Johnson&Johnson

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For immediate release

Health Canada Authorizes RYBREVANT® (amivantamab) in Combination with Carboplatin and Pemetrexed as the Only Targeted First-line Treatment Approved for Patients with Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations

Phase 3 PAPILLON study showed RYBREVANT® in combination with carboplatin and pemetrexed significantly improved progression-free survival, reducing the risk of disease progression or death by 60 per cent versus carboplatin and pemetrexed alone in patients with previously untreated NSCLC with EGFR exon 20 insertion mutations.[1]

TORONTO, July 3, 2024 /CNW/ - Johnson & Johnson (NYSE: JNJ) announced today that Health Canada, through a Priority Review, has issued a Notice of Compliance (NOC) for RYBREVANT® (amivantamab) in combination with platinum-based chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (*EGFR*) Exon 20 insertion mutations.[1]

“Patients with *EGFR* Exon 20 mutated non-small cell lung cancer face an aggressive disease with a worse prognosis than those with other *EGFR* mutations. There is a significant unmet need to improve the effectiveness of treatment for patients with this type of lung cancer,” says Dr. Susanna Cheng*, Medical Oncologist, Sunnybrook Health Sciences Centre. “The approval of novel targeted therapies like RYBREVANT® can bring hope for improved outcomes and quality of life for patients with this rare mutation. The data from the PAPILLON study supports the use of this regimen as the standard-of-care in the first-line treatment of patients with NSCLC harbouring *EGFR* Exon 20 insertion mutations.”

“The treatment of lung cancer has been strongly influenced by an improved understanding of the underlying biology behind this disease. Understanding the mechanism of action of certain genetic alterations such as *EGFR* mutations has allowed exciting new anti-cancer therapies to improve survival in patients touched with these diseases. However, there are still significant treatment gaps to bridge, in particular, in relation to *EGFR* Exon 20 insertion mutations,” says Dr. Kevin Jao**, Medical Oncologist, Hôpital du Sacré-Cœur-de-Montréal. “The emergence of a first line combination therapy with amivantamab and chemotherapy represents a particularly exciting breakthrough for patients diagnosed with this difficult genetic alteration. This represents the first truly meaningful therapy in this setting that gives patients diagnosed with NSCLC with EGFR Exon 20 insertion mutations new hope for a meaningful outcome.”

In Canada, lung cancer is the most commonly diagnosed cancer, with an estimated 31,000 new cases in 2023.[2] It is also responsible for 24 per cent of all cancer deaths among Canadians.[2] An estimated 15 per cent of Canadians with non-squamous NSCLC have an activating *EGFR* mutation.[3] The frequency of *EGFR* mutations is even greater in patients of Asian descent (~39 per cent) and in Asia-Pacific countries (~47 per cent).[4,5] Those with the third most prevalent variant, *EGFR* Exon 20 insertion mutations, tend to have a worse prognosis and shorter survival rates compared with individuals with more common *EGFR* mutations.[6,7,8] In fact, patients newly diagnosed with locally advanced or metastatic NSCLC with *EGFR* Exon 20 insertion mutations have a real-world median overall survival (OS) of 16.2 months, about nine months less than those with the more common *EGFR* Exon 19 deletions/L858R mutations (25.5 months).[9]

"The approval of RYBREVANT® offers a promising and urgently needed new first-line treatment option and represents significant advancement for those battling this rare mutation," says Nina Devito***, Co-chair, Exon20 group-Canada. "The positive study results underscore the importance of ongoing research and innovation in the fight against lung cancer, bringing new possibilities and renewed hope to patients and their loved ones."

The Health Canada NOC is based on results from the Phase 3, randomized, open-label, multicenter PAPILLON study.[1] The study compared treatment with RYBREVANT® in combination with platinum-based chemotherapy to treatment with platinum-based chemotherapy alone in patients with treatment-naïve, locally advanced or metastatic NSCLC with *EGFR* Exon 20 insertion mutations, as identified by local testing.[1] A total of 308 patients were randomized (1:1) to receive RYBREVANT® in combination with platinum-based chemotherapy (N=153) or platinum-based chemotherapy alone (N=155).[1] The results demonstrated RYBREVANT® in combination with platinum-based chemotherapy provides a clinically meaningful and statistically significant improvement in progression-free survival (PFS) and a 60 per cent reduction in the risk of disease progression or death compared to platinum-based chemotherapy alone.[1]

