



## **Pharmacyclics Reports Recent Developments From Clinical Studies of its Btk Inhibitor PCI-32765**

SUNNYVALE, Calif., June 6, 2011 /PRNewswire/ -- Pharmacyclics, Inc. (Nasdaq: PCYC) today announced data from the oral presentation of the Phase IB/II study of the Btk inhibitor, PCI-32765, in chronic lymphocytic leukemia / small cell lymphocytic lymphoma (CLL/SLL) at the 2011 American Society of Clinical Oncology Annual Meeting. The company will also provide a clinical development program update for the Btk Inhibitor, PCI-32765. The update will include 1) efficacy from the Phase IA trial of PCI-32765 in B-cell malignancies including mantle cell lymphoma, follicular lymphoma and diffuse large B-cell lymphoma and 2) a status update for ongoing PCI-32765 clinical studies, and 3) an update on future clinical trials including program expansion opportunities in follicular lymphoma and multiple myeloma. The company will also provide information on the Non-Hodgkins Lymphoma (NHL) market. An investor conference call to discuss the clinical trial results and other company updates will be hosted today at 4:30pm ET, further information is provided below. Slide presentations will be posted on the Pharmacyclics website including the ASCO presentation of the Phase IB/II study results and the Investor Relations presentation.

### **Data Results from the Phase IB/II Study in CLL/SLL as presented at ASCO**

The oral presentation, titled "Activity and tolerability of the Bruton's tyrosine kinase (Btk) inhibitor PCI-32765 in patients with chronic lymphocytic leukemia/small cell lymphocytic lymphoma (CLL/SLL): Interim results of a Phase Ib/II study" was being presented by John C. Byrd, MD today. The presentation included interim data from a single-agent, multi-cohort study evaluating PCI-32765 in CLL/SLL patients with relapsed/ refractory disease or with treatment-naïve disease who were 65 years of age or older. A daily oral dose of 420mg was tested initially, and an additional cohort of patients with relapsed/ refractory disease treated with 840mg daily was enrolled following closure of the 420mg qD relapsed/ refractory cohort. This group of patients had a shorter median follow-up time and were included only for initial response assessment and summary safety data.

Overall, PCI-32765 has been well-tolerated; discontinuation of treatment for adverse events occurred in only 3 of 83 patients. Diarrhea, nausea/ vomiting, and dyspepsia were the most frequently reported events and were typically of modest severity. Significant neutropenia and thrombocytopenia were uncommon in the 420mg qD cohorts, but more frequently observed (18%, 9% respectively) in the 840mg qD cohort in spite of the shorter follow-up. As previously reported, a characteristic pattern of response occurred in the CLL patients, with rapid reduction of lymph node disease and a corresponding initial phase of lymphocytosis. The resolution of lymphocytosis was more rapid in treatment-naïve versus relapsed/ refractory patients, corresponding to a more rapid evolution of overall response per standard criteria in treatment-naïve patients. At a median follow-up of 6.3 months, 67% of patients with treatment-naïve disease had achieved an overall response by standard criteria, with an additional 19% of patients achieving a nodal response. At a median follow-up of 7.8 months in the cohort of relapsed/ refractory patients treated with 420mg qD, the rate of overall objective response was 48% with an additional 41% of patients having achieved a nodal response. The initial response assessment at 2 months in patients with relapsed/ refractory disease appeared similar between the 420mg qD and 840mg qD doses. Additionally, achieving response appeared to be independent of poor-risk features, such as del (17p), del (11q), and lack of mutation in the immunoglobulin heavy chain variable region gene. To date, only three patients have experienced disease progression, and 81% of relapsed/ refractory patients in the more mature 420mg qD cohort are on treatment and free-of-progression at 6 months.

### **Update and Highlights of the PCI-32765 Clinical Development Program**

#### ***Phase IA Study in B-Cell Malignancies - Updated Results***

The previously reported Phase IA trial of PCI-32765 in patients with relapsed or refractory B-cell malignancies was updated. No significant changes in the safety profile have emerged with longer follow-up of this trial. Low-grade diarrhea, fatigue, cough, nausea, and headache were the most frequently reported adverse events; significant neutropenia and thrombocytopenia were uncommon. With longer follow-up, the objective response rate in evaluable patients with CLL/SLL (now 11/14, 79%) and follicular lymphoma (now 6/13, 46%) improved as compared to December 2010. Twenty-two patients remain on the treatment, including five of the nine mantle cell lymphoma patients enrolled in the study.

