, you may not be able to sell the shares of our common stock that you purchase in the rights offering. Certificates representing shares of our common stock that you purchased will be delivered as soon as practicable after expiration of the rights offering. We will not pay you interest on funds delivered to the subscription agent pursuant to the exercise of rights.

***If You Do Not Exercise Your Subscription Rights in Full, Your Percentage Ownership and Voting Rights in Pharmacyclics Will Likely Experience Dilution.***

If you choose not to exercise your subscription rights you will retain your current number of shares of common stock of Pharmacyclics. However, if you choose not to exercise your subscription rights, your percentage ownership and voting rights in Pharmacyclics will experience dilution if and to the extent that other stockholders exercise their subscription rights. In that event, the percentage ownership, voting rights and other rights of all stockholders who do not fully exercise their subscription rights will be diluted. In addition, if Pharmacyclics issues the Additional Shares your percentage ownership, voting rights and other stockholder rights will also be diluted even if you exercise your basic subscription rights, unless you also exercise your oversubscription rights.

***You May Not Revoke Your Subscription Exercise and Could Be Committed to Buying Shares Above the Prevailing Market Price.***

Once you exercise your subscription rights, you may not revoke the exercise. The public trading market price of our common stock may decline before the subscription rights expire. If you exercise your subscription rights and, afterwards, the public trading market price of our common stock falls below the subscription price, you will have committed to buying shares of common stock at a price above the market price. Moreover, you may be unable to sell your shares of our common stock at a price equal to or greater than the price you paid for such shares.

***Because We May Terminate the Offering at Any Time Prior to the Expiration Date, Your Participation in the Rights Offering Is Not Assured.***

We do not intend, but have the right, to terminate the offering at any time prior to the expiration date. If we determine to terminate the offering, we will not have any obligation with respect to the subscription rights except to return any money received from subscribing stockholders as soon as practicable, without interest or deduction.

***You Will Need to Act Promptly and to Carefully Follow the Subscription Instructions, or Your Exercise of Rights May Be Rejected.***

Stockholders who desire to purchase shares in the rights offering must act promptly to ensure that all required forms and payments are actually received by the subscription agent prior to 5:00 pm on July 31, 2009, the expiration date. If you are a beneficial owner of shares, you must act promptly to ensure that your broker, custodian bank or other nominee acts for you and that all required forms and payments are actually received by the subscription agent prior to the expiration date. We shall not be responsible if your broker, custodian or nominee fails to ensure that all required forms and payments are actually received by the subscription agent prior to the expiration date. If you fail to complete and sign the required subscription forms, send an incorrect payment amount, or otherwise fail to follow the subscription procedures that apply to your desired transaction the subscription agent may, depending on the circumstances, reject your subscription or accept it to the extent of the payment received. Neither we nor our subscription agent will undertake to contact you concerning, or attempt to correct, an incomplete or incorrect subscription form or payment. We have the sole discretion to determine whether a subscription exercise properly follows the subscription procedures.

***The Rights Offering Could Impair or Limit the Company's Net Operating Loss Carryforwards and Tax Credit Carryforwards.***

At June 30, 2008, we had net operating loss carryforwards of approximately \$322.4 million for federal income tax reporting purposes and tax credit carryforwards of approximately \$11.0 million for federal reporting purposes. These amounts expire at various times through 2028. Under the Tax Reform Act of 1986, the amounts of and the benefit from net operating losses and tax credit carryforwards that can be carried forward may be impaired or limited in certain circumstances. These circumstances include, but are not limited to, a cumulative stock ownership change of greater than 50%, as defined, over a three year period. Depending on participation in the rights offering, such participation could result in such a stock ownership change.

## COMPANY OVERVIEW

We are a clinical-stage biopharmaceutical company focused on developing and commercializing innovative small-molecule drugs for the treatment of immune mediated disease and cancer. Our purpose is to create a profitable company by generating income from products we develop, license and commercialize, either with one or several potential collaborators/partners or alone as may best forward the economic interest of our stakeholders. We endeavor to create novel, patentable, differentiated products that have the potential to significantly improve the standard of care in the markets we serve.

Presently, we have four product candidates in clinical development and two product candidates in pre-clinical development. It is our business strategy to establish collaborations with large pharmaceutical and biotechnology companies for the purpose of generating present and future income in exchange for adding to their product pipelines. In addition, we strive to generate collaborations that allow us to retain valuable territorial rights and simultaneously fast forward the clinical development and commercialization of our products.

It is our intention to identify product candidates based on exceptional scientific and development expertise, develop them in a rapid, cost-effective manner, and then seek development and/or commercialization partners. We are committed to high standards of ethics, scientific rigor, and operational efficiency as we move each of these programs to viable commercialization.

To date, substantially all of our resources have been dedicated to the research and development of our products, and we have not generated any commercial revenues from the sale of our products. We do not anticipate the generation of any product commercial revenues until we receive the necessary regulatory and marketing approvals to launch one of our products.

We have incurred significant operating losses since our inception in 1991, and as of March 31, 2009 have an accumulated deficit of approximately \$357.5 million. The process of developing and commercializing our products requires significant research and development, preclinical testing and clinical trials, manufacturing arrangements as well as regulatory and marketing approvals. These activities, together with our general and administrative expenses, are expected to result in significant operating losses until the commercialization of our products, or partner collaborations, generate sufficient revenues to cover our expenses. We expect that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial. Our achieving profitability depends upon our ability, to successfully complete the development of our products, obtain required regulatory approvals and successfully manufacture and market our products.

### ***Our Pipeline***

Our pharmaceutical drug development candidates are synthetic small-molecules designed to target key biochemical pathways involved in human diseases with critical unmet needs. We currently have four proprietary drug candidates under clinical development and one drug candidate under preclinical development, and a lead compound undergoing preclinical optimization. This includes a histone deacetylase inhibitor (PCI-24781) about to enter a Phase II clinical trial; an inhibitor of Factor VIIa (PCI-27483) soon to be in a Phase II clinical trial; an inhibitor of Bruton's tyrosine kinase (Btk) (PCI-32765) currently in a Phase I clinical trial targeting oncology applications; a series of Btk inhibitors in advanced preclinical lead optimization and testing targeting autoimmune and allergic indications; and HDAC8 inhibitors

(i.e. PCI-34051 and others) that are currently being optimized for autoimmune and cancer indications. Motexafin gadolinium (MGd) is now in a Phase II trial being conducted by the National Cancer Institute (NCI) in patients with primary brain tumors.

### **Status of Products Under Development**

The table below summarizes our product candidates and their stage of development:

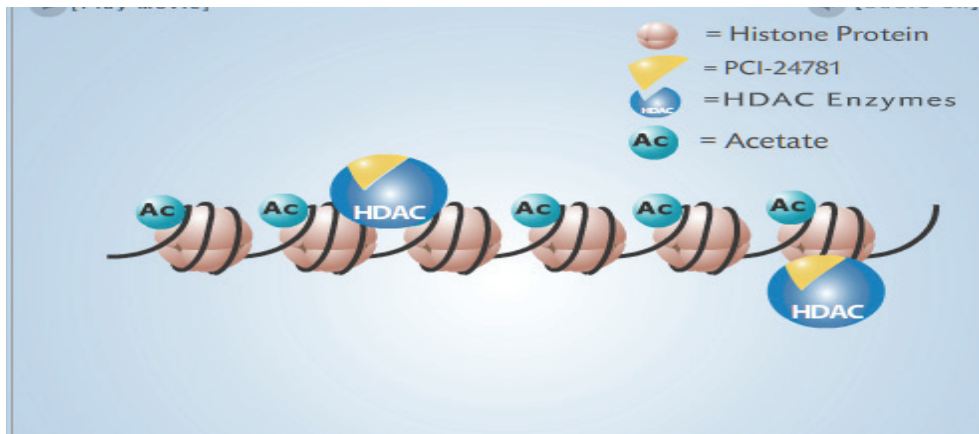
<b>Product Candidate[s]</b>	<b>Disease Indication</b>	<b>Development Status<sup>(1)</sup></b>
PCI-24781 HDAC Inhibitor	Advanced solid tumors Recurrent lymphomas Sarcoma	Phase I – enrolling Phase I/II – enrolling Phase I/II – planned second half 2009
PCI-27483 Factor VIIa Inhibitor	Cancer therapy	Phase I – complete Phase II – planned second half 2009
PCI-32765 B Cell Tyrosine Kinase Inhibitor	B-Cell Lymphomas	Phase I - enrolling
Lead Optimization Series B Cell Tyrosine Kinase Inhibitors	Autoimmune disease and Mast cell disease	Preclinical
Lead Optimization Series HDAC8 Inhibitors	Autoimmune and cancer	Preclinical
MGd	Primary brain tumor <sup>2</sup> Childhood brain tumors <sup>2</sup>	Phase II – enrolling Phase II – complete

1. “Phase I” means initial human clinical trials designed to establish the safety, dose tolerance, pharmacokinetics (i.e. absorption, metabolism, excretion), and pharmacodynamics (i.e. surrogate markers for efficacy) of a compound. “Phase II” means human clinical trials designed to establish safety, optimal dosage and preliminary activity of a compound in a patient population. “Preclinical” means the stage of drug development prior to human clinical trials in which a molecule is optimized for “drug like” properties and evaluated in laboratory animals for efficacy, pharmacokinetics, pharmacodynamics and safety.
2. Studies sponsored by the National Cancer Institute.

### **Histone Deacetylase Inhibitor Program**

The human genome consists of a complex collection of genes which are turned on or off depending on the needs of the cell. Cancer is characterized by genome-wide changes in gene expression within the tumor. Turning off the expression of certain genes favors a tumor’s ability to multiply, to avoid apoptosis (i.e. programmed cell death) or to become resistant to chemotherapy. One of the ways in which genes are turned on or off is by means of chemical modification of histone proteins. Histone proteins are structural components of chromosomes, and form a scaffold upon which DNA, the genetic material, is arranged, see image below. Histone acetylation (i.e. the addition of an acetate group to histones) alters the expression of genes involved in cell cycle control, cell division, and apoptosis. Histone deacetylation reverses histone acetylation by removing the acetyl groups. The process of histone deacetylation is controlled by a family of enzymes known as histone deacetylases (or “HDACs”). HDAC inhibitors prevent deacetylation, leading to an increase in histone acetylation and an increased expression of certain genes. This effect limits the tumor’s ability to multiply, to avoid apoptosis or to become resistant to chemotherapy. HDAC inhibitors block cancer cell proliferation in vitro

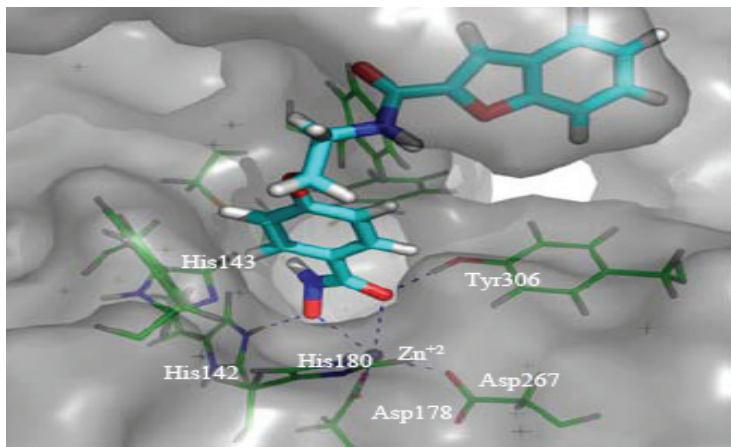
(i.e. in cultured cells) and cancer cell growth arrest is observed in vivo (i.e. in animals) at non-toxic concentrations.



