Pharmacyclics Highlights Important New Data for IMBRUVICA® (ibrutinib) in B-Cell Malignancies

Initial Presentation of Phase III RESONATE™ study and updated results in CLL of single agent IMBRUVICA and also CD20 combination to be presented during ASCO May 30 - Jun 3, 2014

Note: This release corresponds to abstracts 7014, 7009, TPS8611, TPS8615

SUNNYVALE, Calif., May 14, 2014 /PRNewswire/ -- Pharmacyclics, Inc. (NASDAQ: PCYC) today announced IMBRUVICA® (ibrutinib) will be featured in ten abstracts, including both company-sponsored research studies and investigator-sponsored studies. Preliminary data from these abstracts about IMBRUVICA is available as of today on the website of the American Society of Clinical Oncology (ASCO). Updated results will be presented at the 50th Annual Meeting of ASCO being held May 30 through June 3, 2014, in Chicago, IL.

The abstracts presented at ASCO include an oral presentation of long term ibrutinib follow up of 3 years, showing how single agent IMBRUVICA achieved durable responses in patients with treatment naive (TN) or relapsed/refractory (R/R) CLL/SLL including those with deletion 17p, as independently confirmed. The ASCO presentations also include longer term follow up of IMBRUVICA's use in combination with an antibody targeting CD20, ofatumumab. This study shows how the combination is well tolerated and highly active (83% ORR) in patients with previously treated R/R CLL/SLL in all dosing sequences investigated.

“Presentations at ASCO showcase IMBRUVICA's long-term efficacy and safety profile as a single agent, even in high-risk patients, as well as high response rates with long-term durability when IMBRUVICA is administered in combination with an antibody targeting CD20,” said Bob Duggan, CEO and Chairman of the Board, Pharmacyclics.

Oral Presentations
The "Randomized comparison of ibrutinib versus ofatumumab in relapsed or refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma: Results from the phase III RESONATE trial" (Abstract #LBA7008) data have been accepted for presentation at the meeting and are embargoed until May 31, 2014 at 6:30 a.m. CT.

Title: Independent evaluation of ibrutinib efficacy 3 years post-initiation of monotherapy in patients with chronic lymphocytic leukemia/small lymphocytic leukemia including deletion 17p disease (Abstract #7014)
Session: Leukemia, Myelodysplasia, and Transplantation Oral Abstract Session
Date : Tuesday, June 3, 2014
Presentation Time: 11:33 a.m.
Location: McCormick Place, Room E354A
Presenter: Susan O'Brien, M.D., The University of Texas MD Anderson Cancer Center, TX, USA

Dr. O'Brien will present independent assessment of efficacy data 3 years after the initiation of therapy with single agent IMBRUVICA to confirm and further characterize the durability of response. The presented results show that single-agent IMBRUVICA showed durable responses in patients with treatment naive (TN) or relapsed/refractory (R/R) CLL/SLL including those with del17p, as independently confirmed with 3 years of follow-up.

Preliminary results: Of 132 CLL/SLL (31 TN, 101 R/R) patients evaluated, the median age was 68 years, 36 (27.3%) patients (2 TN, 34 R/R) had del17p and 36 (27.3%) had del11q. R/R patients including 34 with del17p had a median of 4 (range, 1-12) prior therapies. The updated ORR (by independent review) was 78.0% for all-treated patients (83.9% TN-, 76.2% R/R and 55.9% for those R/R with del17p). Additionally, 5 R/R patients, 2 with del (17p), had a best response of PR with lymphocytosis. Median DOR was not reached for all-treated patients, and was 25.0 months (range, 4.8-34.3) in patients with del17p. Median time on study was 29.4 months (range, 0.7-38.1) for all-treated patients, and 27.3 months (range, 0.9-37.5) for R/R patients with del17p. Patients receiving prior therapy experienced serious or greater than or equal to Grade 3 adverse events that decreased after 1 year on treatment. No new safety signals were observed in long-term follow-up; 64% of patients remain on treatment with ibrutinib.

Conclusions: Single-agent ibrutinib showed durable responses in patients with TN or R/R CLL/SLL including those with del17p, as independently confirmed with 3 years of follow-up. Further data and analysis will be presented during the oral presentation at ASCO June 3, 2014.

