Ibrutinib Frontline Chronic Lymphocytic Leukemia Study Results Published in The Lancet Oncology

-- Estimated progression-free survival at 24 months was 96.3 percent in this Phase 1b/2 trial--

SUNNYVALE, Calif., Dec. 9, 2013 /PRNewswire/ -- Pharmacyclics, Inc. (NASDAQ: PCYC) today announced that The Lancet Oncology published results of a study evaluating ibrutinib in previously untreated elderly patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). The Phase 1b/2 open-label, multicenter study evaluated 31 patients, 65 years of age and older with CLL or SLL. The primary endpoint of the study was safety, as assessed by the frequency and severity of adverse events (AEs), while the secondary objectives assessed the clinical activity of single agent ibrutinib. Only one patient out of the 31 enrolled in this cohort has had progression of disease.

After a median follow-up of 22.1 months (range, 18.4-23.2), the overall response rate (ORR) for patients was 71 percent (95% CI, 52-86), which included 55 percent partial response, 3 percent nodular partial response and 13 percent complete response. An additional 13 percent of patients achieved a partial response with lymphocytosis. The median time to initial response was 1.9 months (range, 1.5-7.4); the median time to best response and complete response were 5.9 months (range, 1.8-22.1) and 12.0 months (range, 7.1-15.6), respectively.

Across all patients, the estimated progression-free survival (PFS) and overall survival at 24 months were 96.3 percent (95% CI, 76.5-99.5) and 96.6 percent (95% CI, 77.9-99.5), respectively.

"Older patients with CLL and SLL are at particularly high risk, and the standard of care therapies for these patients can often lead to significant and burdensome complications," said lead author Susan O'Brien, M.D., Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center. "There is a need for new treatment options, and we are encouraged by the high response rate and tolerability seen with ibrutinib as a first line therapy."

The majority of AEs that occurred were mild and Grade 1 or 2 in severity. Diarrhea was seen in 21 of 31 patients (68%) and was grade 1 in 14 of 31 patients (45%), grade 2 in three patients (10%), and grade 3 in four patients (13%). There were no episodes of grade 4 diarrhea. Nausea was predominantly grade 1 (12 of 31 patients; 39%), with a maximum grade of 2 (three of 31 patients (10%). Fatigue was seen in 10 of the 31 patients (32%), including five patients (16%) with grade 1, four (13%) with grade 2, and one (3%) with grade 3. Grade 3 infections were noted in three of the 31 patients (10%); no grade 4 or 5 infections were observed. There was one grade 3 neutropaenia and one grade 4 thrombocytopaenia. Two patients discontinued treatment for adverse events that included grade 3 fatigue in one patient and grade 2 viral infection in a second patient.

In this study, response to ibrutinib was assessed on the basis of the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) guidelines for CLL patients, with the exception that lymphocytosis was not a sole criterion for disease progression. Response in SLL patients was assessed by International Working Group for non-Hodgkin lymphoma (IWGNHL) 2007 criteria.

Earlier data from this study were presented at the annual meeting of the American Society of Hematology in December 2012 and the American Society of Clinical Oncology in June 2012. The study was sponsored by Pharmacyclics, Inc.

About CLL/SLL

CLL, a B-cell malignancy, is a slow-growing blood cancer of the white blood cells (lymphocytes), most commonly from B-cells. CLL is the second most common adult leukemia. Approximately 16,000 patients in the U.S. are diagnosed each year with CLL. The prevalence of CLL is approximately 113,000 in the U.S. CLL is a chronic disease that predominantly occurs in the elderly with a five-year survival of approximately 82 percent. Patients commonly receive multiple lines of treatment over the course of their disease. When cancer cells are located mostly in the lymph nodes, the disease is called SLL. CLL and SLL are considered to be different manifestations of the same underlying disease; they share similarities in signs and symptoms, genetic features, disease progression and treatment.

About IMBRUVICA™

IMBRUVICA™ (ibrutinib) is indicated for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy. This indication is based on overall response rate (ORR). An improvement in survival or disease-related
symptoms has not been established. For more information about IMBRUVICA, including the full prescribing information, please visit www.IMBRUVICA.com. IMBRUVICA is a first-in-class, oral therapy and is a new agent that inhibits a protein called Bruton's tyrosine kinase (BTK). BTK is a key signaling molecule of the B-cell receptor signaling complex that plays an important role in the survival of malignant B cells. IMBRUVICA blocks signals that tell malignant B cells to grow and divide uncontrollably. It is one of the first medicines to receive FDA approval via the new Breakthrough Therapy Designation pathway, enabling Pharmacyclics to rapidly bring this medicine to patients in need.

