U.S. FDA Approves IMBRUVICA® (ibrutinib) for Treatment of Waldenstrom's macroglobulinemia (WM)

- First and Only FDA-Approved Treatment for WM Patients
- Approved for All Lines of Therapy in WM
- Fourth Indication for IMBRUVICA

SUNNYVALE, Calif., Jan. 29, 2015 /PRNewswire/ -- Pharmacyclics, Inc. (NASDAQ: PCYC) today announced that the U.S. Food and Drug Administration (FDA) has granted single-agent IMBRUVICA® (ibrutinib) regular (full) approval in all lines of therapy as the first and only treatment for patients with Waldenstrom's macroglobulinemia (WM), a rare, indolent type of B-cell lymphoma. This is the fourth indication for IMBRUVICA, an oral therapy, which received FDA Breakthrough Therapy Designation for this indication in February 2013. IMBRUVICA is being jointly developed and commercialized by Pharmacyclics and Janssen Biotech, Inc.

"Because there has never been an FDA-approved treatment for Waldenstrom's macroglobulinemia since it was first identified over 70 years ago, doctors had to rely on therapies borrowed from similar cancers to treat these patients," Steven P. Treon, M.D., Ph.D., Director of the Bing Center for Waldenstrom's Macroglobulinemia at the Dana-Farber Cancer Institute and Associate Professor at Harvard Medical School, Boston, Mass., and lead investigator of the WM trial data submitted to the FDA for this approval. "I am truly grateful to the FDA for recognizing this need and for approving IMBRUVICA, and I thank those scientists whose hard work and dedication helped discover the genetic cause of this disease and identified ibrutinib as a targeted therapy, and those clinicians at several leading medical centers who diligently enrolled the clinical trial showing that IMBRUVICA is a safe and highly effective therapy for patients with Waldenstrom's macroglobulinemia."

"The FDA's approval of IMBRUVICA for Waldenstrom's macroglobulinemia marks a significant milestone for patients living with this rare disease and has the potential to positively impact the lives of a number of patients," said Carl Harrington, President of the International Waldenstrom's Macroglobulinemia Foundation, who also is a patient living with WM.

The approval is based on results from a multi-center, Phase II study that evaluated the efficacy and tolerability of IMBRUVICA in 63 patients with previously treated WM. In this study, IMBRUVICA demonstrated a response rate of 62% according to an Independent Review Committee. Very good partial responses (VGPR) of 11% and partial responses (PR) of 51% were observed. These responses were maintained and the median duration of response (DOR) has not been reached, with a range of 2.8+ to 18.8+ months.

"IMBRUVICA has demonstrated its effectiveness in patients living with Waldenstrom's macroglobulinemia who, until now, did not have an FDA-approved standard-of-care therapy," said Thorsten Graef, M.D., Ph.D., Head of Hematology at Pharmacyclics. "This approval is a proud moment for our Pharmacyclics and Janssen teams and would not have been possible without the dedication and support of our patients, clinical investigators and the FDA's recognition of IMBRUVICA as a breakthrough therapy for these patients."

WM (a clinically recognized subset of lymphoplasmacytic lymphoma, or LPL) is a slow-growing and rare blood cancer that most commonly originates from B cells, a type of white blood cell (lymphocyte) that develops in the bone marrow. In the United States, approximately 1,000 to 1,500 people are diagnosed each year, with the median age at diagnosis being 60 to 70 years of age. WM occurs as the result of a malfunction in the healthy lifecycle of a B cell, causing the cell to become malignant and reproduce at an abnormal rate. The malignant B cells produce large amounts of an abnormal type of antibody protein called immunoglobulin M (IgM). Excess IgM causes the blood to thicken and causes many of the symptoms of WM.

Consistent with the previous label, the most commonly occurring adverse reactions in WM patients treated with IMBRUVICA (>20%) were neutropenia, thrombocytopenia, diarrhea, rash, nausea, muscle spasms, and fatigue. Six percent of patients receiving IMBRUVICA in the WM trial discontinued treatment due to adverse events. Adverse events leading to dose reduction occurred in 11% of patients.

In addition, the warnings and precautions for IMBRUVICA were updated and reflect the most current safety knowledge based on ongoing clinical investigation and commercial use. Please see the Important Safety Information section below.
IMBRUVICA (ibrutinib) is a first-in-class, oral, once-daily therapy that inhibits a protein called Bruton's tyrosine kinase (BTK). BTK is a key signaling molecule in 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.

IMBRUVICA is approved for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy, CLL patients with del 17p, a genetic mutation that occurs when part of chromosome 17 has been lost, and patients with Waldenstrom's macroglobulinemia.

IMBRUVICA is also approved for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. Accelerated approval was granted for the MCL indication based on overall response rate (ORR). Continued approval for the MCL indication may be contingent upon verification of clinical benefit in confirmatory trials.

