

What we discover today...
creates a wave of change for
a better tomorrow



Letter from the CEO & Chairman of the Board

Building Shareholder Value

Dear Shareholder:

Much has changed in Pharmacyclics corporate development in my brief tenure as Chairman and CEO. The company now has a new board, a new management team, a revitalized strategic direction and a new vigor to achieve significant goals and shareholder value in the coming years.

We are focused on validated molecular targets addressing large unmet medical needs. We have a robust pipeline of four drugs in active clinical trials, several additional programs in late stage lead optimization and an immense patent estate. Each program is being tested in several disease areas to reduce development risk. We utilize molecular biomarkers and predictive screening techniques to target the right drug to the right patient at the right time with the right dose. This greatly reduces the time, cost and risk of clinical programs.

We have highly motivated scientists who collectively hold a large ownership stake in the company. We have a management team that has shown they can conclude corporate partnerships to accelerate drug development. The excitement and encouragement we receive from scientific leaders in the field of immune mediated disease and cancer is exceptional.

I wish to extend my appreciation to all shareholders and I want you to know that in my opinion the work we are engaged in is work worth doing. I, along with my fellow employees, will continue to do everything in our power to make our work worthwhile to all our stakeholders. Please do not hesitate to contact me or other executives at any time with any question you may have. We are here to serve our patients, employees and shareholders.

Sincerely yours

Bob Duggan
CEO & Chairman of the Board



Company Background


Developing a pipeline of novel pharmaceutical drugs for large unmet medical needs

Pharmacyclics Inc. is a clinical-stage biopharmaceutical company focused on developing and commercializing innovative small-molecule drugs for the treatment of immune mediated disease and cancer. 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 three drug candidates under preclinical development. They include:

- » a Bruton's tyrosine kinase (Btk) inhibitor (PCI-32765) currently in a Phase I clinical trial targeting oncology applications and a second Btk inhibitor in advanced preclinical lead optimization and testing targeting autoimmune and allergic indications;
- » a histone deacetylase inhibitor (PCI-24781) about to enter a Phase II clinical trial targeting oncology applications;
- » an inhibitor of Factor VIIa (PCI-27483) soon to be in a Phase II clinical trial, targeting oncology applications;
- » Motexafin gadolinium (MGd) is in two Phase II trials for patients with primary brain tumors;
- » an HDAC8 inhibitor lead (PCI-34051) that is currently being optimized for autoimmune and cancer indications.

To learn about our drugs and to get further explanations and definitions of technical terms please go to www.pharmacyclics.com. If you would like to enroll in one of our trials please call: 408-774-0330

Program	Preclinical	Phase I	Phase II	Phase III
BTK Inhibitors				
PCI-32765 Lymphomas				
Autoimmune Disorders				
PCI-4 series Autoimmune Disorders				
HDAC Inhibitors				Partner
PCI-24781 Lymphomas				
Solid Tumors				
PCI-34051 (HDAC8) Oncology/Inflammation				
Factor VII Inhibitor				
PCI-24783 Pancreatic Cancer				
Motexefin Gadolinium				
Glioblastoma				
Glioma				

Bruton's Tyrosine Kinase Inhibitor

Developing the first small molecule inhibitor of a critical signaling gate for B-cells

Phase I

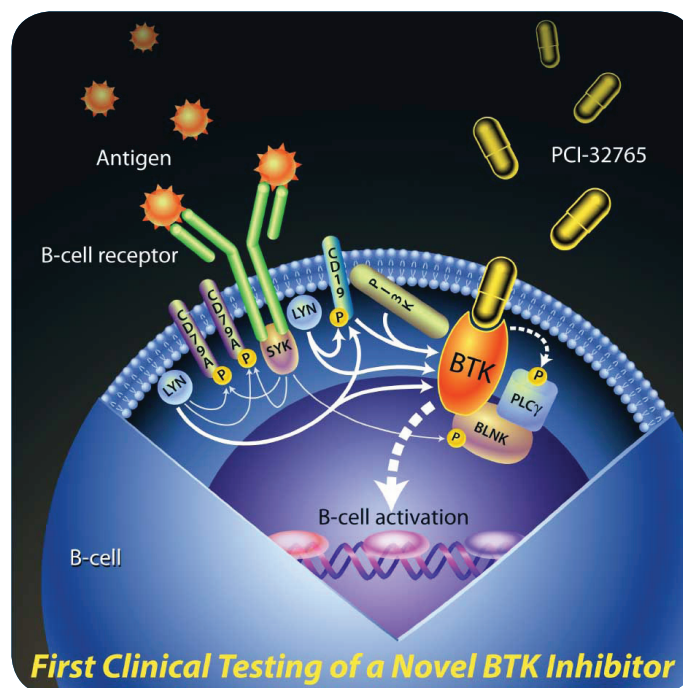
PCI-32765 is an oral small molecule tyrosine kinase inhibitor that targets an enzyme, Bruton's tyrosine kinase (BTK), which is required for B-cell activation and mast cell function.

