Janssen Inc. Receives Health Canada Approval of DARZALEX® (daratumumab) by Priority Review for Patients with Multiple Myeloma Who Have Had At Least One Prior Therapy

DARZALEX® combination therapy significantly improved progression-free survival (PFS) compared to standard of care regimens alone

Toronto, ON, April 17, 2017 – Janssen Inc. announced today that Health Canada has approved DARZALEX® (daratumumab), in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy. 1 Due to the high unmet medical need for multiple myeloma patients, DARZALEX® was granted a Priority Review by Health Canada for this submission.

Multiple myeloma is an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow. 2,3 The disease can be very complex to treat as most patients relapse or become resistant to standard therapies, making the approval of new treatment options so important. 4,5 Janssen looks forward to working with insurers to determine how DARZALEX® can be made available for patients through both private and public insurance plans.

In June 2016, Health Canada issued a Notice of Compliance with Conditions (NOC/c) approving DARZALEX® for those 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 refractory to both a PI and an IMiD (meaning they didn’t respond to treatment). 6 With this new approval, patients can now use DARZALEX® treatment earlier in their disease.

“Canadians living with multiple myeloma have had good reason for hope in recent years with the Health Canada approvals of new treatments like DARZALEX®,” says Aldo Del Col, Co-Founder and Chairman, Myeloma Canada. “While this is encouraging, it is just a first step. There are hurdles to overcome before funding and access to these new treatments are approved by government drug plans.”

Data from two Phase 3 studies supported this new approval. They include the open-label, randomized clinical studies POLLUX (MMY3003) and CASTOR (MMY3004). POLLUX was published in The New England Journal of Medicine, with an accompanying editorial, in October 2016; and CASTOR was published in The New England Journal of Medicine in August 2016. 8

POLLUX showed that DARZALEX®, in combination with lenalidomide and dexamethasone, significantly improved progression free survival (PFS) compared to lenalidomide and dexamethasone alone. 9 While the median PFS had not been reached in patients treated with DARZALEX® in combination with
lenalidomide and dexamethasone, it was 18.4 months for patients treated with lenalidomide and dexamethasone alone. The PFS hazard ratio (HR) was 0.37 (99.39 per cent CI: 0.23, 0.59; p<0.0001), representing a 63 per cent reduction in the risk of disease progression or death in patients treated in the DARZALEX® arm.\textsuperscript{10} The study also showed that DARZALEX® used in combination significantly increased the overall response rate (ORR) (91 per cent vs. 75 per cent, p<0.0001), compared to lenalidomide and dexamethasone alone, also doubling rates of stringent complete response (sCR) (18 per cent vs. 7 per cent) and complete response (CR) (25 per cent vs. 12 per cent), and increasing very good partial response (VGPR) (32 per cent vs. 24 per cent).\textsuperscript{11}

The second study, CASTOR, found the median PFS had not been reached in patients treated with DARZALEX® in combination with bortezomib and dexamethasone and was 7.2 months in the bortezomib and dexamethasone arm. The PFS hazard ratio (HR) was 0.39 (98.98% CI: 0.26, 0.58; p-value < 0.0001), representing a 61 per cent reduction in the risk of disease progression or death for patients in the DARZALEX® arm.\textsuperscript{12} DARZALEX® used in combination was also shown to significantly increase ORR (79 per cent vs. 60 per cent, p<0.0001), compared to bortezomib and dexamethasone alone, also doubling rates of sCR (4 per cent vs. 2 per cent), CR (14 per cent vs. 7 per cent), and VGPR (38 per cent vs. 19 per cent).\textsuperscript{13}

“Having more options in the treatment of multiple myeloma is incredibly important,” says Dr. Michael Sebag, Hematologist at the McGill University Health Centre.* “Not only can DARZALEX® be used as a single agent, but clinical data now show significant efficacy in improved progression-free survival when it is used in combination with two of the most widely used treatment classes. This makes it a versatile option for patients who have received at least one prior therapy.”

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize DARZALEX®.\textsuperscript{14}

**About Multiple Myeloma**

Multiple myeloma is the most common plasma cell cancer\textsuperscript{15} and is characterized by an excess proliferation of plasma cells.\textsuperscript{16} In Canada, there were an estimated 2,700 new cases in 2016 and an estimated 1,450 deaths associated with the disease.\textsuperscript{17} While some patients with multiple myeloma have no symptoms at all, most patients are diagnosed due to symptoms that can include bone fractures or pain, low blood counts, calcium elevation, and kidney problems.\textsuperscript{18}

**About DARZALEX® (daratumumab)**

DARZALEX® is the first CD38-directed monoclonal antibody (mAb) to be approved to treat multiple myeloma. It binds to CD38, a surface protein highly expressed across multiple myeloma cells.\textsuperscript{19}
DARZALEX® induces tumour cell death through cell lysis via multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). DARZALEX® has also demonstrated immunomodulatory effects such as increasing CD4+ and CD8+ T-cells counts, which may contribute to clinical response.

Overall, the safety of the DARZALEX® combination therapy was consistent with the known safety profiles of DARZALEX® monotherapy (D) and lenalidomide plus dexamethasone (Rd), respectively. In data from the POLLUX trial, the most frequent (≥20 per cent) treatment-emergent adverse events (TEAEs) [DRd/Rd] were infusion reactions (48 per cent/0 per cent), diarrhea (47 per cent/28 per cent), nausea (25 per cent/16 per cent), fatigue (35 per cent/29 per cent), pyrexia (21 per cent/11 per cent), upper respiratory tract infection (69 per cent/52 per cent), muscle spasms (27 per cent/20 per cent), cough (32 per cent/15 per cent), dyspnea (23 per cent/14 per cent), constipation (30 per cent/26 per cent), anemia (34 per cent/36 per cent), neutropenia (60 per cent/44 per cent) and thrombocytopenia (28 per cent/30 per cent).

In data from the CASTOR study, the safety of the DARZALEX® combination therapy was consistent with the known safety profiles of DARZALEX® monotherapy (D) and bortezomib plus dexamethasone (Vd), respectively. The most frequent TEAEs [DVd/Vd] (>20 per cent) were infusion reactions (45 per cent/0 per cent), diarrhea (34 per cent/22 per cent), peripheral edema (24 per cent/14 per cent), upper respiratory tract infection (49 per cent/31 per cent), peripheral sensory neuropathy (49 per cent/38 per cent), cough (30 per cent/14 per cent), dyspnea (21 per cent/11 per cent), thrombocytopenia (60 per cent/44 per cent), anemia (28 per cent/32 per cent) and fatigue (22 per cent/25 per cent).

More information about DARZALEX® is available at www.janssen.com/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 at @JanssenCanada.

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

References:

1. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
6. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
10. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
11. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
12. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
20. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
22. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]
23. [DARZALEX™ Product Monograph, Janssen Inc., April 13, 2017]

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the efficacy and availability of DARZALEX® (daratumumab). 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., any of the other Janssen Pharmaceutical Companies 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 clinical success and of obtaining regulatory approvals; uncertainty of obtaining funded access to DARZALEX® for patients; 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 in behavior and spending patterns or financial distress of purchasers of health care products and services; changes to applicable laws and regulations, including global 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 in the sections captioned “Cautionary Note Regarding Forward-Looking Statements” and “Item 1A. Risk Factors,” 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.