To date, nine Phase III trials have been initiated with IMBRUVICA and a total of 37 trials are currently registered on www.clinicaltrials.gov. Janssen and Pharmacyclics entered a collaboration and license agreement in December 2011 to co-develop and co-commercialize IMBRUVICA.

For more information, visit www.IMBRUVICA.com.

About Pharmacyclics

Pharmacyclics® is a 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 and administrative expertise, develop our products in a rapid, cost-efficient manner and pursue commercialization and/or development partners when and where appropriate.

Pharmacyclics markets IMBRUVICA and has two other 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.

Pharmacyclics 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 www.pharmacyclics.com.

The following safety information is described in the package insert for the use of IMBRUVICA in patients with mantle cell lymphoma who have received at least one prior therapy:

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - 5% of patients with MCL had ≥ Grade 3 bleeding events (subdural hematoma, gastrointestinal bleeding, and hematuria). Bleeding events including bruising of any grade occurred in 48% of patients with MCL treated with 560 mg daily. The mechanism for the bleeding events is not well understood. Consider the benefit-risk of ibrutinib in patients requiring antiplatelet or anticoagulant therapies and the benefit-risk of withholding ibrutinib for at least 3 to 7 days pre and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections - Fatal and non-fatal infections have occurred. At least 25% of patients with MCL had infections ≥ Grade 3, according to NCI Common Terminology Criteria for Adverse Events (CTCAE). Monitor patients for fever and infections and evaluate promptly.

Myelosuppression - Treatment-emergent Grade 3 or 4 cytopenias were reported in 41% of patients. These included neutropenia (29%), thrombocytopenia (17%) and anemia (9%). Monitor complete blood counts monthly.

Renal Toxicity - Fatal and serious cases of renal failure have occurred. Treatment-emergent increases in creatinine levels up to 1.5 times the upper limit of normal occurred in 67% of patients and from 1.5 to 3 times the upper limit of normal in 9% of patients. Periodically monitor creatinine levels. Maintain hydration.

Second Primary Malignancies - Other malignancies (5%) have occurred in patients with MCL who have been treated with IMBRUVICA, including skin cancers (4%) and other carcinomas (1%).

Embryo-Fetal Toxicity - Based on findings in animals, IMBRUVICA can cause fetal harm when administered to a pregnant woman. Advise women to avoid becoming pregnant while taking IMBRUVICA. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

ADVERSE REACTIONS
The most commonly occurring adverse reactions (≥ 20%) in the clinical trial were thrombocytopenia*, diarrhea (51%),
neutropenia*, anemia*, fatigue (41%), musculoskeletal pain (37%), peripheral edema (35%), upper respiratory tract infection (34%), nausea (31%), bruising (30%), dyspnea (27%), constipation (25%), rash (25%), abdominal pain (24%), vomiting (23%) and decreased appetite (21%).

*Treatment-emergent decreases (all grades) of platelets (57%), neutrophils (47%) and hemoglobin (41%) were based on laboratory measurements and adverse reactions.

The most common Grade 3 or 4 non-hematological adverse reactions (≥ 5%) were pneumonia (7%), abdominal pain (5%), atrial fibrillation, diarrhea (5%), fatigue (5%), and skin infections (5%). Treatment-emergent Grade 3 or 4 cytopenias were reported in 41% of patients. Ten patients (9%) discontinued treatment due to adverse reactions in the trial (N=111).

The most frequent adverse reaction leading to treatment discontinuation was subdural hematoma (1.8%). Adverse reactions leading to dose reduction occurred in 14% of patients.

**DRUG INTERACTIONS**

**CYP3A Inhibitors** - Avoid concomitant administration with strong or moderate inhibitors of CYP3A. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA dose.

**CYP3A Inducers** - Avoid co-administration with strong CYP3A inducers.

**SPECIAL POPULATIONS - Hepatic Impairment** - Avoid use in patients with baseline hepatic impairment.

Because everyone is different, it is not possible to predict what side effects any one patient will have. Patients with questions or concerns about side effects should talk to their doctor.

Report side effects to the FDA at (800) FDA-1088 or [http://www.fda.gov/medwatch](http://www.fda.gov/medwatch).

For more information please read the IMBRUVICA Full Prescribing Information at [www.IMBRUVICA.com](http://www.IMBRUVICA.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.

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