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Updated Results of Two Phase 2 ibrutinib Studies in Patients with Mantle Cell Lymphoma or Diffuse Large B-cell Lymphoma

SUNNYVALE, Calif., June 16, 2013 /PRNewswire/ -- Pharmacyclics, Inc. (the "Company") (Nasdaq: PCYC) today announced the results of two separate Phase 2 studies suggesting that ibrutinib, an investigational oral Bruton's tyrosine kinase (BTK) inhibitor, showed efficacy when used as a monotherapy in patients with relapsed/refractory mantle cell lymphoma (MCL) or diffuse large B-cell lymphoma (DLBCL). Pharmacyclics sponsored both studies and is jointly developing ibrutinib with Janssen Research & Development, LLC. The data were presented today at the European Hematology Association (EHA) 18th Annual Congress in Stockholm, Sweden.

The findings presented at EHA for patients with MCL or DLBCL expand on the results reported by investigators last year at the American Society of Hematology Congress in December 2012. Ibrutinib was shown to achieve the following key results among patients with relapsed/refractory MCL:

- An overall response rate (ORR) of 68%, including a complete response (CR) of 21% where all signs of cancer are gone, and a partial response (PR) of 47%.
- The estimated median duration of response (DOR) in all responding patients was 17.5 months. The median progression-free survival (PFS) was 13.9 months, and the median overall survival (OS) has not yet been reached, but is estimated to be 58% at 18 months.
- Treatment-emergent adverse events (AEs) reported in greater than 20% of patients included diarrhea (50%), fatigue (41%), nausea (31%), peripheral edema (28%), dyspnea (27%), constipation (25%), upper respiratory tract infection (23%), vomiting (23%) and decreased appetite (21%) and were consistent with previously reported data. Only 8 patients discontinued due to an AE.

Professor Simon Rule, Consultant Haematologist in the Department of Haematology at the Derriford Hospital in Plymouth, United Kingdom, presented the results of this study at the EHA Congress today. He explained, "To see these results from a single agent among MCL patients is quite significant and very promising. The fact that response rates continued to increase over time, with no new safety signals, is particularly reassuring."

In the second study among relapsed/refractory DLBCL patients, investigators examined whether ibrutinib would be more active in the Activated B-cell-like (ABC) subtype of DLBCL compared to the Germinal Center B-cell-like (GCB) subtype. The ABC subtype of DLBCL is dependent on the B-cell antigen receptor (BCR) pathway, of which BTK is a key element. Ibrutinib selectively inhibits BTK, with the aim of inhibiting malignant B-cell growth and proliferation. Results of this study show that:

- Patients with the ABC subtype showed a preferential response to ibrutinib monotherapy compared to those with the GCB subtype (ORR = 41% vs 5%, respectively, p=0.007, Fisher's exact test).
- Median overall survival (OS) was 9.7 months for the ABC subtype, compared to 3.35 months for the GCB subtype.
- Safety data from 70 patients identified no new safety signals. Grade 3 or higher AEs were seen in greater than 3% of patients and included fatigue (9%), hyponatremia (9%), pneumonia (7%), dehydration (4%), and pleural effusion (4%).

"These results indicated that ibrutinib monotherapy was an effective treatment for some study patients who had ABC-subtype DLBCL," noted presenting investigator Sven de Vos, M.D., Ph.D., Associate Professor in the Department of Medicine at the UCLA Medical Center, Los Angeles, U.S.A., who presented the results at the EHA Congress today. "Given that patients with the ABC-subtype of DLBCL are difficult to treat, these results are very promising."

About Ibrutinib
Ibrutinib was designed to specifically target and selectively inhibit an enzyme called BTK. BTK is a key mediator of at least three critical B-cell pro-survival mechanisms occurring in parallel — regulation of apoptosis, cell adhesion and cell migration and homing.

The effectiveness of ibrutinib alone or in combination with other treatments is being studied in several B-cell malignancies, including chronic lymphocytic leukemia/small lymphocytic lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, Waldenstrom's macroglobulinemia and multiple myeloma. To date 7 Phase III trials have been initiated with ibrutinib and a total of 30 ongoing trials are currently registered on http://www.clinicaltrials.gov/. Janssen Biotech, Inc. and Pharmacyclics entered a collaboration and license agreement in December 2011 to co-develop and co-commercialize ibrutinib.

About the MCL Study

111 patients with relapsed/refractory MCL were treated with ibrutinib in this Phase 2 multicenter, open-label, study at 18 sites internationally and had received a median of three prior therapies. Patients were divided into two cohorts based on prior bortezomib exposure — either bortezomib-naive (n=63) or bortezomib-exposed (n=48). Both groups received 560 mg of ibrutinib orally, once a day until disease progression or no longer tolerated by the patient. The primary endpoint of the study was ORR, with secondary endpoints being DOR, PFS, OS and frequency and severity of AEs.

When a disease is described as 'relapsed', it means that it has returned after an initial partial or total remission.[1] 'Refractory' refers to cancer that has become resistant to current treatment.[2]

About the DLBCL Study
The DLBCL study was a Phase 2 multicenter, open-label, study. 70 patients with relapsed/refractory DLBCL with a median of three prior therapies were enrolled, all of whom underwent gene expression profiling to determine which DLBCL subtype they had. All patients received ibrutinib 560 mg orally, once a day, until disease progression or no longer tolerated by the patient. The primary objective of the study was to assess ORR categorized by subtype. Secondary objectives were to assess the safety and tolerability of ibrutinib in people with DLBCL.

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 with partners when and where appropriate.

Presently, Pharmacyclics has three product candidates in clinical development and several preclinical molecules in lead optimization. The Company is committed to high standards of ethics, scientific rigor, and operational efficiency as it moves 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, among others, relating to our future capital requirements, including our expected liquidity position and timing of the receipt of certain milestone payments, and the sufficiency of our current assets to meet these requirements, our future results of operations, our expectations for and timing of ongoing or future clinical trials and regulatory approvals for any of our product candidates, and our plans, objectives, expectations and intentions. 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", "goal", "should", "would", "project", "plan", "predict", "intend", "target" and similar expressions are intended to identify such forward-looking statements. These forward-looking statements are based on information currently available to us and are subject to a number of risks, uncertainties and other factors that could cause our actual results, performance, expected liquidity or achievements to differ materially from those projected in, or implied by, these forward-looking statements. Factors that may cause such a difference include, without limitation, our need for substantial additional financing and the availability and terms of any such financing, the safety and/or efficacy results of clinical trials of our product candidates, our failure to obtain regulatory approvals or comply with ongoing governmental regulation, our ability to commercialize, manufacture and achieve market acceptance of any of our product candidates, for which we rely heavily on collaboration with third parties, and our ability to protect and enforce our intellectual property rights and to operate without infringing upon the proprietary rights of third parties. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, performance or achievements and no assurance can be given that the actual results will be consistent with these forward-looking statements. For more information about the risks and uncertainties that may affect our results, please see the Risk Factors section of our filings with the Securities and Exchange Commission, including our transition report on Form 10-K for the six month period ended December 31, 2012 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.

References

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[1] PubMed Health. Relapse Definition. Available at: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0032674/def-item/glossary_CDR0000045866/?report=objectonly. Accessed November 19, 2012.
[2] PubMed Health. Refractory Cancer Definition. Available at: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0032674/def-item/glossary_CDR0000045863/?report=objectonly. Accessed November 19, 2012.

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