### **PCI-24781 (Pan HDAC Inhibitor)**

PCI-24781 is a novel, potent, small-molecule inhibitor of HDAC enzymes with anti-tumor activity in vitro and in vivo (Buggy et al Mol Cancer Ther 2006; 5 (5), p. 1309-1317). PCI-24781 treatment leads to synergistic efficacy in tumor cells in combination with DNA-damaging agents such as radiation and chemotherapy agents. The mechanism of the synergy may involve inhibition of DNA repair. PCI-24781 has activity against primary human tumors from patients with colon, ovarian, lung and many hematological (i.e. blood related) cancers.

We believe PCI-24781 has a half-life and potency superior to competitor drugs (e.g. Zolinza or LBH-589) that will allow us to achieve an ideal balance of efficacy with minimal toxicity.



Co-crystal of PCI-24781 chemical scaffold with HDAC showing optimized interactions with active site residues

### **Clinical Development -Oncology**

Clinical development began with intravenous administration of PCI-24781 in an initial Phase I study, and has progressed to two clinical studies by the oral route in 2008, both of which are currently enrolling. The first study employing an oral capsule formulation (PCYC-0402) is a Phase I, ascending dose study in patients with solid tumors. This study is open and actively enrolling at four clinical centers: MD Anderson Cancer Center, Marin Oncology, The University of Chicago, and Sarah Cannon Cancer Center ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)). Single agent

stable disease has been achieved in a number of solid tumor histologies including colon, tongue and ovarian carcinoma.

The second study by the oral route (PCYC-0403) is a Phase I/II trial in patients with lymphoma. The improved potency and pharmacokinetic aspects of PCI-24781 served as a basis for the ongoing proof of concept studies in Phase I/II in lymphoma. This trial is now open and actively enrolling at four centers: University of California, San Francisco, University of Nebraska, Northwestern University, and Washington University (St. Louis). Clinical responses have been recorded in this single agent clinical trial, with one partial response and six stable diseases to date in ten evaluated patients. Thrombocytopenia (reduced platelet count) is a reversible effect that has been observed with a number of HDAC inhibitors and is thought to be related to the pharmacologic mechanism of action. In the case of PCI -24781 we had thrombocytopenia, which is being successfully managed through dose scheduling changes. No other drug related serious adverse events have been observed to date.

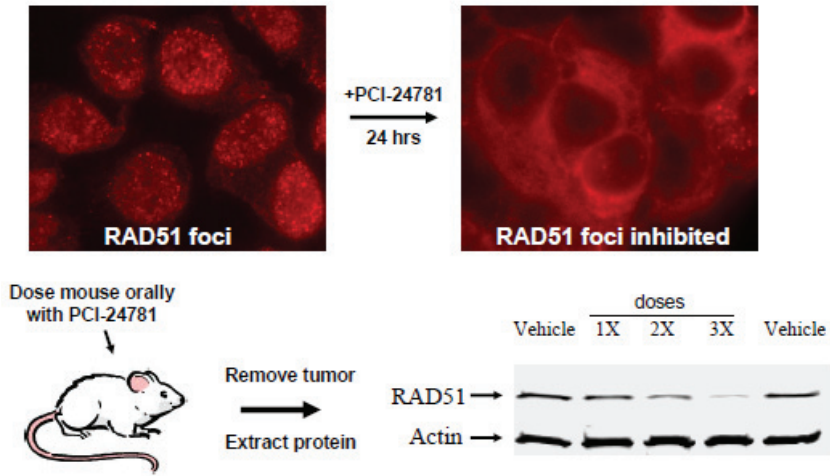
A third clinical study, a Phase I/II, will test PCI-24781 in combination with doxorubicin in patients with soft tissue sarcoma. This trial will be co-sponsored by prominent investigators at Massachusetts General Hospital and Dana-Farber/Harvard Cancer Center, including Drs. George Demetri and Edwin Choy, and is planned to begin in second half of calendar 2009.

### ***Proprietary Predictive Assays***

Following chemotherapy or radiation treatment, some patients' tumors may turn on certain genes as a strategy by the tumor to adapt to the therapy and become resistant to cell death. One example of a genetic change that occurs in many cancers is the activation of the DNA repair gene RAD51. In response to treatment with DNA-damaging chemotherapy or radiation, tumors will often turn on DNA repair genes, such as RAD51, as an adaptive strategy to help the tumor repair the DNA damage done by these agents. In pre-clinical models, PCI-24781 was able to turn off RAD51 (and other DNA repair genes), effectively blocking the ability of the tumor to repair its damaged DNA, sensitizing the tumor to chemotherapy and radiation. PCYC has patented the predictive use of the biomarker RAD51 which was found by Pharmacyclics' scientists to potentially underlie resistance to therapy and may be used as a predictive measure of HDAC inhibitor activity that could be useful in the clinic. This research was published in the Proceedings of the National Academy of Sciences (Proc Natl Acad Sci U S A. 2007;104:19482-7. Epub 2007 Nov 27).

Thus PCI-24781 is effective at inhibiting repair of damaged DNA by downregulating RAD51, which is particularly essential for repair of double-strand breaks (DSB). It was demonstrated by Pharmacyclics that PCI-24781 effectively prevents DSB repair via one of the two major repair pathways, called the homologous recombination pathway, by modulation of RAD51. This allows PCI-24781 to synergize effectively with other agents that damage DNA, such as radiation (Banuelos et al., Clin Cancer Res., v. 13, p. 6816-6826, 2007) and chemotherapeutics i.e. doxorubicin (Adimoolam et al., Proc.Natl.Acad.Sci.U.S.A, v. 104, p. 19482-19487, 2007). We showed recently that RAD51 is over expressed in a majority of human lymphoma samples and that pretreatment with PCI-24781 down regulates RAD51 and potentiates cell killing by subsequent addition of doxorubicin (Balasubramanian et al., Blood (ASH 2007 Abstracts), v. 110, p. 1377.2007). One of our collaborators, Dr. Dina Lev at MD Anderson Cancer Center, has shown that PCI-24781 can also synergize with doxorubicin in sarcoma, both in cells and in animal models (Lopez et al., Clin Cancer Res., In Press. 2009). Accordingly, as mentioned above we plan to begin a Phase I/II trial of PCI-24781 in combination with doxorubicin for treating sarcoma with Dr. Edwin Choy at Massachusetts General Hospital and Dr. George Demetri at Dana-Farber Cancer Institute. These investigators are part of one of

the leading consortiums in sarcoma in the world today. It is anticipated that clinical activity in this trial would pave the way to other indications for PCI-24781 in combination with doxorubicin, which is also used extensively in treatment of other cancers, including lymphoma, breast, lung, ovarian and liver cancer.

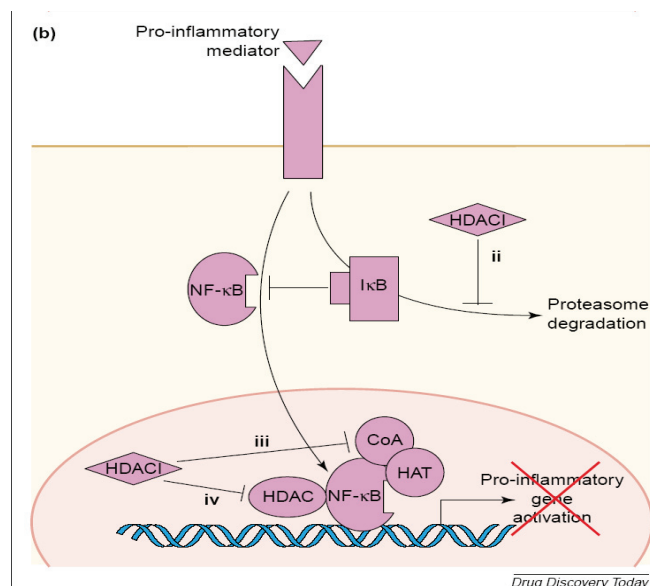


Rad51 is a DNA repair gene that Pharmacocyclics scientists have discovered that predicts sensitivity to PCI-24781. Top: PCI-24781 disrupts nuclear repair foci in colon cancer cells. Bottom: PCI-24781 downregulates RAD51 in tumors grown in mice.

## Market

Pan-HDAC inhibitors have the potential for broad anti-cancer indications in hematologic and solid malignancies when used in combination with numerous chemotherapeutic drugs and radiation.

Specific HDAC enzymes have been implicated in many other physiological processes and there is growing interest in using HDAC inhibitors in many disease areas including metabolic, neurological and immunological disorders as well as for treating bacterial and parasitic infections. For instance, in central nervous system (CNS) indications, HDAC inhibitors have shown activity in models of epilepsy and migraine headaches, dementia, Alzheimer's, Parkinson's and Huntington's disease (recently reviewed in Kazantsev & Thompson, *Nat Rev Drug Discov.* 2008 7(10):854-68; Steffan JS et al. *Nature.* 2001 Oct 18;413(6857):739-43). HDAC inhibitors have shown substantial activity in inflammatory models including rheumatoid arthritis, juvenile RA, multiple sclerosis, psoriasis, lupus, sepsis, diabetes and hemorrhagic shock (reviewed in Chipoy C. *Drug Discovery Today.* 2005 1;10(3):197-20; Gray SG, Dangond F. *Epigenetics.* 2006 Apr-Jun;1(2):67-75. Epub 2006 Mar 5; Susick L et al.; *J Cell Mol Med.* 2009 epub Jan 28). Finally, HDAC inhibitors have shown substantial activity in antiviral, antibacterial and antiparasitic applications (Elaut G, et al. *Curr Pharm Des.* 2007;13(25):2584-620).



The anti-inflammatory effects of HDAC inhibitors can act in multiple ways. One way as shown here is through the inhibition of a major regulator of pro-inflammatory gene expression.

Pharmacyclics is actively involved in exploring many of these non-oncology indications internally as well as with outstanding academic collaborators. Our internal programs include applications for RA, juvenile RA and dermatitis. Currently, Pharmacyclics is reviewing potential clinical options in these areas.

## Patents

Key patent protection in US and international territories will extend beyond 2024 with the possibility of patent term extensions during development.

