Janssen Inc. Announces IMBRUVICA® (ibrutinib) as the First Approved Treatment for Chronic Graft-Versus-Host Disease (cGVHD) Granted by Health Canada Priority Review

October 30, 2017

Approval provides a much-needed option for patients who develop this life-threatening condition following stem cell transplant

TORONTO, Oct. 30, 2017 /CNW/ - Janssen Inc. announced today that following Priority Review, Health Canada has approved IMBRUVICA® (ibrutinib), an oral, once-daily targeted therapy, for the treatment of patients with steroid dependent or refractory chronic graft-versus-host disease (cGVHD).[1]

Chronic GVHD is a potentially life-threatening complication that can develop following a stem cell transplant.[2] It occurs when immune cells of the donor (the graft) mistakenly attack normal tissues of the patient (the host).[3] Chronic GVHD can affect almost any organ in the body.[4] Chronic GVHD is the number one cause of death unrelated to relapses that occur after bone marrow stem cell transplantation.[5]

"Symptoms related to cGVHD can have a significant impact on a patient's quality of life, and for most they come after an already long and difficult battle with a life-threatening disease such as leukemia or lymphoma," says Dr. Andrew Daly, director of the Alberta Blood and Marrow Transplant Program and clinical associate professor at the Cumming School of Medicine, University of Calgary.* "Physicians have had a real challenge finding options with compelling clinical data to treat cGVHD safely and effectively. This approval provides a much-needed new approach for patients who fail initial therapy, as data shows treatment with IMBRUVICA® resulted in improved patient outcomes."

This approval is based on results from an open-label, multi-center, single-arm Phase 1b/2 trial (PCYC-1129) evaluating the safety and efficacy of IMBRUVICA® in 42 patients with cGVHD who required additional therapy after failure of first line corticosteroid therapy (median age of 56 years; range, 19 to 74 years old). The overall response rate (ORR) was 67 per cent (95 per cent CI: 51 per cent, 80 per cent), with 21 per cent of patients achieving complete responses (CR; n=9) and 45 per cent achieving partial responses (PR; n=19).[6] The median steroid dose was reduced over time for the all-treated population, from 0.31 mg/kg/day at baseline to 0.14 mg/kg/day at week 48, and five patients were able to completely discontinue corticosteroids while in response.[7]

"Lymphoma and leukemia patients are among those who may be able to get a stem cell transplant and achieve a potential cure. The procedure also comes with a high risk of cGVHD, which can have a severe impact on a patient's ability to work and go about their day-to-day life," says Robin Markowitz, Chief Executive Officer, Lymphoma Canada. "To date, many patients have had to rely on immunosuppressants and high-dose steroids to treat their cGVHD symptoms, and these come with significant issues. It is great news that patients finally have an approved treatment option."

About Stem Cell Transplants
Stem cell transplants are used when stem cells or bone marrow have been damaged by chemotherapy drugs, radiation therapy or diseases like cancer.[8] There are three main types: 1) Allogeneic - when stem cells from a donor (usually a sibling) are given to a patient; 2) Syngeneic - which are similar to allogeneic, but the stem cells are given by one identical twin to another; and 3) Autologous - where stem cells are taken from the recipient's own bone marrow or blood.[9]

About Chronic Graft-Versus-Host Disease
Chronic GVHD is a life-threatening condition in which the body is attacked by donor immune cells following an allogeneic stem cell or bone marrow transplant.[10,11] Chronic GVHD can cause different issues depending on the organs affected; it commonly affects the skin, mouth, eyes, digestive tract, lungs, and liver.[12] It usually occurs around three months post-stem cell transplant, but in some cases it may not develop until a year or more later.[13] Chronic GVHD occurs in up to 60 per cent of allogeneic transplants,[14] and it is currently the leading cause of long-term morbidity and mortality following allogeneic hematopoietic stem cell transplantation.[15]

About the Study (PCYC-1129)
The overall response rate (ORR) was 67 per cent (95 per cent CI: 51 per cent, 80 per cent), with 21 per cent of patients achieving complete responses (CR; n=9) and 45 per cent achieving partial responses (PR; n=19).[16] Among responders, 71.4% (95 percent CI: 51.3, 86.8) (20 of 28 responders) achieved a sustained response of ≥ 20 weeks.[17] Responses were seen across all organs affected by cGVHD (i.e., skin, mouth, gastrointestinal tract and liver).[18] The recommended dose of IMBRUVICA® for cGVHD is 420 mg (three 140-mg capsules) orally, once-daily.[19]

In the study population, the most common underlying malignancies leading to transplantation were acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL).[20] The median time since cGVHD diagnosis was 14 months, the median number of prior cGVHD treatments was two (range, one to three treatments), and 60 per cent of patients had a Karnofsky performance score of ≤ 80 (which is used to assess a patient's prognosis[21]).[22] The majority of patients (88 per cent) had at least two organs involved at the beginning of the trial, with the most commonly involved organs being mouth (86 per cent), skin (81 per cent) and gastrointestinal tract (33 per cent).[23] Fifty-two per cent of patients were receiving ongoing immunosuppressants in addition to systemic corticosteroids at baseline.[24]