B-cells are lymphocytes with multiple functions in immune response, including antigen presentation, antibody production and cytokine release. Pharmacyclics is currently conducting a Phase I clinical trial in patients with relapsed/refractory B-cell non-Hodgkin's lymphoma (NHL). Our Phase I study is evaluating the safety, pharmacokinetics and pharmacodynamics of PCI-32765. We are utilizing a novel and proprietary pharmacodynamic assay to directly assess BTK inhibition by PCI-32765 in patients and we believe this assay will greatly accelerate the clinical development program. This is the first BTK selective inhibitor to be tested in humans.

PCI-32765 is a novel therapeutic treatment of a variety of B-cell mediated diseases. These include not only oncology applications such as lymphoma, but also autoimmune diseases such as rheumatoid arthritis, Crohn's, multiple sclerosis, idiopathic thrombocytopenic purpura, Sjorgren's, and many others.

Our scientists have also discovered that BTK is critically involved in mast cell degranulation, an important contributor in allergy and asthma. Pharmacyclics is planning to initiate a healthy volunteer study of PCI-32765 in the second half of 2009. Disease areas that such a therapeutic could target are: asthma, allergic rhinitis, food hypersensitivity (peanut, egg, seafood), atopic dermatitis and urticaria.

Anti-B-cell biologics such as Rituxan® and Lymphostat B® cause B-cell depletion and are not orally dosed. The overall non-Hodgkin's lymphoma market is projected to increase from \$3.3 billion in 2007 to \$4.7 billion in 2017. The potential market size in autoimmune indications as an orally administered DMARD is



even larger. Anti-TNF therapies such as Enbrel® and Humira® are T-cell specific with inconvenient subcutaneous injection dosing. Current aggregate market size of anti-TNF therapies is \$5 billion. The market for rheumatoid arthritis (RA) therapies will show robust growth between 2009 and 2017; major market sales are projected to nearly double to \$13.4 billion by 2017. We believe market opportunities in other indications and potential future applications in mast cell mediated diseases such as urticaria, interstitial cystitis, and rhinitis are also quite large.

For further explanation and definitions of technical terms, go to www.pharmacyclics.com/wt/page/btk_inhibitor_pci_32765

Factor VIIa Inhibitor

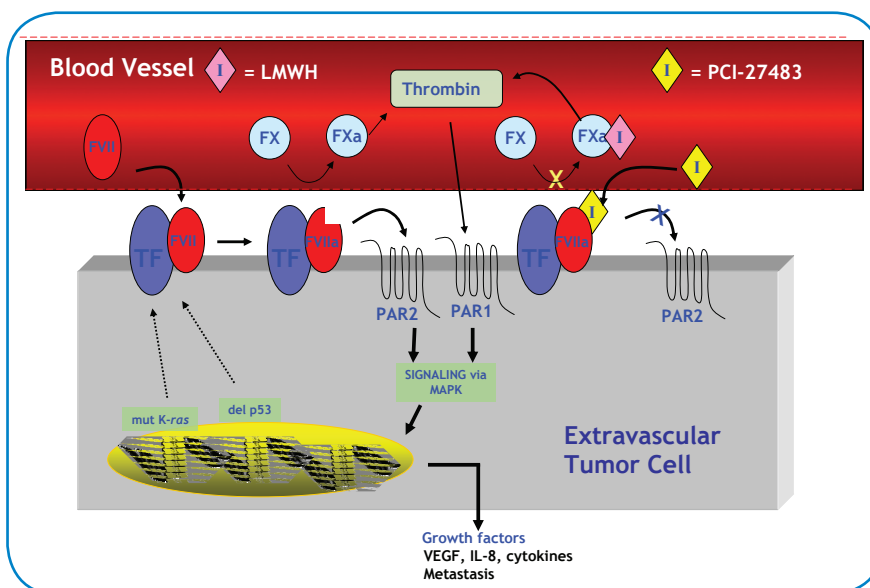
Developing the first small molecule inhibitor of Factor VII