## Competition

Merck's vorinostat (Zolinza®) has been approved by the FDA for cutaneous T-cell lymphoma patients who have progressive, persistent or recurrent disease on or following failure

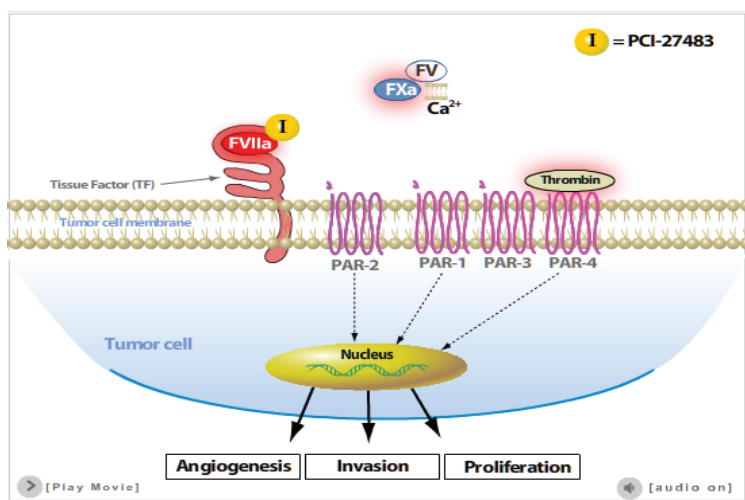
of two systemic therapies, making the oral drug the first in its class to reach the market. A number of structurally distinct HDAC inhibitors are currently in clinical trials including Novartis' LBH-589, the natural product depsipeptide (FK-228) from Gloucester, and the benzamide, SYND 275. HDAC inhibitors have exhibited clinical activity against a variety of human malignancies in initial clinical trials. For example, clinical improvements have been observed in patients with renal cell carcinoma, head and neck squamous carcinoma, mesothelioma, small-cell lung cancer, melanoma, papillary thyroid carcinoma and B- and T-cell lymphomas. Thrombocytopenia (a reduction in platelets, which are cells responsible for clotting blood) was identified as a dose-limiting toxicity for patients administered a number of these agents. Several of the competitors have reported cardiac toxicities such as Grade 3 QTc prolongation, arrhythmias and atrial fibrillation, in addition to fatigue, anorexia, infection, headache and nausea. Preliminary data suggests that PCI-24781 has not shown significant side effects, (other than reversible dose limiting thrombocytopenia) in clinical studies suggesting that PCI-24781 may offer a less toxic modality for the treatment of cancer than its competitors.

### ***Partnering***

On April 16, 2009, the company entered into a collaboration agreement with Servier pursuant to which Pharmacyclics granted to Servier an exclusive license for its Pan-HDAC inhibitors, including PCI-24781, for territories throughout the world excluding the United States. Under the terms of the agreement, Servier acquired the exclusive right to develop and commercialize the Pan-HDAC inhibitor product worldwide except for the United States and will pay a royalty to Pharmacyclics on sales outside of the United States. Pharmacyclics will continue to own all rights within the United States.

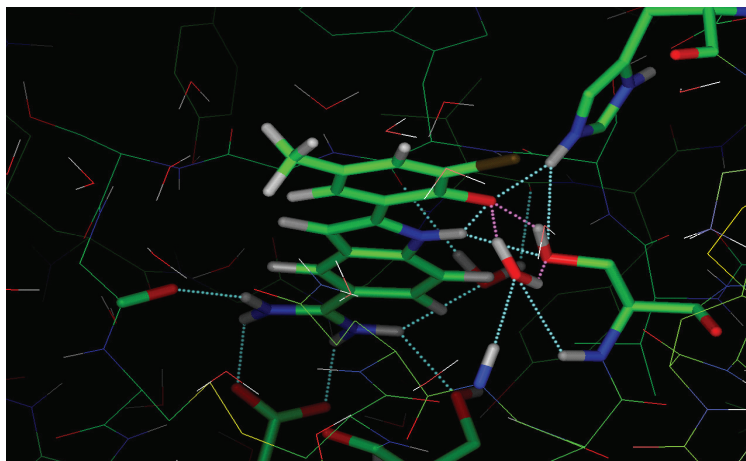
## Factor VIIa Inhibitor Program

Factor VII is an enzyme that becomes activated (fVIIa) by binding to tissue factor (TF, a cell membrane protein). The fVIIa/TF complex triggers the extrinsic coagulation cascade that leads to the formation of a blood clot. Tissue factor is expressed in many cells such as fibroblasts and keratinocytes (i.e. skin cells), but is absent from vascular cells that come in contact with circulating fVII in the blood. Preclinical models of thrombosis (blood clots) in several species have indicated that a selective inhibitor of the Factor VIIa/Tissue Factor (fVIIa/TF) complex may have a greater therapeutic/safety index than inhibition of other coagulation factors. In many cancers, such as those arising from the pancreas, lung, stomach or colon, over expression of tissue factor is associated with an increased incidence in blood clots. Tissue factor over expression also correlates with a worsened prognosis for a number of human cancers (e.g. colorectal, pancreatic, glioblastoma, renal, etc.). Inhibitors of fVIIa/TF complexes have been shown to inhibit the growth of primary and metastatic tumors in mice.



### PCI-27483

PCI-27483 is a highly optimized and first of its kind, small molecule inhibitor of Factor VIIa developed by Pharmacyclics' scientists. This drug selectively inhibits the active form of Factor VII (called Factor VIIa). PCI-27483 is an extremely potent inhibitor of coagulation Factor VII but does not inhibit other coagulation factors, such as Factor XIa, Factor IXa, Factor IIa (Thrombin) and Factor Xa.

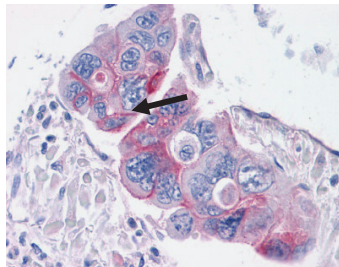


PCI-24783 was developed using rational drug design (Katz, B. A.; *et al. J. Mol. Biol.* **2001**, *307*, 1451-1486) against the target molecule Factor VIIa

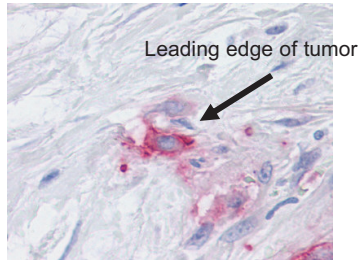
The antithrombotic effects of subcutaneously injected PCI-27483 were determined in a baboon model of arterial thrombosis. Increasing subcutaneous doses of PCI 27483 progressively has an antithrombotic effect similar to that of the low molecular weight heparin (i.e. anti coagulant) product, Lovenox.

In cancer, the Factor VIIa:TF complex triggers a host of physiologic processes that facilitate tumor angiogenesis, growth and invasion. Laboratory studies and animal models indicate that PCI-27483 blocks tumor growth, angiogenesis and metastases.

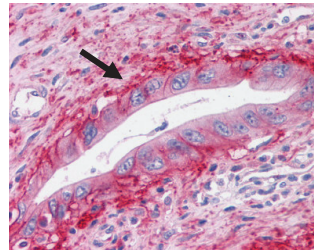
### **Clinical Program**



Malignant Cells 40X



Malignant Cell at Pushing Margin of Invasion 60X



Malignant Cells and Surrounding Fibrocollagenous Matrix 40X

FVIIa was detected in 12/13 pancreatic carcinomas by staining techniques. Staining was detected in malignant cells while all normal cells were negative. Staining often detected at the leading edge of tumor invasion.

Pancreatic cancer is one of the significant causes of death from cancer in the US and Europe. Despite the improvements in the diagnosis and treatment of cancer, patients with locally advanced and/or metastatic pancreatic cancer have a median survival time of approximately 5 to 6 months. Gemcitabine is the most active drug in the treatment of advanced pancreatic cancer; however, the response rates of single agent gemcitabine are between 5% and 11% with a median survival time varying between 5.7 and 6.5 months. Cisplatin, a chemotherapy agent, with gemcitabine has been reported to yield response rates of 10–20% and 4–9 months of median survival times. Clearly, more effective therapy is needed.

TF expression has been observed in 89% of pancreatic cancers, but not within the typical pancreas. Pancreatic cancer patients with high TF expression have a venous thromboembolism rate of 26.3% compared with 4.5% in patients with low TF expression. (Korana et. al. Clin Cancer Res. 2007 May 15;13(10):2870-5). Indeed, thromboembolic complications are increasingly considered to be the leading cause of death in patients with cancer (Levine MN: Cancer Treat Rev 2002;28:145–149). Among 66,000 patients with cancer admitted to US medical centers from 1995 to 2002, patients with pancreatic cancer had the highest risk of thromboembolic complications (12.1% per hospitalization) (Khorana et. al. J Clinical Oncology 2006, 24: 484-490). TF expression occurs early in pancreatic cancer, thus Pharmacyclics believes pancreatic cancer is an excellent focus for development of PCI-27483, which will have a dual mechanism of action of inhibiting tumor growth and thromboembolic events.

We have recently completed our initial Phase I testing of PCI-27483 in healthy volunteers. The primary objective of the ascending dose Phase I study was to assess the

pharmacodynamic and pharmacokinetic profiles of PCI-27483 following a single, subcutaneous injection. In addition, the safety and tolerability of PCI-27483 was evaluated. The drug was well tolerated and no adverse event was observed at any dose level. The International Normalized Ratio (INR) of prothrombin time, a laboratory test for coagulation, was used to measure pharmacodynamic effect at dose levels of 0.05, 0.20, 0.80 and 2.0 mg/kg. Anticoagulation effects can be precisely and accurately measured a few hours following dosing with a simple blood test. A mean peak INR of 2.7 was achieved without adverse effects at the highest dose level administered. The target INR range for oral anti-coagulants i.e. Coumadin, is between 2 and 3. The half-life of PCI-27483 was 9 to 10 hours, which compares favorably to the single-dose half-life of the low molecular weight heparin Lovenox (4.5 hours) and Fragmin (3 to 5 hours).

A multicenter Phase II study is planned to begin second half of calendar 2009. The target patient population is locally advanced (non-metastasized) pancreatic cancer within 2 months of diagnosis either receiving or planned to receive gemcitabine therapy. The goals will be to; a) assess the safety of PCI-27483 at pharmacologically active dose levels; b) to assess potential survival benefit and c) obtain initial information of the effects on the incidence of thromboembolic events.

### ***Market***

Each year 230,000 individuals worldwide are diagnosed with pancreatic cancer (in the US more than 34,000 are diagnosed each year). The overall pancreatic cancer market is forecasted to double to \$1.2 billion in 2016. There are approximately 870,000 new cases of gastric cancer worldwide per year, with 670,000 deaths. Worldwide incidence of other cancers types that also have been shown to have high TF expression include: colon cancer (940,000 new cases per year); ovarian (190,000 new cases per year); breast (1.2 million new cases per year), and lung cancer (1.2 million new cases per year).

### ***Patents***

PCI-27483 (as a compound, in pharmaceutical compositions and in uses for treating a variety of diseases) is covered by US patent applications (issued and pending) and PCT national phase patent applications in 14 other jurisdictions, including Europe, Canada, Japan, China, India, South Korea, Australia and Brazil. The projected expiration of this coverage is through at least 2024 (without including patent term extensions in the various territories).