The most common (≥20 per cent) adverse drug reactions (ADRs) of all Grades in the cGVHD trial were fatigue (57 per cent), bruising (40 per cent), diarrhea (36 per cent), stomatitis (29 per cent), muscle spasms (29 per cent), nausea (26 per cent), hemorrhage (26 per cent), and pneumonia (21 per cent). [25] Atrial fibrillation occurred in one patient (2 per cent), which was Grade 3.[26] Serious adverse reactions occurred in 52 per cent of patients.[27] The most common serious adverse reactions (2 or more patients) were pneumonia, sepsis (septic shock), cellulitis, headache, and pyrexia.[28] There were two fatal events, one case of pneumonia and one case of pulmonary aspergillosis.[29] Twenty-four per cent of patients receiving IMBRUVICA® in

the cGVHD trial discontinued treatment due to adverse reactions.[30] The most common adverse reactions leading to discontinuation were fatigue and pneumonia.[31] Adverse reactions leading to dose reduction occurred in 26 per cent of patients.[32]

About IMBRUVICA® (ibrutinib)
IMBRUVICA® contains the medicinal ingredient ibrutinib which is the first and only approved targeted inhibitor of Bruton's tyrosine kinase (BTK). Ibrutinib blocks BTK activity.[33]

This is the sixth approval for IMBRUVICA® in Canada. In addition to the cGVHD indication, IMBRUVICA® is also indicated for the treatment of patients with previously untreated active chronic lymphocytic leukemia (CLL), including those with 17p deletion. It is also approved for the treatment of patients with CLL who have received at least one prior therapy, including those with 17p deletion. IMBRUVICA® is indicated in combination with bendamustine and rituximab for the treatment of patients with CLL who have received at least one prior therapy. IMBRUVICA® is approved for the treatment of patients with Waldenström's macroglobulinemia (WM), and approved for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL).

IMBRUVICA® is co-developed by Cilag GmbH International (a member of the Janssen Pharmaceutical Companies) and Pharmacyclics LLC, an AbbVie company. Janssen Inc. markets IMBRUVICA® in Canada.

About the Janssen Pharmaceutical Companies
At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com/canada. Follow us on Twitter @JanssenCanada.

* Dr. Daly was not compensated for any media work. Dr. Daly has been a paid consultant to Janssen Inc.

Cautions Regarding Forward-Looking Statements
This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding anticipated benefits of IMBRUVICA®. 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 Inc. and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of continued clinical success and regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes to applicable laws and regulations, including health care reforms; and trends toward health care cost containment. A further list and descriptions 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 January 1, 2017, including under "Item 1A. Risk Factors," its most recent Quarterly Report on Form 10-Q, including in the section captioned "Cautionary Note Regarding Forward-Looking Statements," 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.

References:

[1] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.

[2] Leukemia and Lymphoma Society of Canada. Graft Versus Host Disease. Available from: http://www.llscanada.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease. Accessed October 2017.

[3] Leukemia and Lymphoma Society of Canada. Graft Versus Host Disease. Available from: http://www.llscanada.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease. Accessed October 2017.

[4] Leukemia and Lymphoma Society of Canada. Graft Versus Host Disease. Available from: http://www.llscanada.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease. Accessed October 2017.

[5] Canadian Stem Cell Foundation. About GVHD. Available from: http://stemcellfoundation.ca/en/diseases/gvhd/. Accessed October 2017.

[6] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.

[7] American Society of Hematology Blood Journal. Ibrutinib for Chronic Graft-Versus-Host Disease After Failure of Prior Therapy. Available from: http://www.bloodjournal.org/content/early/2017/09/18/blood-2017-07-793786?sso-checked=true. Accessed October 2017.

[8] Canadian Cancer Society. Stem Cell Transplant. Available from: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/stem-cell-transplant/?region=on. Accessed October 2017.

[9] Canadian Cancer Society. Stem Cell Transplant. Available from: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/stem-cell-transplant/?region=on. Accessed October 2017.

[10] Leukemia and Lymphoma Society of Canada. Graft Versus Host Disease. Available from: http://www.llscanada.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease. Accessed October 2017.

[11] MedlinePlus, U.S. National Library of Medicine. Graft-versus-host-disease. Available from: http://www.nlm.nih.gov/medlineplus/ency/article/001309.htm. Accessed October 2017.

[12] Canadian Cancer Society. Graft Versus Host Disease. Available from: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/stem-cell-transplant/side-effects-of-stem-cell-transplant/graft-versus-host-disease-gvhd/?region=on. Accessed October 2017.

[13] Leukemia and Lymphoma Society of Canada. Graft Versus Host Disease. Available from: http://www.llscanada.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease. Accessed October 2017.

[14] Canadian Cancer Society. Graft Versus Host Disease. Available from: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/stem-cell-transplant/side-effects-of-stem-cell-transplant/graft-versus-host-disease-gvhd/?region=on. Accessed October 2017.

[15] Socie G et al. Blood. 2014; 124(3): 374-384.

[16] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.

[17] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[18] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[19] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[20] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[21] Canadian Cancer Society. Karnofsky Performance Status Scale. Available from: http://info.cancer.ca/glossary/default.aspx?Lang=E&cceid=10505. Accessed October 2017.
[22] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[23] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[24] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[25] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[26] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[27] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[28] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[29] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[30] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[31] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[32] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.
[33] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated October 25, 2017.

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