Entering Phase II

Factor VII is a blood protein with a critical controlling function in blood clotting. Many types of cancer, such as lung, breast, pancreatic, colorectal, gastric and others, express high levels of a cell surface protein known as tissue factor (TF). After binding to TF, the Factor VIIa/TF complex becomes activated and triggers a host of pathologic processes in the tumor microenvironment that facilitates growth, invasion and metastasis of many cancers. Furthermore, studies have shown that many tumors historically associated with an increased TF expression have an increased incidence of life threatening venous thromboembolism.

PCI-27483 potently and selectively targets the FVIIa and the tissue factor complex. PCI-27483 has a dual activity profile: it inhibits tumor growth directly and inhibits thromboembolic complications seen in cancer patients with high TF expressing tumors. Preclinical models of thrombosis in several species have indicated that a selective inhibitor of the FVIIa/TF complex may have a greater therapeutic/safety index than inhibition of other coagulation factors.

Pharmacyclics is currently preparing for initiation of a Phase II trial that will evaluate PCI-27483's effect in patients with pancreatic cancer. Patients diagnosed with pancreatic cancer have a 5-year survival rate of less than 3%, making pancreatic cancer one of the most deadly forms of cancer. Worldwide there were approximately 250,000 patients with pancreatic cancer incidence



in 2007. Recent clinical studies have shown that approximately 90% of pancreatic cancers express TF and also about 25% have VTEs (Venous Thromboembolisms). We also believe there is great opportunity for this drug in addressing the high incidence of gastric cancer in Asia. This cancer type also expresses large amounts of TF and is a clear unmet medical need.

For further explanation and definitions of technical terms, go to www.pharmacyclics.com/wt/page/pci_27483

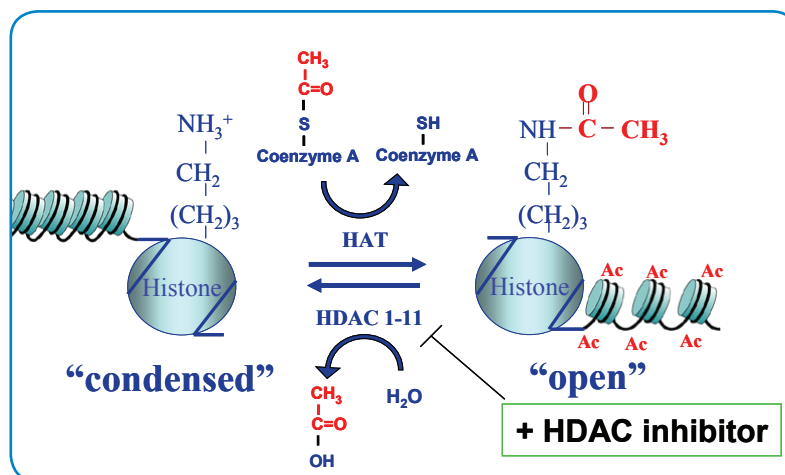
Histone Deacetylase Inhibitor (HDAC)

Developing a less toxic HDACi for use in a wide variety of cancers

Entering Phase II

Histone deacetylase inhibitors (HDAC) inhibitors induce differentiation of cancer cells and block cancer cell proliferation. PCI-24781 is a novel, potent, orally active small molecule inhibitor of HDAC that has substantial anti-tumor activity in many preclinical tumor models (Buggy et al Mol Cancer Ther 2006; 5 (5), p. 1309-1317) and activity against primary human tumors from patients with colon, ovarian, lung and many hematological cancers. PCI-24781 treatment leads to synergistic efficacy in tumor cells in combination with chemotherapeutic agents including platinum agents, inhibitors of NF- κ B, PARP inhibitors as well as radiation. PCI-24781 has an optimized half life, oral bioavailability, potency, and duration of exposure to achieve an ideal balance of efficacy with minimal toxicity.

A number of HDAC inhibitors are in advanced clinical studies, many being used in combination with chemotherapy, and we expect good news from the field as a whole. PCI-24781 is ideally positioned in the competitive HDAC market. Competitors are often weakly potent, toxic or not orally bioavailable. Since these drugs are limited by significant toxicities including fatigue, nausea and cardiotoxicities, they consequently have narrow therapeutic windows.