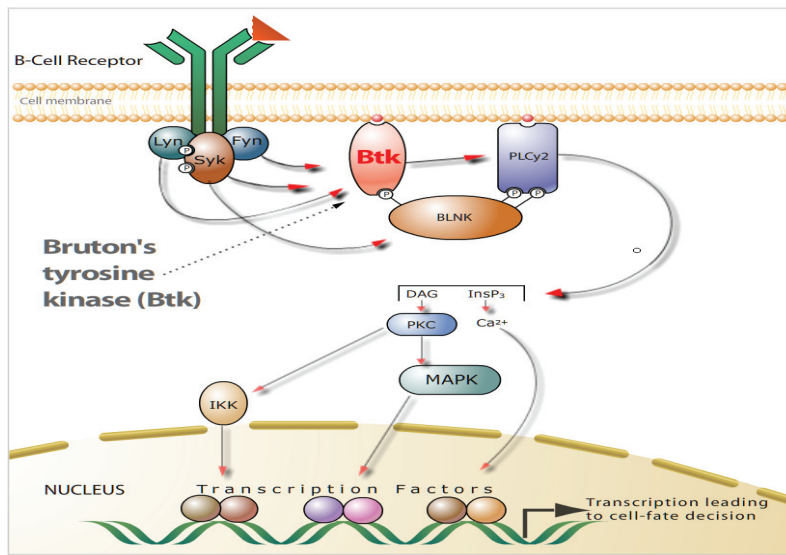
### ***Partnering***

Pharmacyclics will seek a partner to co-develop PCI-27483. We believe this unique drug may be competitively positioned for a significant partnership following the successful achievement of further clinical milestones.

### **Btk Inhibitors**

Pharmacyclics is pioneering the development of orally bioavailable inhibitors of Bruton's tyrosine kinase (Btk), a signaling molecule that is critically important for the activity of B-cells (i.e. cells that lead to the productions of antibodies) and mast cell (i.e. a cell involved in allergic responses). When B-cells are overactive, the immune system produces inflammatory cells and antibodies that begin to attack the body's own tissue, leading to autoimmune diseases. Also, B-cell lymphomas and leukemias, which are common blood cancers, result from mutations acquired during normal B-cell development leading to uncontrolled B-cell proliferation and B-cell

malignancies. Specific cancer indications include non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and as a potential inhibitor of tumor stem cells (also known as Tumor Initiating Cells or TIC's) that have been identified in certain cancers. In addition, Btk inhibitors have potential for treatment of autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and allergic diseases such as eosinophilic esophagitis. Pharmacyclics has developed two programs of proprietary and chemically distinct inhibitors, producing one candidate optimized for oncology (PCI-32765) and currently in a Phase I clinical trial; and a series of BTK inhibitor molecules currently being optimized for autoimmune and allergic indications for an anticipated IND in the second half of 2010.



Btk plays a critical role in signaling via B-cell receptor (BCR) signaling. Btk inhibitors block B-cell activation and auto-antibody formation.

### **Genetic Validation of Inhibiting the Target in Humans**

Unlike competing programs for inhibiting B-cell signaling such as with Syk inhibition, a human genetic mutation exists which helps to validate Btk as a drug target. Bruton's agammaglobulinemia (XLA) is an X-linked disease (only male offspring being effected) occurring in approximately 1 in 250,000 males, which disrupts the function of BTK. In the absence of Btk, B-cells do not come about or mature. Males with XLA have a total or almost total absence of B-cells and very low levels of circulating antibodies. Therefore, Btk is absolutely necessary for the proliferation and the differentiation of B-cells. A point mutation in mice also causes X-linked immunodeficiency (xid), with ~50% fewer conventional B2 B-cells, absent B1 B-cells, and reduced levels of antibodies.

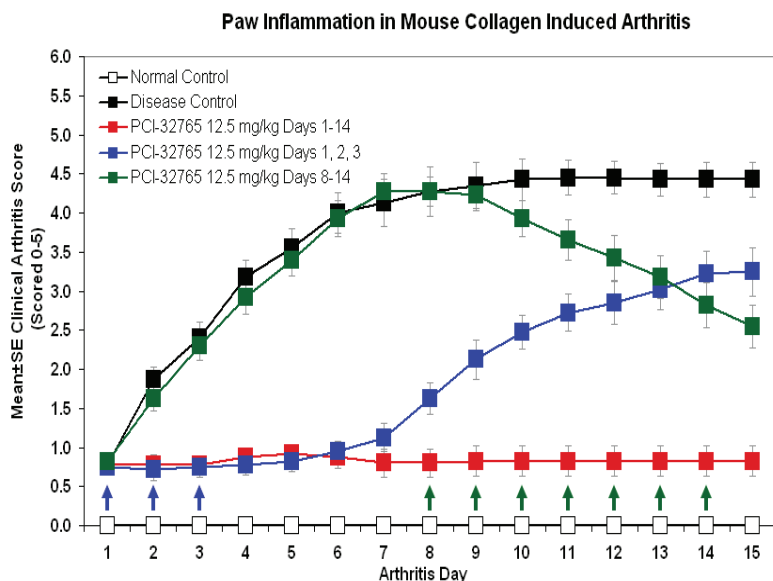
### **PCI-32765 for Oncology**

We have developed highly selective, small-molecule inhibitors of Btk using a proprietary scaffold and demonstrated oral efficacy in preclinical models of lymphoma and spontaneous lymphoma in dogs. Our inhibitors take advantage of a unique and proprietary mechanism to achieve potency and selectivity over other kinases (i.e. signaling molecules). PCI-32765 inhibits purified Btk with an IC50 of 0.46 nM. In ex vivo stimulation assays in whole blood, PCI-32765 inhibits human B-cell receptor activation (IC50 • 200 nM), while not affecting T-cell activation. We have also confirmed that PCI-32765 inhibits key phosphorylation events downstream of the B-cell receptor at similar concentrations. A one hour pulse of PCI-32765 is sufficient to inhibit B-cell activation for ~18 hours in cellular assays.

Based on available information we believe PCI-32765 is uniquely selective over closely related kinases. B-cell receptor signaling is implicated in the survival of B-cell derived Non-Hodgkin's lymphoma. Studies have shown that PCI-32765 inhibits the proliferation of B-cell lymphoma and leukemia cells. We have demonstrated that PCI-32765 kills a subset of lymphoma cell lines (GI50 <1 mM). We have recently initiated a trial of PCI-32765 in spontaneous canine lymphoma in companion animals. Thus far, in five dogs, with monoclonal B-cell Lymphoma, we have observed two partial responses (by RECIST criteria) following treatment with PCI-32765.

### ***PCI-32765 Preclinical Proof of Concept for Autoimmune diseases***

In animal models of rheumatoid arthritis, oral administration of PCI-32765 leads to the regression of established disease. In vivo, once daily oral dosing of PCI-32765 inhibited collagen induced arthritis (CIA) in the mouse (ED50 = 4.55 mg/kg/day). In a scheduling study (below), PCI-32765 rapidly regressed disease even when dosing was initiated at day 8, when inflammation was maximal. In addition, three days of PCI-32765 dosing resulted in inhibition of disease for six days, suggesting that intermittent dosing of PCI-32765 may result in sustained therapeutic effect. No PCI-32765-related weight loss was observed in the arthritis studies when dosed up to 200 mg/kg/day for 10 days. PCI-32765 also prevents the progression of anti-collagen induced arthritis at doses as low as 3 mg/kg.



In mouse models of collagen induced arthritis, orally administered PCI-32765 actually reversed disease. Shown are two dosing schedules for PCI-32765. In blue, animals were dosed for three days then the drug was withdrawn. The induction of the disease was delayed for four days. In green, the animals were allowed to develop the disease, and at day 8, the animals were dosed with PCI-32765. Within one day, the degree of disease severity was decreased.

PCI-32765 also prevents mast cell activation in vitro and inhibits mast cell-dependent anaphylaxis in vivo. Dual inhibition of mast cell and B-cell activation may explain the significant efficacy of PCI-32765 in animal models and may provide a treatment modality for a variety of allergic diseases including asthma and allergy.

### ***Clinical Development of PCI-32765***

A robust kilogram-scale synthesis, developed to the standards of Good Manufacturing Practices (GMP), has been developed and drug substance, technically described as Active Pharmaceutical Ingredient (API), is available to support clinical studies. An optimized capsule formulation has been developed.

We have developed multiple pharmacodynamic assays to monitor inhibition of B-cells in peripheral blood including a proprietary assay that can be used to monitor active-site occupancy of Btk by our inhibitors. We have confirmed that efficacy in our autoimmune models is correlated with doses that lead to Btk occupancy. In addition, we have adapted the probe assay so that it can be used to monitor Btk occupancy by PCI-32765 in human blood. This assay will be used to determine what dose levels of PCI-32765 lead to occupancy of Btk in clinical trials. In addition, we can measure inhibition of B-cell signaling and mast cell activation ex vivo using samples from PCI-32765 treated patients.

A Phase I trial in surface immunoglobulin positive B-cell lymphoma has begun at three clinical sites in the US. The objective of this study will be to determine the safety and tolerability of a 28-day oral dosing regimen and to evaluate effects on pharmacodynamic assays and tumor response.

### ***Potential New Oral Disease Modifying Anti-Rheumatic Drug (DMARD)***

Using the same chemical scaffold as PCI-32765, work was initiated on a second generation Btk inhibitor with the goal of optimizing for use in chronic disease. New chemical entities are being screened in a series of efficacy, pharmacokinetic, and safety assays designed to identify compounds that retained potent inhibition of Btk while exhibiting better selectivity and better pharmaceutical properties. Our current lead molecule, PCI-45261 was identified in December 2008. Btk inhibition by PCI-45261 is >2500-fold selective over the tyrosine kinases EGFR and JAK-3. We have confirmed that orally dosed PCI-45261 is highly efficacious in a mouse model of collagen induced arthritis. Relatively low efficacious doses are predicted for humans based on interspecies scaling. We are currently in the final stages of optimizing a series of molecules based on PCI-45261.

Data to date for PCI-32765 and our series of BTK inhibitors (i.e. PCI-45261 and others) demonstrates improvements in signs of inflammation in rheumatoid arthritis models. Based on the mechanism of action, we expect that the optimized drug from this series will delay the progression of the disease and be classified as a DMARD (disease modifying anti-rheumatic drug).

### ***Market Size***

Pharmacyclics will generate proof-of-concept data in both lymphoma and RA indications. Pharmacyclics is not aware of any other competitors in clinical trials with other Btk inhibitors. The anti-B-cell biologics such as Rituxan® and Lymphostat B all have a distinction of massive B-cell depletion and lack of convenient oral dosing. The overall Non Hodgkin's Lymphoma market is projected to increase from \$3.3 billion in 2007 to \$4.7 billion in 2017 (3.6% a year). The market for rheumatoid arthritis (RA) therapies will show robust growth between 2009 and 2017; major market sales will nearly double to \$13.4 billion in 2017.

### ***Patents***

A variety of non-provisional PCT applications have been filed for methods, uses and composition of the lead and second generation compounds including PCI-32765 and for the Btk fluorescent probe (PD marker). For lead clinical candidate (PCI-32765), we expect global patent protection till at least December 2026 (without including pharmaceutical extensions).

## ***Partnering***

We are evaluating multiple partner candidates for further discussions, which will likely depend on further product development progress. Pharmacyclics will be seeking strategic pharma / biotech partnership(s) to further develop and commercialize PCI-32765 and our series of BTK inhibitors.