IMBRUVICA is being studied alone and in combination with other treatments in several blood cancers. Over 5,100 patients have been treated in clinical trials of IMBRUVICA conducted in 35 countries by more than 800 investigators. Currently, 13 Phase III trials have been initiated with IMBRUVICA and 58 trials are registered on www.clinicaltrials.gov.

IMBRUVICA was one the first medicines to receive U.S. FDA approval via the new Breakthrough Therapy Designation pathway, and is the only product to have received three Breakthrough Therapy Designations.

INDICATIONS
IMBRUVICA is indicated to treat people with:

- Chronic lymphocytic leukemia (CLL) who have received at least one prior therapy
- Chronic lymphocytic leukemia (CLL) with 17p deletion
- Waldenström's macroglobulinemia
- Mantle cell lymphoma (MCL) who have received at least one prior therapy - accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

Patients taking IMBRUVICA for CLL or WM should take 420 mg taken orally once daily (or three 140 mg capsules once daily).

Patients taking IMBRUVICA for MCL should take 560 mg taken orally once daily (or four 140 mg capsules once daily).

Capsules should be taken orally with a glass of water. Capsules should be taken whole. Do not open, break, split or chew the capsules.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (subdural hematoma, gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA®.

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. Grade 3 or greater infections occurred in 14% to 26% of patients. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA®. Monitor patients for fever and infections and evaluate promptly.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 19 to 29%), thrombocytopenia (range, 5 to 17%), and anemia (range, 0 to 9%) occurred in patients treated with IMBRUVICA®. Monitor complete blood counts monthly.
Atrial Fibrillation - Atrial fibrillation and atrial flutter (range, 6 to 9%) have occurred in patients treated with IMBRUVICA®, particularly in patients with cardiac risk factors, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (eg, palpitations, lightheadedness) or new-onset dyspnea should have an ECG performed. If atrial fibrillation persists, consider the risks and benefits of IMBRUVICA® treatment and dose modification.

Second Primary Malignancies - Other malignancies (range, 5 to 14%) including non-skin carcinomas (range, 1 to 3%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4 to 11%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been reported with IMBRUVICA® therapy. Monitor patients closely and take appropriate precautions in patients at risk for tumor lysis syndrome (e.g. high tumor burden).

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 common adverse reactions (≥25%) in patients with B-cell malignancies (MCL, CLL, WM) were thrombocytopenia, neutropenia, diarrhea, anemia, fatigue, musculoskeletal pain, bruising, nausea, upper respiratory tract infection, and rash. Seven percent of patients receiving IMBRUVICA® discontinued treatment due to adverse events.

DRUG INTERACTIONS

CYP3A Inhibitors - Avoid co-administration with strong and moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA® dose.

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

SPECIFIC POPULATIONS

Hepatic Impairment - Avoid use in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA® dose.

For additional important safety information, please see Full Prescribing Information at http://www.imbruvica.com/downloads/Prescribing_Information.pdf.

Patient Access to IMBRUVICA

Patients who are prescribed IMBRUVICA® can receive access support through a variety of programs:

- The YOU&i Start™ program enables eligible patients who are experiencing insurance coverage delays to access free product for a limited time.
- The YOU&i Access™ Instant Savings Program helps commercially insured, eligible patients who have difficulties with out-of-pocket expenses for IMBRUVICA. Eligible patients may receive support to reduce their monthly out-of-pocket costs to $10 per month.
- The YOU&i Access Service Center assists patients with all access-related administration issues.
- Pharmacyclics makes donations to the Johnson & Johnson Patient Assistance Foundation (JJPAF), an independent, nonprofit organization that provides assistance to patients who need access to IMBRUVICA who are eligible based on financial need and if they are uninsured.

For more information about these comprehensive patient access programs, call or visit 1-877-877-3536 or www.IMBRUVICA.com.

About Pharmacyclics

Pharmacyclics, Inc. (NASDAQ: PCYC) is a biopharmaceutical company focused on developing and commercializing innovative small-molecule drugs for the treatment of cancer and immune mediated diseases. The company's mission 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 needs. It will do so by identifying and controlling promising product
candidates based on scientific development and administrative expertise, developing its products in a rapid, cost-efficient manner and, pursuing 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 commercialization. Pharmacyclics is headquartered in Sunnyvale, CA. To learn more, please visit 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 Form 10-K for the year ended December 31, 2013 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.

*Disclaimer: Dr. Treon served as principal investigator of this Dana-Farber Cancer Institute-sponsored clinical study. He has served as a paid advisor to both Pharmacyclics and Janssen in developing the compound ibrutinib. Dr. Treon does not have a financial interest in either company. The Dana-Farber Cancer Institute has received research funding from Pharmacyclics in conjunction with this clinical trial.

IMBRUVICA is a registered trademark of Pharmacyclics, Inc.

1 IMBRUVICA Prescribing Information, January 2015


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