Selected Poster Presentation
Title: A phase 1b/2 study evaluating activity and tolerability of the BTK inhibitor ibrutinib in combination with ofatumumab in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and related diseases (Abstract #7009)

Session: Leukemia, Myelodysplasia, and Transplantation Poster Highlights Session

Date: Saturday, May 31, 2014

Presentation Time: 1:15 p.m.

Location: McCormick Place, Room S405, Poster #1

Presenter: Samantha Jaglowski, M.D., M.P.H., The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA

Dr. Jaglowski will present efficacy data from three cohorts of patients receiving IMBRUVICA and ofatumumab, an anti-CD20 antibody, in three different administration sequences.

Preliminary results: A total of 71 patients (27, 20, 24 in G1, 2, 3) were enrolled and treated with IMBRUVICA daily and ofatumumab in 28-day cycles until progressive disease. Median age was 64 years; 61% had Rai stage III/IV; 65 patients had CLL, 1 SLL, 2 Prolymphocytic leukemia (PLL) and 3 Richter’s Transformation (RT); 75% had lymph nodes greater than or equal to 5 cm; 44% had del17p; 31% had del11q. Group 1 (G1) received one cycle of IMBRUVICA monotherapy, followed by ofatumumab. Group 2 (G2) received ofatumumab on Day 1 of Cycle 1, and IMBRUVICA on Day 2 of Cycle 1. Group 3 (G3) received two cycles of ofatumumab monotherapy, and IMBRUVICA on Day 1 of Cycle 3. Most common grade 3-4 adverse events (AE) was neutropenia in 17%; 39% had serious adverse events (SAEs); 45% had infusion related reactions (IRR) (with greater than or equal to g 3 in 1 pt in G2); 6 patients had AEs leading to ibrutinib discontinuation; 9 patients died within 30 days of last dose and 2 within f/u period. Overall response rate per investigator in CLL/SLL was 100% in G1, 79% in G2, and 71% in G3. G3 had 4 patients who progressed before taking ibr. At study end, 52/58 responders (90%) were progression-free with f/u of 16, 12 and 11 months for G1, 2 and 3, respectively. Two patients achieved a partial response with lymphocytosis. Three RT patients had disease control followed by progressive disease (PD) on Day 471, 168, and 137. At 12 months, PFS was 89%, 85%, and 90% in G1, 2 and 3, respectively; 76% continued on IMBRUVICA in a long-term extension study; 2 patients had a transplant.

Conclusions: IMBRUVICA combined with ofatumumab is well tolerated and highly active (83% ORR) in patients with pre-treated R/R CLL/SLL in all 3 dosing sequences investigated. Because of these compelling results, randomized trials evaluating anti-CD20 antibody in combination with IMBRUVICA with a PFS endpoint are ongoing. Further data and analysis will be presented during the data presentation at ASCO May 31, 2014.

Other Company Sponsored Presentations

Trial in Progress Title: A phase 3 study of ibrutinib in combination with either bendamustine and rituximab (BR) or rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in patients with previously treated follicular lymphoma or marginal zone lymphoma. (Abstract TPS8611*)

Session: Lymphoma and Plasma Cell Disorders General poster session

Date: Monday, June 2, 2014

Presentation Time: 1:15 p.m.

Location: S Hall A2

Presenter: Nathan Fowler, M.D., The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Trial in Progress Title: A randomized, double-blind, placebo-controlled phase 3 study of ibrutinib in combination with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in subjects with newly diagnosed nongerminatal center B-cell subtype of diffuse large B-cell lymphoma (DLBCL). (Abstract TPS8615*)

Session: Lymphoma and Plasma Cell Disorders General poster session

Date: Monday, June 2, 2014

Presentation Time: 1:15 p.m.

Location: S Hall A2.

Presenter: Anas Younes, M.D., Memorial Sloan Kettering Cancer Center, New York, NY, USA

INDICATIONS

IMBRUVICA is indicated for the treatment of:

- Patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
- Patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy.

These indications are based on overall response rate. An improvement in survival or disease-related symptoms has not been established.