### **HDAC8-specific inhibitor program: PCI-34051**

Pharmacyclics' scientists have been in the forefront of research into inhibitors for specific HDAC enzymes beginning with the cloning of the human HDAC8 in 2000 (Buggy et al., *Biochem.J.*, v. 350 Pt 1, p. 199-205, 2000). Since then, we were the first to publish the crystal structure of a human HDAC (HDAC8) in 2004 (Somoza et al., *Structure.*, v. 12, p. 1325-1334, 2004), the first to publish the most selective inhibitor of human HDAC8 (PCI-34051) in 2008 (Balasubramanian et al., *Leukemia.*, v. 22, p. 1026-1034, 2008), and the first to discover a novel anti-inflammatory activity of a HDAC8 inhibitor (Balasubramanian et al., in preparation 2009). This has led to a strong intellectual property position, with multiple patents on the gene, protein and a large selective inhibitor panel, and worldwide recognition of our efforts with seminar and poster presentations at major international conferences including the first HDAC inhibitors conference in 2007 and a subsequent one in 2008, as well as AACR and ASH conferences.

Using our unique knowledge of the crystal structure of HDAC8 complexed with multiple pan- and selective inhibitors, we have discovered a novel HDAC8 selective inhibitor, PCI-34051, which inhibits HDAC8 with a  $K_i$  of 10 nM (a measure of potency) with >200 fold selectivity over the other HDACs tested. With this very important tool compound, we have identified multiple clinical applications for this class of drugs.

T-cell lymphoma: PCI-34051 induces growth arrest and apoptosis in T-cell lymphomas and leukemias, but not in any other hematologic and most solid tumors (Balasubramanian et al., *Leukemia.*, v. 22, p. 1026-1034, 2008). Thus, it has the potential to offer an improved therapeutic index in these indications over non selective HDAC inhibitors such as vorinostat, which was approved for CTCL in 2006 but has been associated with multiple toxicities in the clinic.

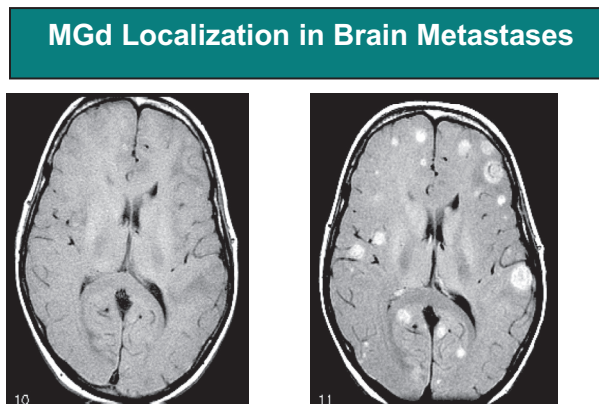
Pediatric neuroblastoma: HDAC8, uniquely among all HDAC enzymes, is overexpressed in pediatric neuroblastoma tumors, and a high HDAC8 expression level is strongly associated with a poor prognosis (Oehme et al., *Clin Cancer Res.*, v. 15, p. 91-99, 2009). HDAC8-specific inhibitors induce growth inhibition and differentiation into non-tumor forms of neuroblastoma cells. Thus, HDAC8-specific inhibitors could prove valuable in treating this disease for which there is no curative therapy at present.

Inflammatory disease: We have discovered that PCI-34051 inhibits the secretion of many pro-inflammatory proteins from blood cells (Balasubramanian et al., in preparation 2009). It is particularly effective at modulating the proteins interleukin-1 beta (IL1b) and interleukin-18, both of which are associated with many autoimmune disorders. Anti-IL1b protein therapeutics have proven effective in treatment of RA and systemic juvenile RA (Pascual et al., *J Exp.Med.*, v. 201, p. 1479-1486, 2005), Adult-onset Still's Disease (Lequerre et al., *Ann.Rheum.Dis.*, v. 67, p. 302-308, 2008), Familial Cold Syndrome and Muckle-Wells syndrome (Farasat et al., *Arch.Dermatol.*, v. 144, p. 392-402, 2008). We have also shown that PCI-34051 is effective at reducing IL1b secretion from blood cells of patients with RA and psoriasis (Balasubramanian et

al., in preparation, 2009). Thus, HDAC8-specific inhibitors offer a unique therapeutic modality in treatment of these autoimmune disorders.

### **Motexafin Gadolinium (MGd)**

MGd is a radiation and chemotherapy sensitizing agent with a novel mechanism of action. MGd is designed to accumulate selectively in cancer cells. Once inside cancer cells, MGd in combination with radiation induces apoptosis (programmed cell death) by disrupting redox-dependent pathways. MGd is also detectable by magnetic resonance imaging (MRI) and may allow for more precise tumor detection. The National Cancer Institute (NCI) is currently sponsoring two Phase II trials which have and continue to provide valuable developmental insights and directions.



We are currently evaluating MGd in glioblastoma multiforme (GBM), wherein proof-of-efficacy relies on extending survival time. GBM is the most common primary brain tumor in adults accounting for 40% of primary central nervous system tumors. Radiation increases median survival by approximately 4 to 9 months, addition of temozolomide increases this to 14 months, but despite numerous studies of other potential therapies, the outcome of GBM has not changed beyond this. Previous collaborators, led by Dr. Judith Ford (*Int. J. Rad. Oncol. Biol. Phys* pp 1-8, 2007), showed that in a case matched analysis, patients treated with MGd (n=31) had a median survival of 16.1 months compared to the matched RTOG (Radiation Therapy Oncology Group) database patients with a median survival of 11.8 months. MGd is currently in a RTOG sponsored Phase II multi-center study in GBM in combination with radiation therapy and temozolomide ([www.clinicaltrials.gov](http://www.clinicaltrials.gov); 113 patients study). The principal investigator, Dr. David G. Brachman, is heading this study at the Barrow Neurological Institute at St. Joseph's Hospital in Phoenix, AZ. Previous studies in malignant gliomas headed by Dr. William Shapiro from the Barrow Institute have shown that the combination of MGd and temozolomide has no additional overlapping toxicities when used in combination. MGd is also in a Children's Oncology Group (COG) sponsored Phase II study in children with pontine gliomas in combination with radiation therapy ([www.clinicaltrial.gov](http://www.clinicaltrial.gov); 60 patients). The principal investigator, Dr. Kristin A. Bradley is heading this multi-center study at the University of Wisconsin. The study has completed enrollment.

## Our Business Strategy

The key elements of our business strategy include:

- *Focusing on creating novel, patentable, differentiated biopharmaceutical products.* We are leveraging our expertise in chemistry and clinical development to create multiple novel drug candidates.
- *Focusing on proprietary drugs that address large markets of unmet medical need for the treatment of oncology and immune mediated diseases.* Although our versatile technology platform can be used to develop a wide range of pharmaceutical agents, we have focused most of our initial efforts in oncology and immune mediated diseases where we have established strength in preclinical and clinical development.
- *Utilize biomarkers and predictive pharmacodynamic assays wherever possible.* Targeting the right drug to the right patient at the right time with the right dose has the potential to greatly expedite intelligent clinical development and reduce the time, cost and risk of clinical programs.
- *Provide major pharmaceutical companies access to validated drug candidates.* Major pharmaceutical companies have a need for promising drug candidates, which still may require large clinical trials. We focus on satisfying this need for novel, best in class or first in class drugs. A partnership with Pharmacyclics may provide these companies the opportunity to leverage the innovation and excellence of a creative, focused and experienced scientific team.
- *Establish strategic alliances and collaborations.* Except for the rights which we license to Servier, we own the worldwide rights to our multiple product candidates. At the opportune time in the clinical development path we intend to establish strategic alliances and collaborations for the development and commercialization of our products.
- *Leverage development with outsourcing.* We utilize outside vendors with expertise and capability in manufacturing and clinical development to more efficiently develop our multiple product candidates.
- *Create a large clinical pipeline.* We reduce risk of failure by taking multiple 'shots on goal'.

We are subject to risks common to pharmaceutical companies developing products, including risks inherent in our research, development and commercialization efforts, preclinical testing, clinical trials, uncertainty of regulatory and marketing approvals, uncertainty of market acceptance of our products, history of and expectation of future operating losses, reliance on collaborative partners, enforcement of patent and proprietary rights, and the need for future capital. In order for a product to be commercialized, we must conduct preclinical tests and clinical trials, demonstrate efficacy and safety of our product candidates to the satisfaction of regulatory authorities, obtain marketing approval, enter into manufacturing, distribution and marketing arrangements, build a U.S. commercial oncology franchise, obtain market acceptance and, in many cases, obtain adequate coverage of and reimbursement for our products from government and private insurers. We cannot provide assurance that we will generate revenues or achieve and sustain profitability in the future.

## USE OF PROCEEDS

The purpose of this rights offering is to raise equity capital in a cost-effective manner that gives all of our stockholders the opportunity to participate. Assuming adequate net proceeds which we anticipate to be approximately \$23.5 million (approximately \$28.2 million if all of the Additional Shares are issued), we plan to use those net proceeds for general working capital purposes. As part of working capital use, \$6.4 million of the net proceeds from this rights offering will be used to repay Pharmacyclics' obligations under a Promissory Note made by Pharmacyclics in favor of affiliates of Robert W. Duggan, our Chairman of the Board and Chief Executive Officer, and the beneficial owner of approximately 27% of Pharmacyclics' outstanding common stock.

Mr. Duggan has indicated to us that he intends to exercise all of his rights, but has not made any formal commitment to do so, for a total exercise of 5,106,000 shares equaling approximately \$6.5 million, an amount sufficient to satisfy the indebtedness owed by Pharmacyclics to Mr. Duggan in its entirety. The reason we decided to raise up to approximately \$24 million in cash and/or securities, as provided herein, in this rights offering was to ensure that even if no other stockholders participated in the rights offering, Mr. Duggan would be able to participate up to his proportionate 27% interest and Pharmacyclics would receive at least the necessary amount required satisfy the Company's indebtedness. The initial loan of \$5.0 million was approved by a majority of the disinterested members of the Registrant's Board of Directors and the amendment to the loan for an additional \$1.4 million was unanimously approved by the Board of Directors. Under the terms of the loan, Pharmacyclics is to pay to affiliates of Robert W. Duggan, the principal sum of \$6.4 million on the earlier of (i) July 1, 2010 or (ii) upon the closing of this rights offering (provided that the loan shall only accelerate up to the amount of net proceeds raised in this rights offering). The initial loan of \$5.0 million had an interest rate of 1.36% from December 30, 2008 until March 31, 2009 and the \$6.4 million combined note bears interest as follows: (i) the rate of interest in effect for such day as publicly announced from time to time by Citibank N.A. as its "prime rate" from April 1, 2009 until December 31, 2009 and (ii) the prime rate plus 2% from January 1, 2010 until the expiration of the note. Interest is to be paid annually.