To date, over 70 patients have been treated with PCI-24781. Single agent stable disease has been achieved in a number of solid tumor histologies including colon, gall bladder, prostate, medullary thyroid and fibrosarcoma. Clinical responses have also been recorded in lymphoma including follicular, SLL, CTCL, Hodgkin's and PTCL.

For further explanation and definitions of technical terms, go to www.pharmacyclics.com/wt/page/hdac

Motexafin Gadolinium (MGd)

Awaiting survival data on two Phase II trials

Phase II

MGd is a radiation and chemotherapy sensitizing agent with a novel mechanism of action. MGd is designed to accumulate selectively in cancer cells and induce 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. Currently, MGd is under

evaluation in multicenter studies sponsored by the NCI, including a Phase II trial in adults with newly diagnosed glioblastoma and a Phase II trial in children with brain stem gliomas.

For further explanation and definitions of technical terms, go to www.pharmacyclics.com/wt/page/xcytrin

Scientific Advisory Board

Our new Scientific Advisory Board includes two former ASCO Presidents (Drs. Paul Bunn from University of Colorado and Margaret Tempero, Director of Clinical Sciences at UCSF); one former FASEB President (Dr. Frederick Rickles) and one former AACR President (Dr. Daniel Von Hoff). Dr. Von Hoff has been involved in 33 of the last 36 oncology drug submissions to the FDA. Dr. Steven Weitman was recently the principal investigator in clinical trials for the first pediatric drug approved in over 30 years (clofarabine). Dr. Branimir Sikic is Co-Director of Stanford's Center for Clinical Development and a renowned expert in oncology. Dr. Barton Kamen is CMO of the Leukemia and Lymphoma Society and pioneer of metronomic dosing. Dr. Edward Sausville is a

Daniel D. Von Hoff, MD, PhD (TGen Institute, Arizona)
Physician in Chief & Director; CSO of US Oncology, past AACR President

Branimir I. Sikic, MD (Stanford University)
Co-Director, Stanford Center for Clinical and Translational Education and Research Director, Clinical and Translational Research Unit

Mark C. Genovese, MD (Stanford University)
Co-Chief of Immunology & Rheumatology, 2008 Henry Kunkel Award (ACR)

Paul Bunn, MD (University of Colorado)
James Dudley Endowed Chair of Cancer Research, Past ASCO President

Margaret Tempero, MD (University of California, San Francisco)
Chaired Professor; Deputy Director & Director Clinical Sciences, Past ASCO President

Edward A. Sausville, MD (University of Maryland)
Professor of Medicine, former Associate Director, Division of Cancer Treatment & Diagnosis of NCI

Steven D. Weitman, MD (Industry Consultant)
PI of clofarabine

Barton A. Kamen, MD, PhD (CMO Leukemia and Lymphoma Society)
Executive VP & Chief Medical Officer; Professor, Pediatrics & Pharmacology at Robert Wood Johnson Medical School

Randall K. Johnson, PhD (Industry Consultant)
Former Head of SmithKline/GSK Oncology, NIH, over 30 years experience with cancer drugs

Leaders in the Field Helping to Guide the Way

former Associate Director at the NCI and an expert on preclinical models. Dr. Randall Johnson is former head of GSK oncology and a world famous chemist. Dr. James Abruzzese is Chairman of Gastrointestinal Oncology at MD Anderson. Dr. Minesh Mehta is Chairman of Radiology at the University of Wisconsin and has pioneered many ground breaking clinical trials. Dr. David Smith is a former FDA oncology reviewer and world class clinical trial statistician. Dr. Mark Genovese is Co-Chair of Rheumatology at Stanford and an industry expert in development of new medicines. This team is sharing cutting edge science, strategy, and clinical and regulatory advice. Importantly, all are great advocates and emissaries of our science and drugs.

James L. Abruzzese, MD (MD Anderson)
Chairman, Department of Gastrointestinal Medical Oncology; M.G. and Lillie A. Johnson Chair for Cancer Treatment

Minesh P. Mehta, MD (University of Wisconsin)
Professor of Medicine, Chair of FDA Radiological Devices Panel, International Expert on CNS tumors

Frederick R. Rickles, MD (George Washington University)
Professor of Medicine, Pediatrics, Pharmacology & Physiology, former Exec Director of FASEB

David Smith, PhD (City of Hope)
Senior Biostatistician, former FDA Oncology Division Reviewer





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