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 or chronic lymphocytic leukemia who have received at least one prior therapy. These indications are based on overall response rate. An improvement in survival or disease-related symptoms has not been established:
The most commonly occurring adverse reactions (greater than or equal to 20%) in the clinical trial were IMBRUVICA. IMBRUVICA is a first-in-class, oral therapy and is a new agent that inhibits a disease received at least one prior therapy. These indications are based on overall response rate. An improvement in survival or IMBRUVICA is indicated for the treatment of patients with mantle cell lymphoma or chronic lymphocytic leukemia who have About For the full prescribing information, visit www.IMBRUVICA.com. IMPORTANT SAFETY INFORMATION WARNINGS AND PRECAUTIONS Hemorrhage - Five percent of patients with MCL and 6% of patients with CLL had Grade 3 or higher bleeding events (subdural hematoma, ecchymoses, gastrointestinal bleeding, and hematuria). Overall, bleeding events including bruising of any grade occurred in 48% of patients with MCL treated with 560 mg daily and 63% of patients with CLL treated at 420 mg daily. The mechanism for the bleeding events is not well understood. IMBRUVICA may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies. Consider the benefit-risk of withholding IMBRUVICA 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 with IMBRUVICA therapy. At least 25% of patients with MCL and 35% of patients with CLL had infections Grade 3 or greater 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 with MCL and 35% of patients with CLL. These included neutropenia (29%), thrombocytopenia (17%) and anemia (9%) in patients with MCL and neutropenia (27%) and thrombocytopenia (10%) in patients with CLL. Monitor complete blood counts monthly. Renal Toxicity - Fatal and serious cases of renal failure have occurred with IMBRUVICA therapy. Treatment-emergent increases in creatinine levels up to 1.5 times the upper limit of normal occurred in 67% of patients with MCL and 23% of patients with CLL. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 9% of patients with MCL and 4% of patients with CLL. Periodically monitor creatinine levels. Maintain hydration. Second Primary Malignancies - Other malignancies have occurred in 5% of patients with MCL and 10% of patients with CLL who have been treated with IMBRUVICA. Four percent of patients with MCL had skin cancers, and 1% had other carcinomas. Eight percent of patients with CLL had skin cancers and 2% had other carcinomas. 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 - MCL: The most commonly occurring adverse reactions (greater than or equal to 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 (greater than or equal to 5%) were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), 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. CLL: The most commonly occurring adverse reactions (greater than or equal to 20%) in the clinical trial were thrombocytopenia*, diarrhea (63%), bruising (54%), neutropenia*, anemia*, upper respiratory tract infection (48%), fatigue (31%), musculoskeletal pain (27%), rash (27%), pyrexia (25%), constipation (23%), peripheral edema (23%), arthralgia (23%), nausea (21%), stomatitis (21%), sinusitis (21%), and dizziness (21%). *Treatment-emergent decreases (all grades) of platelets (71%), neutrophils (54%) and hemoglobin (44%) were based on laboratory measurements per IWCLL criteria and adverse reactions. The most common Grade 3 or 4 non-hematological adverse reactions (greater than or equal to 5%) were pneumonia (8%), hypertension (8%), atrial fibrillation (6%), sinusitis (6%), skin infection (6%), dehydration (6%), and musculoskeletal pain (6%). Treatment-emergent Grade 3 or 4 cytopenias were reported in 35% of patients. Five patients (10%) discontinued treatment due to adverse reactions in the trial (N=48). These included 3 patients (6%) with infections and 2 patients (4%) with subdural hematomas. Adverse reactions leading to dose reduction occurred in 13% 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. For the full prescribing information, visit http://www.imbruvica.com/downloads/Prescribing_Information.pdf About IMBRUVICA IMBRUVICA is indicated for the treatment of patients with mantle cell lymphoma or chronic lymphocytic leukemia who have received at least one prior therapy. These indications are based on overall response rate. 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 and spread of malignant B cells. IMBRUVICA blocks signals that tell malignant B cells to multiply and spread uncontrollably. It is one of the first medicines to file for FDA approval via the new Breakthrough Therapy Designation pathway, enabling Pharmacyclics to rapidly bring this medicine to patients in need.

To date, 11 Phase III trials have been initiated with ibrutinib and a total of 44 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.

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 and control promising product candidates based on scientific development and administrational 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 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.

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.

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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