## THE RIGHTS OFFERING

### Subscription Rights

#### *Basic Subscription Rights*

We will distribute to each holder of our common stock who is a record holder of our common stock on the record date, which is July 15, 2009, at no charge, one non-transferable subscription right for each share of common stock owned. The subscription rights will be evidenced by non-transferable subscription rights certificates. Each subscription right will entitle the rights holder to purchase 0.6808 shares of our common stock at a price of \$1.28 per share, the subscription price, which shall be paid in cash or by the delivery to the Company by the holder of an equivalent amount of principal and accrued and unpaid interest of indebtedness owed by the Company to such holder, or a combination thereof, upon timely delivery of the required documents and payment of the subscription price. We will not issue fractional shares, but rather will round up or down the aggregate number of shares you are entitled to receive to the nearest whole number. If rights holders wish to exercise their subscription rights, they must do so prior to 5:00 p.m., New York City time, on July 31, 2009, the expiration date for the rights offering, subject to extension. After the expiration date, the subscription rights will expire and will have no value. See below “— Expiration of the Rights Offering and Extensions, Amendments and Termination.” You are not required to exercise all of your subscription rights. We will deliver to the record holders who purchase shares in the rights offering certificates representing the shares purchased as soon as practicable after the rights offering has expired.

#### *Oversubscription Rights*

Subject to the allocation described below, each subscription right also grants the holder an oversubscription right to purchase additional shares of our common stock that are not purchased by other rights holders pursuant to their basic subscription rights. You are entitled to exercise your oversubscription right only if you exercise your basic subscription right in full.

If you wish to exercise your oversubscription right, you should indicate the number of additional shares that you would like to purchase in the space provided on your rights certificate, as well as the number of shares that you beneficially own without giving effect to any shares to be purchased in this offering. When you send in your rights certificate, you must also send the full purchase price in cash and/or securities, as provided herein, for the number of additional shares that you have requested to purchase (in addition to the payment in cash and/or securities, as provided herein, due for shares purchased through your basic subscription right). If an insufficient number of shares of Common Stock are available to fully satisfy all properly exercised oversubscription rights requests, the Company shall have the right, at its discretion, to increase the number of shares available for issuance in the rights offering by up to an amount equal to 3,750,000 Additional Shares in order to satisfy additional properly exercised oversubscription rights requests. If Pharmacyclics does not elect to issue Additional Shares, or if the Additional Shares are not sufficient to satisfy all of the properly exercised oversubscription rights requests, then the available shares will be prorated among those who properly exercised oversubscription rights based on the number of shares each rights holder subscribed for under the basic subscription right. The subscription agent will return any excess payments in the form in which made, or if made in a combination of cash and indebtedness, in the form indicated, or if not indicated, Company indebtedness will be applied to payment first, followed by cash, by mail without interest or deduction promptly after the expiration of the subscription period.

As soon as practicable after the expiration date, the subscription agent will determine the number of shares of common stock that you may purchase pursuant to the oversubscription right. You will receive certificates representing these shares as soon as practicable after the expiration date and after all allocations and adjustments have been effected. If you request and pay for more shares than are allocated to you, we will refund the overpayment in the form in which made, or if made in a combination of cash and indebtedness, in the form indicated, or if not indicated, Company indebtedness will be applied to payment first, followed by cash, without interest or deduction. In connection with the exercise of the oversubscription right, banks, brokers and other nominee holders of subscription rights who act on behalf of beneficial owners will be required to certify to us and to the subscription agent as to the aggregate number of subscription rights exercised, and the number of shares of common stock requested through the oversubscription right, by each beneficial owner on whose behalf the nominee holder is acting.

### **Expiration of the Rights Offering and Extensions, Amendments and Termination**

You may exercise your subscription rights at any time prior to 5:00 p.m., New York City time, on July 31, 2009, the expiration date for the rights offering. If you do not exercise your subscription rights before the expiration date of the rights offering, your subscription rights will expire and will have no value. We will not be required to issue shares of our common stock to you if the subscription agent receives your rights certificate or payment, after the expiration date, regardless of when you sent the rights certificate and payment, unless you send the documents in compliance with the guaranteed delivery procedures described below.

We may, in our sole discretion, extend the time for exercising the subscription rights. We may extend the expiration date at any time after the record date. If the commencement of the rights offering is delayed for a period of time, the expiration date of the rights offering may be similarly extended. We will extend the duration of the rights offering as required by applicable law, and may choose to extend the duration of the rights offering for any reason. We may extend the expiration date of the rights offering by giving oral or written notice to the subscription agent on or before the scheduled expiration date. If we elect to extend the expiration date of the rights offering, we will issue a press release announcing such extension no later than 9:00 a.m., New York City time, on the next business day after the most recently announced expiration date. In no event will we extend the expiration date beyond 90 days from the date we distribute the rights.

We reserve the right, in our sole discretion, to amend or modify the terms of the rights offering. We also reserve the right to terminate the rights offering at any time prior to the expiration date for any reason, in which event all funds received in connection with the rights offering will be returned without interest or deduction to those persons who exercised their subscription rights as soon as practicable.

### **Conditions to the Rights Offering**

We may terminate the rights offering, in whole or in part, if at any time before completion of the rights offering there is any judgment, order, decree, injunction, statute, law or regulation entered, enacted, amended or held to be applicable to the rights offering that in the sole judgment of our Board of Directors would or might make the rights offering or its completion, whether in whole or in part, illegal or otherwise restrict or prohibit completion of the rights offering. We may waive any of these conditions and choose to proceed with the rights offering even if one or more of these events occur. If we terminate the rights offering, in whole or in part, all affected subscription rights will expire without value and all subscription payments in the form in which received by the subscription agent will be returned in the form in which paid, without

interest or deduction, as soon as practicable. See also “— Expiration of the Rights Offering and Extensions, Amendments and Termination.”

### **Method of Exercising Subscription Rights**

The exercise of subscription rights is irrevocable and may not be cancelled or modified. Your subscription rights will not be considered exercised unless the subscription agent receives from you, your broker, custodian or nominee, as the case may be, all of the required documents properly completed and executed and your full subscription price payment in cash and/or securities, as provided herein, prior to 5:00 p.m., New York City time, on July 31, 2009, the expiration date of the rights offering. Rights holders may exercise their rights as follows:

#### *Subscription by Registered Holders*

Rights holders who are registered holders of our common stock may exercise their subscription privilege by properly completing and executing the rights certificate together with any required signature guarantees and forwarding it, together with payment in full in cash and/or securities, as provided herein, of the subscription price for each share of the common stock for which they subscribe, to the subscription agent at the address set forth under the subsection entitled “— Delivery of Subscription Materials and Payment,” on or prior to the expiration date.

#### *Subscription by DTC Participants*

Banks, trust companies, securities dealers and brokers that hold shares of our common stock on the rights offering record date as nominee for more than one beneficial owner may, upon proper showing to the subscription agent, exercise their subscription privilege on the same basis as if the beneficial owners were record holders on the rights offering record date through the Depository Trust Company, or DTC. Such holders may exercise these rights through DTC’s PSOP Function on the “agents subscription over PTS” procedure and instructing DTC to charge their applicable DTC account for the subscription payment for the new shares or indicating to DTC that such holder intends to pay for such rights through the delivery to the Company by the holder of an equivalent amount of principal and accrued and unpaid interest of indebtedness owed by the Company to such holder, or a combination thereof, and deliver such amount to the subscription agent. DTC must receive the subscription instructions and payment for the new shares by the rights expiration date. Except as described under the subsection titled “— Guaranteed Delivery Procedures,” subscriptions accepted by the subscription agent via a Notice of Guaranteed Delivery must be delivered to the subscription agent with payment before the expiration of the subscription period.

#### *Subscription by Beneficial Owners*

Rights holders who are beneficial owners of shares of our common stock and whose shares are registered in the name of a broker, custodian bank or other nominee, and rights holders who hold common stock certificates and would prefer to have an institution conduct the transaction relating to the rights on their behalf, should instruct their broker, custodian bank or other nominee or institution to exercise their rights and deliver all documents and payment (whether cash and/or Company indebtedness), on their behalf, prior to the expiration date. A rights holder’s subscription rights will not be considered exercised unless the subscription agent receives from such rights holder, its broker, custodian, nominee or institution, as the case may be, all of the required documents and such holder’s full subscription price payment.

## Method of Payment

Payments must be made in full in:

- U.S. currency by:
  - uncertified check drawn against a U.S. bank payable to “Computershare Trust Company, N.A. (acting as Subscription Agent for Pharmacyclics)”;
  - bank draft (cashier’s check) drawn against a U.S. bank payable to “Computershare Trust Company, N.A. (acting as Subscription Agent for Pharmacyclics)”;
  - U.S. Postal money order payable to “Computershare Trust Company, N.A. (acting as Subscription Agent for Pharmacyclics)”.
- the delivery to the Company by the holder of an equivalent amount of principal and unpaid interest of indebtedness owed by the Company to such holder.

Rights certificates received after that time will not be honored, and we will return your payment to you in the form received as soon as practicable, without interest or deduction.

The subscription agent will be deemed to receive payment upon:

- clearance of any uncertified check deposited by the subscription agent;
- receipt by the subscription agent of any certified bank check draft drawn upon a U.S. bank;
- receipt by the subscription agent of any U.S. Postal money order; or
- the receipt by the subscription agent of the original evidence of indebtedness owed by the Company to such holder.

You should read the instruction letter accompanying the rights certificate carefully and strictly follow it. **DO NOT SEND RIGHTS CERTIFICATES OR PAYMENTS TO US.** Except as described below under “— Guaranteed Delivery Procedures,” we will not consider your subscription received until the subscription agent has received delivery of a properly completed and duly executed rights certificate and payment of the full subscription amount. The risk of delivery of all documents and payments is on you or your nominee, not us or the subscription agent.

The method of delivery of rights certificates and payment of the subscription amount to the subscription agent will be at the risk of the holders of rights, but, if sent by mail, we recommend that you send those certificates and payments by overnight courier or by registered mail, properly insured, with return receipt requested, and that a sufficient number of days be allowed to ensure delivery to the subscription agent and clearance of payment before the expiration of the subscription period.

Unless a rights certificate provides that the shares of common stock are to be delivered to the record holder of such rights or such certificate is submitted for the account of a bank or a broker, signatures on such rights certificate must be guaranteed by an “Eligible Guarantor

Institution,” as such term is defined in Rule 17Ad-15 of the Exchange Act, subject to any standards and procedures adopted by the subscription agent. See “— Medallion Guarantee May be Required.”

**Medallion Guarantee May Be Required**

Your signature on each subscription rights certificate must be guaranteed by an eligible institution, such as a member firm of a registered national securities exchange or a member of the Financial Industry Regulatory Authority, Inc., or a commercial bank or trust company having an office or correspondent in the United States, subject to standards and procedures adopted by the subscription agent, unless:

- your subscription rights certificate provides that shares are to be delivered to you as record holder of those subscription rights; or
- you are an eligible institution.

**Subscription Agent**

The subscription agent for this rights offering is Computershare Inc. We will pay all fees and expenses of the subscription agent related to the rights offering and have also agreed to indemnify the subscription agent from certain liabilities that it may incur in connection with the rights offering.