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Among 151 patients who received RYBREVANT® in combination with platinum-based chemotherapy, the median duration of treatment was 9.7 months (range: 0.1 to 26.9 months), with 76% were exposed for 6 months or longer and 38% were exposed for greater than one year.[1] Serious adverse events occurred in 37.1 per cent of patients who received RYBREVANT® in combination with platinum-based chemotherapy.[1] Fatal adverse events, irrespective of relatedness to treatment, occurred in 7 patients (4.6 per cent) who received RYBREVANT® in combination with platinum-based chemotherapy.[1] The most common treatment-emergent adverse events (≥ 20 per cent) were rash, neutropenia, paronychia, anaemia, stomatitis, infusion-related reactions, hypoalbuminaemia, edema, constipation, leukopenia, nausea, thrombocytopenia, decreased appetite, fatigue, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, COVID-19, hypokalaemia, vomiting, and diarrhea.[1] The most common Grade 3 to 4 laboratory abnormalities (≥ 2 per cent) were decreased albumin, increased ALT, increased gamma-glutamyltransferase, decreased sodium, decreased potassium, decreased magnesium and decreases in white blood cells, hemoglobin, neutrophils, platelets, and lymphocytes.[1]

“This approval reinforces our commitment to developing novel therapies, particularly for underserved patient populations with significant unmet needs,” says Berkeley Vincent, President, Janssen Inc., a Johnson & Johnson Company. “With RYBREVANT® in combination with carboplatin and pemetrexed, we are redefining care for patients with newly diagnosed NSCLC with *EGFR* exon 20 insertion mutations by offering a targeted treatment that may delay progression of their disease versus carboplatin and pemetrexed alone. This milestone takes us one step closer to our aim of getting in front of cancer.”

About RYBREVANT®

RYBREVANT® is a fully-human *EGFR-MET* bispecific antibody that acts by targeting tumours with activating and resistance *EGFR* mutations and *MET* mutations and amplifications, and by harnessing the immune system.[1] It binds extracellularly, or to the outside of the cell, slowing or inhibiting tumour growth and leading to tumour cell death.[1] RYBREVANT®, indicated as a monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC with activating *EGFR* Exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy, has been issued a marketing authorization with conditions.[1] RYBREVANT®, indicated in combination with platinum-based chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with locally advanced (not amenable to curative therapy) or metastatic NSCLC with activating *EGFR* Exon 20 insertion mutations, has been issued a market authorization without conditions.[1] A validated test is required to identify *EGFR* Exon 20 insertions mutation-positive status prior to treatment.[1]

About the PAPILLON Study

PAPILLON (NCT04538664) is a Phase 3 randomized, open-label study evaluating the efficacy and safety of RYBREVANT® in combination with platinum-based chemotherapy (carboplatin and pemetrexed), compared with platinum-based chemotherapy alone, in newly diagnosed patients with advanced or metastatic NSCLC characterized by *EGFR* exon 20 insertion mutations. The primary endpoint of the study is PFS (using RECIST v1.1 guidelines[§]) as assessed by blinded independent central review (BICR). Secondary endpoints include overall response rate (ORR) and overall survival (OS). Patients who received platinum-based chemotherapy alone were allowed to receive RYBREVANT® monotherapy in the second-line setting after confirmation of disease progression.[10]

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com and https://www.janssen.com/canada. Follow us at @JNJInnovMedCAN.

Cautions Concerning Forward-Looking Statements

This press release contains “forward-looking statements” as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of RYBREVANT® (amivantamab). 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 clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including

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technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior and spending patterns 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 December 31, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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 Janssen Inc. nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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** Dr. Kevin Jao was not compensated for this media work. He has been compensated previously by J&J for other professional engagements.

*** Nina Devito was not compensated for this media work. Exon20 group-Canada has been compensated previously by J&J for other professional engagements.

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[1] RYBREVANT® Product Monograph, Toronto, ON: Janssen Inc. June 28, 2024.
[2] 2023 Faces of Lung Cancer Report. Lung Cancer Canada. p.11. https://www.lungcancercanada.ca/getattachment/Resources/Faces-of-Lung-Cancer-Reports/LCC1010ENG_FOLCR_Report_2023_v8-digital.pdf.aspx
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[10] ClinicalTrials.gov. A Study of Combination Amivantamab and Carboplatin-Pemetrexed Therapy, Compared With Carboplatin-Pemetrexed, in Participants With Advanced or Metastatic Non-Small Cell Lung Cancer Characterized by Epidermal Growth Factor Receptor (EGFR) Exon 20 Insertions (PAPILLON).

Source: Johnson & Johnson