Janssen to Demonstrate Breadth of Oncology Portfolio with 42 Clinical Data Presentations at the 2014 American Society of Hematology (ASH) Annual Meeting

November 6, 2014
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- ***Note: This release corresponds to ASH abstracts 22, 31, 78, 84, 176, 327, 505, 2096, 2312, 3448, 3474, 4454, 4469, 4680***

RARITAN, NJ, November 6, 2014 - Janssen Research & Development, LLC (Janssen) will present new data across more than eight disease areas at the 56th American Society of Hematology (ASH) Annual Meeting being held December 6-9, 2014, in San Francisco, Calif., USA. More than 40 abstracts from Janssen company-sponsored or supported studies across four compounds have been accepted for presentation during the ASH meeting, seven of which are included in the oral sessions. Presentations will discuss data for IMBRUVICA® (ibrutinib), daratumumab, SYLVANT® (siltuximab) and DOXIL® (doxorubicin HCl liposome injection). Accepted meeting abstracts are currently available on the ASH website.

"The breadth of data across our cancer portfolio at ASH reflects our commitment to urgently advancing research and solutions for unmet needs of patients with blood cancers," said Peter F. Lebowitz, M.D., Ph.D., Global Oncology Head, Janssen. "We're particularly excited about the ibrutinib data which will be featured in nearly three dozen presentations, across eight distinct disease areas. Additional studies submitted by external groups will include ibrutinib and other treatments used in combination. We also look forward to discussing promising, early daratumumab data exploring its potential in multiple myeloma."

Abbreviated List of Company-Sponsored or Supported Research to be Presented
IMBRUVICA (ibrutinib)
IMBRUVICA will be featured in more than 37 abstracts, including both company-sponsored and investigator-initiated studies evaluating its use as a single agent and in combination with other therapies. There are eight studies selected for oral presentation, including the following five, sponsored by either Janssen or Pharmacyclics, Inc. IMBRUVICA is being jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics, Inc.:
Oral Presentations:

- **Ibrutinib, Single Agent or in Combination with Dexamethasone, in Patients with Relapsed or Relapsed/Refractory Multiple Myeloma (MM): Preliminary Phase 2 Results (Abstract 31)**
  Myeloma: Therapy, excluding Transplantation I. Saturday, December 6 at 12:00 p.m. PT in the West Building, 2001-2003-2014-2016
  Lead Author: Ravi Vij, M.D., The Washington University School of Medicine, St. Louis, MO, USA
- **Complex Karyotype, Rather Than Del(17p), Is Associated with Inferior Outcomes in Relapsed or Refractory CLL Patients Treated with Ibrutinib-Based Regimens (Abstract 22)**
  CLL: Therapy, excluding Transplantation: Phase 3 Trials and More. Saturday, December 6, 2014 at 12:45 p.m. PT at the South Building, Gateway Ballroom 104
  Lead Author: Philip A. Thompson, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
- **Mutational Analysis of Patients with Primary Resistance to Single-Agent Ibrutinib in Relapsed or Refractory Mantle Cell Lymphoma (MCL) (Abstract 78)**
  Non-Hodgkin Lymphoma: Biology, excluding Therapy: Genomic. Sunday, December 7 at 1:15 p.m. PT in the South Building, Gateway Ballroom 104
  Lead Author: Sriram Balasubramanian, Ph.D., Janssen Research & Development, LLC, Springhouse, PA, USA
- **Efficacy and Safety of Ibrutinib in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Leukemia with 17p Deletion: Results from the Phase II RESONATE™-17 Trial (Abstract 327)**
  CLL: Therapy, excluding Transplantation: Novel Therapies. Monday, December 8 at 7:30 a.m. PT in the West Building, 3001-3003-3014-3016
  Lead Author: Susan O'Brien, M.D., The University of Texas MD Anderson Cancer Center, Houston, TX, USA
- **Combination Of Ibrutinib and BCL-2 or SYK Inhibitors In Ibrutinib Resistant ABC-Subtype Of Diffuse Large B-Cell Lymphoma (Abstract 505)**
  Lymphoma: Pre-Clinical - Chemotherapy and Biologic Agents. Monday, December 8 at 2:45 p.m. PT in the West Building, 2005-2007-2018-2020
  Lead Author: Hsu-Ping Kuo, Ph.D., Pharmacyclics Inc., Sunnyvale, CA, USA

Daratumumab

There are six company-sponsored or supported daratumumab abstracts scheduled for presentation at ASH:

- **Modulation of CD38 Expression Levels on MM Tumor Cells by All-Trans Retinoic Acid Improves the Efficacy of the Anti-CD38 Monoclonal Antibody Daratumumab (Abstract 2096)**

Myeloma: Pathophysiology and Pre-Clinical Studies, excluding Therapy: Poster I. Saturday, December 6, 2014 at 5:30 p.m. in the West Building, Level 1
Lead Author: Inger S. Nijhof, M.D., Department of Hematology, University Medical Center Utrecht, Utrecht, Netherlands

- **Safety and Efficacy of Daratumumab with Lenalidomide and Dexamethasone in Relapsed or Relapsed, Refractory Multiple Myeloma (Abstract 84)**
  Myeloma: Therapy, excluding Transplantation II. Sunday, December 7, 2014 at 1:15 p.m. in the West Building, 2001-2003-2014-2016
  Lead Author: Torben Plesner, M.D., Vejle Hospital, Vejle, Denmark
- **An Open-label, Multicenter, Phase 1b Study of Daratumumab in Combination with Backbone Regimens in Patients with Multiple Myeloma (Abstract 176)**
  Myeloma: Therapy, excluding Transplantation: First Line Treatments. Sunday, December 7, 2014 at 4:45 p.m. in the South Building, Esplanade 303-305-307
  Lead Author: Philippe Moreau, M.D., University Hospital, Nantes, France
- **Anti-Leukemic Activity Of Daratumumab In AML Cells And Patient-Derived Xenografts (Abstract 2312)**
  Acute Myeloid Leukemia: Novel Therapy, excluding Transplantation: Poster II. Sunday, December 7, 2014 at 6:00 p.m. in the North Building, Hall E
  Lead Author: Cedric Dos Santos, Ph.D., The University of Pennsylvania, Philadelphia, PA, USA
- **Direct In Vitro Comparison of Daratumumab with Surrogate Analogs of CD38 Antibodies MOR03087, SAR650984 and Ab79 (Abstract 3474)**
  Myeloma: Therapy, excluding Transplantation: Poster II. Sunday, December 7, 2014 at 6:00 p.m. in West Building, Level 1
  Lead Author: Jeroen Lammerts van Bueren, Genmab BV, Utrecht, Netherlands
- **Daratumumab shows anti-tumor activity in CLL and hampers leukemia-microenvironment interactions (Abstract 4680)**
  Therapy, excluding Transplantation: Poster III. Monday, December 8, 2014 at 6:00 p.m. in the West Building, Level 1
  Lead Author: Alba Matas-Céspedes, M.S., Department of Hemato-Oncology, IDIBAPS, Barcelona, Spain

SYLVANT (siltuximab)

There are two company-sponsored SYLVANT abstracts scheduled for presentation as posters at ASH:

- **Superior Restoration of Health with Siltuximab Among Multicentric Castleman's Disease Patients When Measured By SF-36 (Abstract 4469)**
  Lymphoma: Therapy with Biologic Agents, excluding Pre-Clinical Models: Poster III. Monday, December 8, 2014 at 6:00 p.m. PT in the West Building, Level 1
  Lead Author: Frits van Rhee, M.D., Ph.D., University of Arkansas for Medical Sciences, Little Rock, AR, USA

DOXIL (doxorubicin HCl liposome injection)

- **Final Overall Survival Results of a Randomized Trial Comparing Bortezomib Plus Pegylated Liposomal Doxorubicin with Bortezomib Alone in Subjects with Relapsed or Refractory Multiple Myeloma (Abstract 3448)**
  Myeloma: Therapy, excluding Transplantation: Poster II. Sunday, December 7 at 6:00 p.m. in the West Building, Level 1
  Lead Author: Robert Orlowski, M.D., Ph.D., The University of Texas MD Anderson Cancer Center, Houston, TX, USA

About IMBRUVICA
IMBRUVICA was one of the first therapies to receive U.S. approval via the FDA's Breakthrough Therapy Designation. IMBRUVICA works by blocking a specific protein called Bruton's tyrosine kinase (BTK).[1] The BTK protein transmits important signals that tell B cells to mature and produce antibodies and is needed by specific cancer cells to multiply and spread.[1,2] IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.[1] For more information, visit www.IMBRUVICA.com.

