AstraZeneca, Pharmacyclics And Janssen Partner On Immuno-Oncology Combination Trials With IMBRUVICA® For Hematologic Cancers

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LONDON, SUNNYVALE, CA and RARITAN, NJ, November 4, 2014 -- AstraZeneca, Pharmacyclics, Inc. and Janssen Research & Development LLC ("Janssen") today announced they have entered into a clinical trial collaboration to evaluate the efficacy and safety of AstraZeneca's investigational anti-PD-L1 immune checkpoint inhibitor, MEDI4736, in combination with IMBRUVICA® (ibrutinib), an oral Bruton's tyrosine kinase inhibitor, co-developed and co-commercialized by Pharmacyclics and Janssen Biotech, Inc. The study will assess the combination as a treatment for patients with hematologic cancers including Diffuse Large B-Cell Lymphoma and Follicular Lymphoma, which are investigational uses for both compounds.

MEDI4736 blocks the signals that help tumors avoid detection by the immune system, countering the tumor's immune-evading tactics. Ibrutinib blocks signals that tell malignant B cells (white blood cells that produce antibodies) to multiply and spread uncontrollably. Preclinical evidence suggests that the combination of these two agents may lead to an enhanced anti-tumor immune response.

The Phase I part of the trial is expected to establish a recommended dose regimen for the combination of MEDI4736 and ibrutinib, and the Phase II part of the study will assess the safety and efficacy of the investigational combination. Under the terms of the agreement, the trial will be conducted by Pharmacyclics. The financial terms of the agreement have not been disclosed.

Briggs Morrison, Executive Vice President, Global Medicines Development & Chief Medical Officer, AstraZeneca, said: "We are committed to progressing our strong immuno-oncology pipeline as rapidly as possible. Our partnership with Pharmacyclics and Janssen supports our exploration of the potential of anti-PD-L1 in hematological cancers and is further evidence of our belief that combination therapies have the potential to be one of the most effective ways of treating cancer."

"We are delighted by our strategic collaboration with AstraZeneca as we explore the potential of IMBRUVICA in combination with immunotherapy to address a variety of hematologic cancers in which we already have deep experience and an ongoing scientific interest," said Bob Duggan, Chairman & CEO, Pharmacyclics. "We look forward to working with our partners as we advance our understanding of different ways by which to continue to evolve treatment paradigms and expand treatment options for patients with certain B-cell malignancies."

"Cancer drug development is at one of its most exciting, productive periods in history," said Peter Lebowitz, MD, PhD, Global Oncology Head, Janssen. "This collaboration reflects the common goal of all three companies to better understand new treatment options and combinations - with the ultimate goal of making a difference to the lives of people with hematologic malignancies."

About MEDI4736

MEDI4736 is an investigational human monoclonal antibody directed against programmed cell death ligand 1 (PD-L1). Signals from PD-L1 help tumors avoid detection by the immune system. MEDI4736 blocks these signals, countering the tumor's immune-evading tactics. MEDI4736 is being developed, alongside other immunotherapies, to empower the patient's immune system and attack the cancer.

MEDI4736 is in development as monotherapy in solid tumors, with Phase III clinical trials due to commence in 2014 for patients with non-small cell lung cancer and squamous cell carcinoma of the head of neck. AstraZeneca and MedImmune, its biologics research and development arm, also have a broad program of immuno-oncology combination trials underway, including MEDI4736 + tremelimumab (CTLA-4), MEDI4736 + MEDI0680 (PD-1) and MEDI4736 + MEDI6469 (OX40) and MEDI4736 + IRESSA (epidermal growth factor receptor-tyrosine kinase inhibitor).

About IMBRUVICA®

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 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. IMBRUVICA is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics.

IMBRUVICA® INDICATIONS

IMBRUVICA is indicated to treat people with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy
  - Accelerated approval was granted for this indication based on overall response rate. Improvements in survival or disease-related symptoms have not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.
- Chronic lymphocytic leukemia (CLL) who have received at least one prior therapy
- Chronic lymphocytic leukemia (CLL) with 17p deletion

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - 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 anti-platelet or anti-coagulant 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. Twenty-five percent of patients with MCL and 26% of patients with CLL had Grade 3 or greater NCI Common Terminology Criteria for Adverse Events (CTCAE). Monitor patients for fever and infections and evaluate promptly.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 23 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 10%) including 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 8%).

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 common 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 (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.
Fatal and serious cases of renal failure have occurred. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 9% of patients.

CLL: The most common adverse reactions (≥20%) in the clinical trials were thrombocytopenia (56%), neutropenia (51%), diarrhea (51%), anemia (37%), fatigue (28%), musculoskeletal pain (28%), upper respiratory tract infection (28%), rash (26%), nausea (25%), and pyrexia (24%).
Approximately 5% of patients receiving IMBRUVICA® discontinued treatment due to adverse events. These included infections, subdural hematomas, and diarrhea. Adverse events leading to dose reduction occurred in approximately 6% 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.

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

Please see full prescribing information: http://www.imbruvica.com/downloads/Prescribing_Information.pdf

About AstraZeneca
AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.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, visit www.pharmacyclics.com.

About the Janssen Pharmaceutical Companies of Johnson & Johnson
At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology,

neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Janssen Research & Development LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit http://www.janssenrnd.com for more information.

Pharmacyclics Safe Harbor Statement

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.

Johnson & Johnson Note on Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in new product development, including obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to laws and regulations and domestic and foreign health care reforms; and general industry conditions, including trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2013, including in Exhibit 99 thereto, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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