**Information Agent**

The information agent for this rights offering is Georgeson Inc. We will pay all fees and expenses of the information agent related to the rights offering and have also agreed to indemnify the information agent from certain liabilities that it may incur in connection with the rights offering. The information agent can be contacted at the following address and telephone number:

Georgeson Inc.  
199 Water Street  
New York, New York 10038  
(800) 279-5722

**Delivery of Subscription Materials and Payment**

You should deliver your subscription rights certificate and payment of the subscription price in cash and/or securities, as provided herein, or, if applicable, notice of guaranteed delivery, to the subscription agent by one of the methods described below:

<i>By mail:</i>	<i>By overnight courier:</i>
<p><i>Computershare c/o Voluntary Corporate Actions - Pharmacyclics Rights Offering Suite V P.O. Box 43011 Providence, RI 02941-3011</i></p>	<p><i>Computershare c/o Voluntary Corporate Actions - Pharmacyclics Rights Offering 250 Royall Street Suite V Canton, MA 02021</i></p>

Your delivery to an address or by any method other than as set forth above will not constitute valid delivery and we may not honor the exercise of your subscription rights.

You should direct any questions or requests for assistance concerning the method of subscribing for the shares of common stock or for additional copies of this prospectus to the information agent.

### **Guaranteed Delivery Procedures**

The subscription agent will grant you three business days after the expiration date to deliver the rights certificate if you follow the following instructions for providing the subscription agent notice of guaranteed delivery. On or prior to the expiration date, the subscription agent must receive payment in full in cash and/or securities, as provided herein, for all shares of common stock subscribed for through the exercise of the subscription privilege, together with a properly completed and duly executed notice of guaranteed delivery substantially in the form accompanying this prospectus either by mail or overnight courier, that specifies the name of the holder of the rights and the number of shares of common stock subscribed for. If applicable, it must state separately the number of shares of common stock subscribed for through the exercise of the subscription privilege and a member firm of a registered national securities exchange, a member of the Financial Industry Regulatory Authority, Inc., or a commercial bank or trust company having an office or correspondent in the United States must guarantee that the properly completed and executed rights certificate for all shares of common stock subscribed for will be delivered to the subscription agent within three business days after the expiration date. The subscription agent will then conditionally accept the exercise of the rights and will withhold the certificates for shares of common stock until it receives the properly completed and duly executed rights certificate within that time period.

In the case of holders of rights that are held of record through DTC, those rights may be exercised by instructing DTC to transfer rights from that holder's DTC account to the subscription agent's DTC account, together with payment of the full subscription price. The notice of guaranteed delivery must be guaranteed by a commercial bank, trust company or credit union having an office, branch or agency in the United States or by a member of a Stock Transfer Association approved medallion program such as STAMP, SEMP or MSP.

Notices of guaranteed delivery and payments should be mailed or delivered to the appropriate addresses set forth under "— Delivery of Subscription Materials and Payment."

### **Calculation of Subscription Rights Exercised**

If you do not indicate the number of subscription rights being exercised, or do not forward full payment in cash and/or securities, as provided herein, of the total subscription price payment for the number of subscription rights that you indicate are being exercised, then you will be deemed to have exercised your subscription right with respect to the maximum number of subscription rights that may be exercised with the aggregate subscription price payment in cash and/or securities, as provided herein, you delivered to the subscription agent. If we do not apply your full subscription price payment to your purchase of shares of our common stock, we or the subscription agent will return in cash (unless the holder paid for the rights through indebtedness owed by the Company) the excess amount to you by mail, without interest or deduction, as soon as practicable after the expiration date of the rights offering.

## **Escrow Arrangements**

The subscription agent will hold funds received in payment of the subscription price or evidence of Company indebtedness in a segregated account until the rights offering is completed or withdrawn and terminated.

## **Notice to Beneficial Holders**

If you are a broker, a trustee or a depository for securities who holds shares of our common stock for the account of others as of the record date, you should notify the respective beneficial owners of such shares of the rights offering as soon as possible to find out their intentions with respect to exercising their subscription rights. You should obtain instructions from the beneficial owners with respect to their subscription rights, as set forth in the instructions we have provided to you for your distribution to beneficial owners. If a beneficial owner so instructs, you should complete the appropriate subscription rights certificates and submit them to the subscription agent with the proper payment. If you hold shares of our common stock for the account(s) of more than one beneficial owner, you may exercise the number of subscription rights to which all such beneficial owners in the aggregate otherwise would have been entitled had they been direct record holders of our common stock on the record date, provided that you, as a nominee record holder, make a proper showing to the subscription agent by submitting the form entitled "Nominee Holder Certification" that we will provide to you with your rights offering materials. If you did not receive this form, you should contact the subscription agent to request a copy.

## **Beneficial Owners**

If you are a beneficial owner of shares of our common stock or will receive subscription rights through a broker, custodian bank or other nominee, we will ask your broker, custodian bank or other nominee to notify you of the rights offering. If you wish to exercise your subscription rights, you will need to have your broker, custodian bank or other nominee act for you. If you hold certificates of our common stock directly and would prefer to have your broker, custodian bank or other nominee act for you, you should contact your nominee and request it to effect the transactions for you. To indicate your decision with respect to your subscription rights, you should complete and return to your broker, custodian bank or other nominee the form entitled "Beneficial Owners Election Form". You should receive the "Beneficial Owners Election Form" from your broker, custodian bank or other nominee with the other rights offering materials. If you wish to obtain a separate subscription rights certificate, you should contact the nominee as soon as possible and request that a separate subscription rights certificate be issued to you. You should contact your broker, custodian bank or other nominee if you do not receive this form but you believe you are entitled to participate in the rights offering. We are not responsible if you do not receive this form from your broker, custodian bank or nominee or if you receive it without sufficient time to respond.

## **Subscription Price**

In determining the subscription price for this rights offering, a pricing committee of our board of directors has been established. In setting the subscription price, the pricing committee reviewed and considered a number of factors, including the amount of proceeds desired, our need for liquidity and equity capital, alternatives available to us for raising equity capital, the historic market price, moving averages and volume weighted moving averages of our common stock, the pricing of similar transactions, the liquidity and the historic volatility of the market price of our common stock, the historic trading volume of our common stock, our business prospects,

our recent and anticipated operating results, the price at which our stockholders might be willing to participate in the rights offering, the desire to provide an opportunity to our stockholders to participate in the rights offering on a pro rata basis and general conditions in the securities market. The subscription price is not necessarily related to the book value of our assets, net worth, past operations, cash flows, losses, financial condition, or any other established criteria for valuing Pharmacyclics and may or may not be considered the fair value of our common stock to be offered in the rights offering. You should not assume or expect that, after the rights offering, our common shares will trade at or above the subscription price. The Company can give no assurance that our common shares will trade at or above the subscription price in any given time period.

We also cannot assure you that the market price of our common shares will not decline during or after the rights offering. We also cannot assure you that you will be able to sell common shares purchased during the rights offering at a price equal to or greater than the subscription price. We urge you to obtain a current quote for our common shares before exercising your subscription rights.

### **Determinations Regarding the Exercise of Your Subscription Rights**

We will decide all questions concerning the timeliness, validity, form and eligibility of the exercise of your subscription rights and any such determinations by us will be final and binding. We, in our sole discretion, may waive, in any particular instance, any defect or irregularity, or permit, in any particular instance, a defect or irregularity to be corrected within such time as we may determine. We will not be required to make uniform determinations in all cases. We may reject the exercise of any of your subscription rights because of any defect or irregularity. We will not accept any exercise of subscription rights until all irregularities have been waived by us or cured by you within such time as we decide, in our sole discretion. Our interpretations of the terms and conditions of the rights offering will be final and binding.

Neither we, nor the subscription agent, will be under any duty to notify you of any defect or irregularity in connection with your submission of subscription rights certificates and we will not be liable for failure to notify you of any defect or irregularity. We reserve the right to reject your exercise of subscription rights if your exercise is not in accordance with the terms of the rights offering or in proper form. We will also not accept the exercise of your subscription rights if our issuance of shares of our common stock to you could be deemed unlawful under applicable law.

### **No Revocation or Change**

Once you submit the form of rights certificate to exercise any subscription rights, you may not revoke or change your exercise or request a refund of monies paid. All exercises of rights are irrevocable, even if you subsequently learn information about us that you consider to be unfavorable. You should not exercise your rights unless you are certain that you wish to purchase additional shares of our common stock at the subscription price.

### **Non-Transferability of the Rights**

The subscription rights granted to you are non-transferable and, therefore, may not be assigned, gifted, purchased, sold or otherwise transferred to anyone else. Notwithstanding the foregoing, you may transfer your rights to any affiliate of yours and your rights also may be transferred by operation of law; for example, a transfer of rights to the estate of the recipient upon the death of the recipient would be permitted. If the rights are transferred as permitted,

evidence satisfactory to us that the transfer was proper must be received by us prior to the expiration date.

### **Rights of Subscribers**

You will have no rights as a stockholder with respect to shares you subscribe for in the rights offering until certificates representing shares of common stock are issued to you. You will have no right to revoke your subscriptions after you deliver your completed rights certificate, payment in cash and/or securities, as provided herein, and any other required documents to the subscription agent.

### **Intended Purchases**

Robert W. Duggan has indicated to us that he intends to exercise all of his rights, but has not made any formal commitment to do so, for a total exercise of 5,106,000 shares equaling approximately \$6.5 million, an amount sufficient to satisfy the indebtedness owed by Pharmacyclics to Mr. Duggan in its entirety (he currently holds approximately 27% of the outstanding shares of the Company's common stock).

### **Foreign Stockholders and Stockholders with Army Post Office or Fleet Post Office Addresses**

The subscription agent will not mail rights certificates to you if you are a stockholder whose address is outside the United States or if you have an Army Post Office or a Fleet Post Office address. Instead, we will have the subscription agent hold the subscription rights certificates for your account. To exercise your rights, you must notify the subscription agent prior to 11:00 a.m., New York City time, at least three business days prior to the expiration date, and establish to the satisfaction of the subscription agent that it is permitted to exercise your subscription rights under applicable law. If you do not follow these procedures by such time, your rights will expire and will have no value.

### **No Board Recommendation**

An investment in shares of our common stock must be made according to your evaluation of your own best interests and after considering all of the information herein, including the "Risk Factors" section of this prospectus. Neither we nor our Board of Directors are making any recommendation regarding whether you should exercise your subscription rights.

### **Shares of Common Stock Outstanding After the Rights Offering**

Based on the 27,539,378 shares of our common stock currently outstanding, and the potential that Pharmacyclics may issue as many as 18,750,000 shares (22,500,000 shares if all of the Additional Shares are issued) pursuant to this rights offering, 46,289,378 shares of our common stock (50,039,378 shares if all of the Additional Shares are issued) may be issued and outstanding following the rights offering, which represents an increase in the number of outstanding shares of our common stock of approximately 68% (82% if all of the Additional Shares are issued).

## **Fees and Expenses**

Neither we, nor the subscription agent, will charge a brokerage commission or a fee to subscription rights holders for exercising their rights. However, if you exercise your subscription rights through a broker, dealer or nominee, you will be responsible for any fees charged by your broker, dealer or nominee.

## **Questions About Exercising Subscription Rights**

If you have any questions or require assistance regarding the method of exercising your subscription rights or requests for additional copies of this document or any document mentioned herein, you should contact the subscription agent at the address and telephone number set forth above under “— Delivery of Subscription Materials and Payment.”