Additional Information about 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 (e.g., 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 Daratumumab
In August 2012, Genmab A/S granted Janssen Biotech, Inc. an exclusive worldwide license to develop, manufacture and commercialize daratumumab. Daratumumab is an investigational human $IgG1_{1K}$ monoclonal antibody (mAb) that binds with high affinity to CD38 on the surface of multiple myeloma cells. Daratumumab is in Phase 3 clinical development for multiple myeloma, and may also have potential in other malignant and pre-malignant diseases on which CD38 is expressed. In May 2013, daratumumab was granted Breakthrough Therapy Designation by the FDA for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), or who are double refractory to a PI and IMiD.

About SYLVANT® (siltuximab)
SYLVANT is an anti-interleukin-6 (IL-6) chimeric monoclonal antibody that binds to human IL-6.[3] IL-6 is a multifunctional cytokine produced by various cells such as T cells, B cells, monocytes, fibroblasts and endothelial cells. Dysregulated overproduction of IL-6 from activated B cells in affected lymph nodes has been implicated in the pathogenesis of, or mechanism causing, Multicentric Castleman's Disease (MCD).[4] Information about ongoing studies with siltuximab can be found at www.clinicaltrials.gov.

On April 23, 2014, the U.S. FDA approved SYLVANT for the treatment of patients with MCD who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative. SYLVANT was not studied in patients with MCD who are HIV positive or HHV-8 positive because SYLVANT did not bind to virally produced IL-6 in a nonclinical study. In June 2014, Janssen announced the European Commission (EC) approved the use of SYLVANT for the treatment of adult patients with MCD who are HIV negative and HHV-8 negative. SYLVANT is the first medicine approved in the U.S. and Europe for the treatment of MCD.

Additional Information about SYLVANT®
INDICATION - SYLVANT® (siltuximab) is indicated for the treatment of patients with multicentric Castleman's disease (MCD) who are human

immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

Limitation of Use. SYLVANT® was not studied in patients with MCD who are HIV positive or HHV-8 positive because SYLVANT® did not bind to virally produced IL-6 in a nonclinical study.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS - Severe hypersensitivity reaction to siltuximab or any of the excipients in SYLVANT®.

Concurrent Active Severe Infections - Do not administer to patients with severe infections until the infection resolves. SYLVANT® may mask signs and symptoms of acute inflammation including suppression of fever and of acute phase reactants such as C-reactive protein (CRP). Monitor patients closely for infections. Institute prompt anti-infective therapy and do not administer further SYLVANT® until the infection resolves.

Vaccinations - Do not administer live vaccines to patients receiving SYLVANT® because interleukin-6 (IL-6) inhibition may interfere with the normal immune response to new antigens.

Infusion Related Reactions and Hypersensitivity - Stop the infusion if the patient develops signs of anaphylaxis. Discontinue further therapy.

Stop the infusion if the patient develops mild to moderate infusion reactions. If the reaction resolves, the infusion may be restarted at a lower infusion rate. Consider medicating with antihistamines, acetaminophen, and corticosteroids. Discontinue SYLVANT® if the patient does not tolerate the infusion following these interventions. *[see Adverse Reactions (6)]*.

Administer SYLVANT® in a setting that provides resuscitation equipment, medication, and personnel trained to provide resuscitation.

Gastrointestinal (GI) Perforation - Use with caution in patients who may be at increased risk for GI perforation. Promptly evaluate patients presenting with symptoms that may be associated with or suggestive of GI perforation.

Adverse Reactions - The most common adverse reactions (>10% compared to placebo) in the MCD clinical trial were pruritus, increased weight, rash, hyperuricemia, and upper respiratory tract infection.

Drug Interactions - Cytochrome P450 (CYP450) Substrates - Upon initiation or discontinuation of SYLVANT®, in patients being treated with CYP450 substrates with narrow therapeutic index, perform therapeutic monitoring of effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) as needed and adjust dose. Exercise caution when SYLVANT® is co-administered with CYP3A4 substrate drugs where a decrease in effectiveness would be undesirable (e.g., oral contraceptives, lovastatin, atorvastatin).

For more information on SYLVANT®, including the full prescribing information, visit www.SYLVANT.com.

About DOXIL®
DOXIL is indicated for the treatment of patients with ovarian cancer whose disease has progressed or recurred after prior platinum based therapy. DOXIL in combination with VELCADE® (bortezomib) is indicated for the treatment of patients with multiple myeloma who have not previously received VELCADE and have received at least one prior therapy. DOXIL is also indicated for the treatment of AIDS-related Kaposi's sarcoma in patients after failure of prior systemic chemotherapy or intolerance to such therapy.