#### ***Broad Clinical Development Progress for Btk Inhibitor PCI-32765 in B-cell Malignancies***

In 2010-2011, Pharmacyclics initiated a Phase II clinical development program in chronic lymphocytic leukemia, mantle cell lymphoma and diffuse large B-cell lymphoma. This program was designed to allow for Phase III decisions in these indications based upon ongoing analysis of the clinical data. We have enrolled over 220 patients to date on trials of PCI 32765.

Throughout 2011 we will continue to execute this clinical trials program, and will analyze data from these trials on an ongoing basis. Below is an update on each of our current PCI-32765 clinical development programs.

**-- Chronic Lymphocytic Leukemia / Small Cell Lymphocytic Lymphoma (CLL/SLL)**

Our CLL/SLL program has enrolled 137 patients through May 2011. We have completed enrollment of 87 patients in the Phase IB/II CLL/SLL single-agent study noted above. The interim results of this study were presented today at the 2011 Annual Meeting of ASCO and the full ASCO presentation is posted on our website.

Two ongoing studies, initiated in Q1 2011, are evaluating PCI-32765 in combination with standard therapies for CLL/SLL. We have enrolled 34 patients in these studies and anticipate completing enrollment in 2011.

From these studies, we expect to be able to analyze initial 3-month safety data for ofatumumab/PCI-32765 and bendamustine/rituximab/PCI-32765 in the second half of 2011. To date the preliminary safety data from these combination studies suggests that these combinations are likely to be safe.

Based on the significant single-agent activity in CLL/SLL from the ongoing Phase IB/II trial, and contingent upon confirmation of 3-month combination safety data, Phase III planning is currently underway. We expect to initiate a Phase III study in CLL/ SLL in the first half of 2012.

**-- Mantle Cell Lymphoma (MCL)**

A Phase II study of single-agent PCI-32765 in relapsed or refractory MCL (PCYC-1104) began enrolling patients in late February 2011. To date, we have enrolled 30 patients on this trial and anticipate completing enrollment by the end of calendar 2011. Initial review of early data from this ongoing study suggests that the high overall response rate observed in Phase I is likely to be similar in Phase II. We anticipate submitting an abstract with interim results for presentation at the 2011 American Society of Hematology (ASH) Meeting. Contingent upon the ongoing analysis of PCYC-1104, we will soon begin Phase III planning in MCL. We anticipate that a Phase III study will be initiated in 2012.

**-- Diffuse Large B-Cell Lymphoma (DLBCL)**

A multicenter, open-label, Phase II study of PCI-32765 in patients with relapsed or refractory DLBCL (PCYC-1106) began enrollment in May 2011. This study is designed to assess the activity of PCI-32765 in two genetically distinct subtypes of DLBCL, the activated B-cell (ABC) subtype and the germinal center (GC) subtype. We have enrolled 3 out of the planned 60 patients and expect to complete enrollment in the first quarter of calendar 2012. Other trials evaluating the combination of PCI-32765 with chemotherapy in DLBCL are under development.

A separate pilot study of PCI-32765 in patients with ABC subtype DLBCL is currently being conducted at the NIH Clinical Center. Thus far, 8 out of a planned 10 patients have been enrolled. While it is too early to report full results of this study, objective responses, including complete responses, have been observed. We anticipate that this study once completed will be submitted for presentation at the 2011 American Society of Hematology Meeting

**-- Follicular Lymphoma (FL)**

Updated results from the Phase IA study have shown an improvement in the objective response rate in follicular lymphoma. We are encouraged by this preliminary signal and are developing a Phase II program in this histology. We anticipate the initiation of a Phase II trial in follicular lymphoma in the first half of 2012.

**-- Multiple Myeloma (MM)**

Ongoing pre-clinical studies, both internally as well as through external collaborations, have suggested a vital role for Btk in both malignant plasma cells and osteoclasts, which are involved in the bone complications of this disease. Therefore, we believe that Btk represents a viable therapeutic target in MM, and we are developing a Phase II trial of PCI-32765 in MM, which we expect to initiate in early 2012.

"In February 2009 Pharmacylics dosed the first patient with PCI-32765, a Bruton tyrosine kinase irreversible inhibitor. Bottom line, we have now dosed 230 patients across multiple hematologic histologies. The results have exceeded the expectations of most all involved to this point in time. We look forward to continued progress as well as playing a meaningful role in the coming new era of patient friendly oncology therapy," said Mr. Duggan, CEO and Chairman of the Board.

