European Medicines Agency (EMA) Issues Positive Opinion, Recommends Full Approval of IMBRUVICA® (ibrutinib) for Treatment of Two Blood Cancers

SUNNYVALE, Calif., July 25, 2014 /PRNewswire/ -- Pharmacyclics, Inc. (NASDAQ: PCYC) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending the granting of full marketing approval for IMBRUVICA® (ibrutinib) in the European Union.

IMBRUVICA is being jointly developed and commercialized in the United States by Pharmacyclics and Janssen Biotech, Inc. In Europe, once approved, Janssen-Cilag International NV (Janssen) will be the marketing authorization holder. Janssen will market IMBRUVICA in EMEA (Europe, Middle East, Africa), as well as the rest of the world, outside of the United States.

The CHMP recommendation for IMBRUVICA is for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL), or adult patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy. The positive opinion was based on data from the Phase II study (PCYC-1104) in MCL, and a Phase III RESONATE™ study (PCYC1112-CA) and a Phase II study (PCYC-1102) in CLL.

The European Medicines Agency is a decentralized agency of the European Union responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the 28 countries of the European Union. The positive opinion of the EMA's CHMP will be reviewed by the European Commission, and a final decision on IMBRUVICA is anticipated later this year. In addition to European markets, a worldwide regulatory filing program for ibrutinib currently is underway.

"We are pleased with the CHMP's positive opinion for a full approval and with their recognition of the statistically significant overall survival and progression-free survival benefits of ibrutinib in CLL, as well as the strength of our MCL data," said Bob Duggan, Chairman & CEO, Pharmacyclics. "Today, we are one big step closer to offering an important, potentially paradigm-changing, new treatment option to patients around the world with these complex and challenging blood cancers."

IMBRUVICA received accelerated approval from the U.S. Food and Drug Administration (FDA) for two indications based on overall response rate: for the treatment of patients with MCL and CLL who have received at least one prior therapy.

The following results are from the CHMP analysis as part of its review of ibrutinib.

**MCL Study Efficacy Results**

In a multi-center, single-arm, open-label Phase II study (PCYC 1104), the efficacy of ibrutinib in 111 patients with relapsed or refractory MCL were evaluated. A response rate of 68% was observed, with a complete response rate of 21%, and a partial response rate of 47%, with an estimated median follow up of 15.3 months, the estimated median response duration was 17.5 months; the estimated median progression-free survival was 13.9 months.

**CLL Study Efficacy Results**

RESONATE™ (PCY1112) is a Phase III, randomized, multi-center, open-label, international, head-to-head study of single-agent, orally-administered ibrutinib versus the intravenous monoclonal antibody ofatumumab targeting the CD 20 antigen. The study enrolled 391 relapsed or refractory patients with CLL/SLL.

In this study, single-agent ibrutinib demonstrated a statistically significant improvement in progression-free survival (PFS), overall survival (OS), and overall response rate (ORR), regardless of baseline characteristics, as compared with patients treated with ofatumumab.

The median PFS in the ofatumumab arm was 8.1 months and was not reached in the ibrutinib arm because progression events occurred more slowly. The PFS results represent a 78% reduction in the risk of progression or death in patients treated with ibrutinib compared to ofatumumab. The OS median was not reached in either arm, but the results represent a 57% reduction in the risk of death in patients receiving ibrutinib versus those in the ofatumumab arm. Results were consistent across all baseline sub-groups, including those with del 17p.

**MCL and CLL Study Safety Results**

The most commonly occurring adverse reactions ( > 20%) were diarrhea, musculoskeletal pain, upper respiratory tract infection, bruising, rash, nausea, pyrexia, neutropenia, and constipation. The most common grade 3/4 reactions ( > 5%) were...
anemia, neutropenia, pneumonia, and thrombocytopenia.

About Ibrutinib
Ibrutinib is a Bruton's tyrosine kinase (BTK) inhibitor. BTK is an important protein involved in mediating the cellular signaling pathways which control B cell maturation and survival. In certain malignant B cells, there is excessive signaling through the B cell receptor signaling pathway, which includes BTK. The malignant cell ignores the natural signal to die and continues to develop and proliferate, upon which it migrates and adheres to protective environmental areas such as the lymph nodes, continuing to proliferate and survive. Ibrutinib is specifically designed to target and inhibit BTK. Ibrutinib forms a strong covalent bond with BTK, which inhibits the excessive transmission of cell survival signals within the malignant B cells and stops their excessive build-up in these protected environmental areas.

Ibrutinib is an investigational agent being studied alone and in combination with other treatments in several blood cancers including CLL, MCL, Waldenstrom's macroglobulinemia (WM), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and multiple myeloma (MM).

About MCL
MCL is a rare and aggressive type of B-cell lymphoma that can be challenging to treat and is associated with a poor prognosis. MCL is considered a rare disease, characterized by high unmet need and small patient populations, and has a median age at diagnosis of 65. Median overall survival typically is three to four years, and only one to two years in patients following their first relapse. MCL typically involves the lymph nodes, but can spread to other tissues, such as the bone marrow, liver, spleen and gastrointestinal tract.

About CLL
Chronic lymphocytic leukemia is the most common adult leukemia in the Western world, with a median age of 72 years at diagnosis. In most patients, CLL is a slow growing cancer, starting from white blood cells in the bone marrow. When cancer cells are located mostly in the lymph nodes, the disease is called small lymphocytic lymphoma (SLL). CLL/SLL is a chronic disease which often progresses. Patients are faced with fewer treatment options, and generally are prescribed multiple lines of therapy as they relapse or become resistant to treatments. Median overall survival ranges between 18 months and more than 10 years depending on the stage of disease.

Deletion 17p (del 17p) and TP53 mutation are associated with aggressive, treatment-resistant disease. The deletion results in the loss of a key gene, TP53, which senses the presence of abnormal DNA and triggers either DNA repair mechanisms or cell death, and is important in tumour suppression. Approximately 7% to 13% of patients have del 17p or TP53 mutation at diagnosis. However, incidence rises to > 30% in patients who have relapsed or who have refractory disease. The median predicted survival for patients with the deletion 17p mutation or TP53 mutation is just two to three years.

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 five 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, 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 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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