INDICATIONS

- DOXIL® (doxorubicin HCl liposome injection) is indicated for the treatment of patients with ovarian cancer whose disease has progressed or recurred after platinum-based chemotherapy.
- DOXIL® in combination with bortezomib is indicated for the treatment of patients with multiple myeloma who have not previously received bortezomib and have received at least one prior therapy.
- DOXIL® is administered intravenously by your healthcare professional.
- DOXIL® is also indicated for the treatment of AIDS-related Kaposi's sarcoma in patients after failure of prior systemic chemotherapy or intolerance to such therapy.

IMPORTANT SAFETY INFORMATION

Serious and possibly permanent heart-related side effects that may lead to congestive heart failure can occur in patients treated with DOXIL®. Inform your doctor of any history of heart disease, radiation to your chest, or prior anticancer therapy. Your doctor will monitor your heart function.

Infusion reactions may also occur during administration. Be sure to tell your doctor if you have any symptoms during infusion, including: flushing, shortness of breath, facial swelling, headaches, chills, back pain, tightness in your chest or throat, dizziness, or lightheadedness. For most patients, these reactions have resolved within several hours to a day once the infusion is stopped, or for some patients with slowing of the infusion rate. However, in some cases, these reactions may be serious and sometimes life-threatening and may be fatal.

DOXIL® may severely reduce the number of blood cells (red blood cells, white blood cells, and cells that prevent bleeding called platelets) in your body that may potentially increase risk of infections, anemia, and bleeding. Speak to your doctor if you notice any changes in your health. Your doctor will monitor your blood laboratory results.

Talk to your doctor if you have a history of heart disease or liver disease, or have received prior radiation therapy and/or anticancer therapy.

If you are pregnant, planning to become pregnant, or nursing inform your doctor. Nursing should be discontinued during treatment with DOXIL®.

You should not take DOXIL® if you have a prior history of allergic reactions to doxorubicin or other ingredients found in the formulation. Please inform your doctor about your history of allergic reactions to medications or other substances.

Very rare cases of oral cancer have been reported in people who had taken DOXIL® more than one year or who had taken a total dose greater than 720 mg/m2. The oral cancer was diagnosed during treatment and up to 6 years after the last dose. Your doctor will examine you at regular times for

the signs and symptoms of oral cancer.

The most common side effects reported in at least 20% of patients treated with DOXIL® during clinical studies were: weakness, fever, nausea, vomiting, stomatitis (painful redness, swelling, or sores in the mouth), diarrhea, and rash, loss of appetite, low white blood cell count, low platelet count, anemia, tiredness, and constipation. Hand-foot syndrome, which may lead to tingling or burning, redness, flaking, bothersome swelling, small blisters, or small sores on palms of hands or soles of feet, was reported as well. In certain cases, this reaction can be more severe leading to serious infections, interfering with walking and other daily activities. In the treatment of multiple myeloma, nerve damage called peripheral neuropathy, which may lead to pain, numbness, burning sensation, tingling, and more serious symptoms, was reported in >40% of patients. Be sure to tell your doctor immediately if you experience any of these or other symptoms.

DOXIL® may make the side effects of other anticancer therapies worse when used in combination.
Following administration, DOXIL® may turn urine and other bodily fluids a reddish-orange color. This is due to the color of DOXIL® and will go away as the drug leaves the body.

Your doctor may prescribe antinausea medications before or during your DOXIL® treatment.
Please talk to your doctor or nurse if you have any additional questions regarding DOXIL®.

For more information about DOXIL® therapy, please visit www.DOXIL.com. **Please see full Prescribing Information for more details.**

You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

About Janssen Research & Development, LLC
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.

Janssen in Oncology
In oncology, our goal is to fundamentally alter the way cancer is understood, diagnosed and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include a focus on hematologic malignancies, prostate cancer and lung cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualized use of our therapies; as well as safe and effective identification and treatment of early changes in the tumor microenvironment.

References:

[1] IMBRUVICA Prescribing Information, July 2014.

[2] Genetics Home Reference. Isolated growth hormone deficiency. Available from: http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed October 2014

[3] SYLVANT Prescribing Information. April 2014.

[4] El-Osta HE, Kurzrock R. Castleman's disease: from basic mechanisms to molecular therapeutics. Oncologist. 2011;16(4):497-511.

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