**ASCO Conference Call and Webcast Details**

Date: Monday, June 6, 2011

Time: 4:30 pm ET

Participant Dial In (Toll Free): 877-407-8133

Participant Dial In (International): 201-689-8040

Slides used in the ASCO presentation from today and during the conference call are posted on the Investor Relations Section of our website, under Events & Webcasts: <http://ir.pharmacylics.com/events.cfm>

To access the live audio broadcast or the subsequent archived recording, log on to <http://ir.pharmacylics.com/events.cfm>. The archived version of the webcast will be available for 30 days on the Investor Relations section of the company's Web site at

### **Large unmet needs in Non-Hodgkin's Lymphoma (NHL) Market**

There are over 25 distinct subtypes of B-cell malignancies; the common NHLs include the following: follicular lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma, diffuse large B-cell lymphoma and mantle cell lymphoma. The NHL therapy market will experience robust annual growth (7.6% per year) and more than double in size over the years 2009-2019 from approximately \$4.1 billion in 2009 to approximately \$8.4 billion in 2019, as forecasted by Decision Resources, Inc. in the Non-Hodgkin's Lymphoma Onkos Study, April 2011.

There are significant and distinct areas of unmet medical need across the NHL subtypes. Within the indolent lymphomas, we believe a need exists for active therapies that avoid the toxicities typically seen with conventional chemotherapies. Such active therapies are needed as part of effective combinations early in the course of treatment, and also as effective single-agent treatments later in the course of disease progression. In particular, drugs which are well tolerated and which do not limit subsequent treatment options because of bone marrow or other organ toxicity are demanded. In the aggressive lymphomas, it is our belief that the need exists for agents that can combine with standard therapies to improve cure rate, and for agents that are effective in patients that fail potentially curative therapy.

A typical treatment of NHL includes a diverse combination of chemotherapies in addition to rituximab or other monoclonal antibodies. Such treatments, particularly in combination, can exceed a cost of \$100,000 for a 12-month treatment period.

In the major pharmaceutical markets in the US, Europe and Japan, Decision Resources, Inc. estimates the following for 2011: There are 305,440 prevalent cases living with DLBCL, with 50,180 patients estimated to be in the first line setting and 34,320 patients estimated to be in the relapsed/refractory setting. CLL/SLL constitutes about one-third of the B-cell malignancy population. There are 172,630 prevalent cases living with CLL, with 39,390 patients estimated to be in the first line setting and 33,550 patients estimated to be in the relapsed/refractory CLL setting. Follicular lymphoma (FL) constitutes about 20% of the B-cell malignancy population and is considered an indolent, yet incurable, disease. There are 136,450 prevalent cases living with FL, with 21,050 patients estimated to be in the first line setting and 14,270 patients estimated to be in the relapsed/refractory setting. MCL, generally an aggressive form of lymphoma, comprises approximately 5% of the newly diagnosed B-cell malignancies. There are 32,180 prevalent cases living with MCL, with 5,300 patients estimated to be in the first line setting and 4,140 patients estimated to be in the relapsed/refractory setting.

The prevalence of NHL is large and according to the Leukemia & Lymphoma Society, in 2010 there were approximately 475,000 people in the United States alone living with NHL (active disease or in remission).

### **About Pharmacyclics**

Pharmacyclics® is a clinical-stage biopharmaceutical company focused on developing and commercializing innovative small-molecule drugs for the treatment of cancer and immune mediated diseases. Our mission and goal is to build a viable biopharmaceutical company that designs, develops and commercializes novel therapies intended to improve quality of life, increase duration of life and resolve serious unmet medical healthcare needs; and to identify promising product candidates based on scientific development expertise, develop our products in a rapid, cost-efficient manner and pursue commercialization and/or development partners when and where appropriate.

Presently, Pharmacyclics has four product candidates in clinical development and several preclinical molecules in lead optimization. We are committed to high standards of ethics, scientific rigor, and operational efficiency as we move each of these programs to viable commercialization.

The Company is headquartered in Sunnyvale, California and is listed on NASDAQ under the symbol PCYC. To learn more about how Pharmacyclics advances science to improve human healthcare visit us at <http://www.pharmacyclics.com>.

**NOTE:** This announcement may contain forward-looking statements made in reliance upon the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations and beliefs regarding our future results or performance. Because these statements apply to future events, they are subject to risks and uncertainties. When used in this announcement, the words "anticipate", "believe", "estimate", "expect", "expectation", "should", "would", "project", "plan", "predict", "intend" and similar expressions are intended to identify such forward-looking statements. Our actual results could differ materially from those projected in the forward-looking statements. Additionally, you should not consider past results to be an indication of our future performance. For a discussion of the risk factors and other factors that may affect our results, please see the Risk Factors section of our filings with the Securities and Exchange Commission, including our annual report on Form 10-K and quarterly reports on Form 10-Q. We do not intend to update any of the forward-looking statements after the date of this announcement to conform these statements to actual results, to changes in management's expectations or otherwise, except as may be required by law.