## **Other Matters**

Pharmacyclics is not making the rights offering in any state or other jurisdiction in which it is unlawful to do so, nor is Pharmacyclics distributing or accepting any offers to purchase any shares of our common stock from subscription rights holders who are residents of those states or of other jurisdictions or who are otherwise prohibited by federal or state laws or regulations to accept or exercise the subscription rights. Pharmacyclics may delay the commencement of the rights offering in those states or other jurisdictions, or change the terms of the rights offering, in whole or in part, in order to comply with the securities law or other legal requirements of those states or other jurisdictions. Subject to state securities laws and regulations, Pharmacyclics also has the discretion to delay allocation and distribution of any shares you may elect to purchase by exercise of your subscription rights in order to comply with state securities laws. Pharmacyclics may decline to make modifications to the terms of the rights offering requested by those states or other jurisdictions, in which case, if you are a resident in one of those states or jurisdictions or if you are otherwise prohibited by federal or state laws or regulations from accepting or exercising the subscription rights you will not be eligible to participate in the rights offering.

## **MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES**

The following discussion is a summary of the material United States Federal income tax consequences of the rights offering to holders of our common stock. This discussion assumes that the holders of our common stock hold such common stock as a capital asset for United States Federal income tax purposes. This discussion is based on the Internal Revenue Code of 1986, as amended, Treasury Regulations promulgated thereunder, Internal Revenue Service rulings and pronouncements and judicial decisions in effect on the date hereof, all of which are subject to change (possibly with retroactive effect) and to differing interpretations. The following summary does not purport to be a complete analysis of all of the potential U.S. Federal income tax considerations, applies only to holders that are United States persons and does not address all aspects of United States Federal income taxation that may be relevant to holders in light of their particular circumstances or to holders who may be subject to special tax treatment under the Internal Revenue Code, including, without limitation, holders who are dealers in securities or foreign currency, foreign persons, insurance companies, tax-exempt organizations, banks, financial institutions, broker-dealers, holders who hold our common stock as part of a hedge, straddle, conversion or other risk reduction transaction, or who acquired our common stock pursuant to the exercise of compensatory stock options or otherwise as compensation.

This summary is of a general nature only and is not intended to constitute a complete analysis of all tax consequences relating to the receipt, exercise, disposition and expiration of the subscription rights and the ownership and disposition of our common shares. It is not intended to constitute, and should not be construed to constitute, legal or tax advice to any particular holder. Holders should consult their own tax advisors as to the tax consequences in their particular circumstances. To ensure compliance with Treasury Department Circular 230, holders are hereby notified that (1) any discussion of U.S. federal income tax issues herein or any other document referred to herein is not intended or written to be used, and cannot be used, by such holders for the purpose of avoiding penalties that may be imposed under the Internal Revenue Code, (2) such discussions are for use in connection with the promotion or marketing of the transactions or matters addressed herein, and (3) holders should seek advice based on their particular circumstances from an independent tax advisor.

We intend to treat the distribution of subscription rights pursuant to the rights offering as a non-taxable transaction for United States Federal income tax purposes and the remaining portion of this summary describes the United States Federal income tax consequences of such treatment. However, there can be no assurance that the Internal Revenue Service will take a similar view or would agree with the tax consequences described below. We have not sought, and will not seek, an opinion of counsel or a ruling from the Internal Revenue Service regarding the United States Federal income tax consequences of the rights offering or the related share issuance. The following summary does not address the tax consequences of the rights offering or the related share issuance under foreign, state, or local tax laws. **ACCORDINGLY, EACH HOLDER OF OUR COMMON STOCK SHOULD CONSULT ITS TAX ADVISOR WITH RESPECT TO THE PARTICULAR TAX CONSEQUENCES OF THE RIGHTS OFFERING AND THE RELATED SHARE ISSUANCE TO SUCH HOLDER.**

The United States Federal income tax consequences to a holder of our common stock of the receipt and exercise of subscription rights under the rights offering will be as follows:

- A holder will not recognize taxable income for United States Federal income tax purposes in connection with the receipt of subscription rights in the rights offering.

- A holder's tax basis in its subscription rights will depend on the relative fair market value of the subscription rights received by such holder and the common stock owned by such holder at the time the subscription rights are distributed. If either (i) the fair market value of the subscription rights on the date such subscription rights are distributed is equal to at least 15% of the fair market value on such date of the common stock with respect to which the subscription rights are received or (ii) the holder elects, in its United States Federal income tax return for the taxable year in which the subscription rights are received, to allocate part of its tax basis in such common stock to the subscription rights, then upon exercise of the subscription rights, the holder's tax basis in the common stock will be allocated between the common stock and the subscription rights in proportion to their respective fair market values on the date the subscription rights are distributed. If the subscription rights received by a holder have a fair market value that is less than 15% of the fair market value of the common stock owned by such holder at the time the subscription rights are distributed, the holder's tax basis in its subscription rights will be zero unless the holder elects to allocate its adjusted tax basis in the common stock owned by such holder in the manner described in the previous sentence. Holders exercising subscription rights will be notified by us in the event that the fair market value of the subscription rights on the date such subscription rights are distributed equals or exceeds 15% of the fair market value of the common stock on such date.

- A holder which allows the subscription rights received in the rights offering to expire will not recognize any gain or loss, and the tax basis in the common stock owned by such holder with respect to which such subscription rights were distributed will be equal to the tax basis in such common stock immediately before the receipt of the subscription rights in the rights offering.

- A holder will not recognize any gain or loss upon the exercise of the subscription rights received in the rights offering. The tax basis in the common stock acquired through exercise of the subscription rights will equal the sum of the subscription price for the common stock and the holder's tax basis, if any, in the rights as described above. The holding period for the common stock acquired through exercise of the subscription rights will begin on the date the subscription rights are exercised.

## PLAN OF DISTRIBUTION

On or about July 16, 2009, we will distribute the rights, rights certificates and copies of this prospectus to individuals who owned shares of common stock on the record date. We have not employed any brokers, dealers or underwriters in connection with the solicitation or exercise of rights in the rights offering and no commissions, fees or discounts will be paid in connection with the rights offering. While certain of our directors, officers and other employees may solicit responses from you, those directors, officers and other employees will not receive any commissions or compensation for their services other than their normal compensation. If you wish to exercise your subscription rights and purchase shares of common stock, you should complete the subscription rights certificate and return it with payment in cash and/or securities, as provided herein, for the shares of common stock, to the subscription agent, Computershare Inc., at the following address:

***By Mail:***

*Computershare  
c/o Voluntary Corporate Actions -  
Pharmacyclics Rights Offering  
Suite V  
P.O. Box 43011  
Providence, RI 02941-3011*

***By Overnight Delivery:***

*Computershare  
c/o Voluntary Corporate Actions -  
Pharmacyclics Rights Offering  
250 Royall Street  
Suite V  
Canton, MA 02021*

In the event that the rights offering is not fully subscribed, holders of rights who exercise all of their rights pursuant to their basic subscription privilege will have the opportunity to subscribe for unsubscribed rights pursuant to the over-subscription privilege. See further the section of this prospectus entitled "The Rights Offering."

We have not agreed to enter into any standby or other arrangement to purchase or sell any rights or any of our securities. Robert W. Duggan, which beneficially owns approximately 27% of our common stock, has indicated his intention to exercise all of his rights under the rights offering, but it has made no formal binding commitment to do so.

We have not entered into any agreements regarding stabilization activities with respect to our securities.

If you have any questions, you should contact the information agent, Georgeson Inc., 199 Water Street, New York, New York 10038 by telephone at (212) 806-6859 (call collect) or 800-279-5722 (toll-free) or by email at [pharmacyclics@gerogeson.com](mailto:pharmacyclics@gerogeson.com). We have agreed to pay the subscription agent and information agent a fee plus certain expenses, which we estimate will total approximately \$22,000. We estimate that our total expenses in connection with the rights offering will be approximately \$448,339.

We have engaged an investor relations firm to assist us in providing access to and enhancing relationships with our shareholders and the investment community.

Other than as described herein, we do not know of any existing agreements between any stockholder, broker, dealer, underwriter or agent relating to the sale or distribution of the shares of common stock.

## LEGAL MATTERS

The validity of the rights and shares of common stock offered by this prospectus have been passed upon for us by Olshan Grundman Frome Rosenzweig & Wolosky LLP, New York, New York.

## EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended June 30, 2008, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

## INCORPORATION BY REFERENCE

We incorporate by reference into this prospectus information we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is deemed to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede that information. This prospectus incorporates by reference the documents set forth below, that we have previously filed with the SEC. These documents contain important information about us and our financial condition.

- our Annual Report on Form 10-K for the year ended June 30, 2008, filed with the SEC on September 5, 2008;
- our Quarterly Reports on Form 10-Q for the period ended September 30, 2008, filed with the SEC on October 31, 2008, for the period ended December 31, 2008, filed with the SEC on February 13, 2009, and for the period ended March 31, 2009, filed with the SEC on May 12, 2009;
- our Current Reports on Form 8-K filed with the SEC on July 15, 2008, August 14, 2008, September 15, 2008, September 18, 2008, October 1, 2008, October 16, 2008, October 30, 2008, November 13, 2008, November 26, 2008, December 16, 2008, January 6, 2009, January 22, 2009, February 11, 2009, February 13, 2009, February 23, 2009, February 25, 2009, March 19, 2009, April 6, 2009, April 14, 2009, April 17, 2009, April 22, 2009, April 23, 2009, June 1, 2009 and June 5, 2009;
- our Definitive Proxy Statement on Schedule 14A filed with the SEC on October 28, 2008; and
- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on October 20, 1995, including any amendment or report filed for the purpose of updating that description.

All documents filed by us under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and prior to the date of the completion of the offering of the securities described in this prospectus shall also be deemed to be incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents. Any statement contained in this prospectus or in a previously filed document incorporated or

deemed to be incorporated by reference in this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document that also is or was deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

The information relating to us contained in this prospectus should be read together with the information in the documents incorporated by reference. Documents incorporated by reference are available from us without charge, excluding any exhibits to those documents, unless the exhibit is specifically incorporated by reference as an exhibit in this document. You can obtain documents incorporated by reference in this document, at no cost, by requesting them in writing or by telephone from us at the following address or telephone number:

Pharmacyclics, Inc.  
Attention: Corporate Secretary  
995 E. Arques Avenue  
Sunnyvale, California 94085-4521  
(408) 774-0330

#### **WHERE YOU CAN FIND ADDITIONAL INFORMATION**

We file reports, proxy statements and other information with the SEC. Information filed with the SEC can be inspected and copied at the public reference facilities maintained by the SEC at Headquarters Office, 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Section of the SEC, Headquarters Office, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. Further information on the operation of the SEC's public reference room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website that contains reports, proxy statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

We filed a registration statement on Form S-3 to register with the SEC the securities offered by this prospectus. This prospectus is a part of that registration statement. As allowed by the rules of the SEC, this prospectus does not contain all of the information you can find in our registration statement or the exhibits to the registration statement.

Our common stock is traded on the NASDAQ Global Market under the symbol "PCYC." Our website is located at <http://www.pharmacyclics.com>. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

