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For Immediate Release

Johnson & Johnson receives positive CHMP opinion for RYBREVANT®▼ (amivantamab) in combination with chemotherapy for the first-line treatment of patients with advanced non-small cell lung cancer with activating EGFR exon 20 insertion mutations

This positive CHMP opinion establishes amivantamab as a new option, and the first fully-human EGFR-MET bispecific antibody, in the first-line treatment of EGFR exon 20 insertion-mutated NSCLC

The recommendation is supported by data from the Phase 3 PAPILLON study, which showed amivantamab plus chemotherapy significantly improved progression-free survival in adult patients, versus chemotherapy alone[1]

BEERSE, BELGIUM (26 April 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended the approval of RYBREVANT®▼ (amivantamab) in combination with chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations.

"The PAPILLON study results represent an important advancement in the EGFR exon 20 insertion NSCLC treatment landscape, demonstrating significantly improved progression-free survival with first-line amivantamab plus chemotherapy, versus chemotherapy alone," said trial investigator Professor Nicolas Girard, Head of Medical Oncology, Institut Curie, and Professor of Thoracic Oncology and Respiratory Medicine at the Paris Saclay University, France.* "Notably, we observed improvements in functional status and reduction in lung cancer-related symptoms, underscoring the potential of this regimen to redefine standards of care for these patients, offering hope for improved quality of life and patient-relevant treatment outcomes."

An urgent need exists for innovative treatments in NSCLC, particularly for patients with EGFR exon 20 insertion driver mutations, due to the significant disease burden.[2] EGFR exon 20 insertion mutations are the third most common activating EGFR mutation and are associated with real-world five-year overall survival rates as low as 8%.[2] This reinforces the critical demand for targeted therapeutic approaches, tailored to address the unique complexities of EGFR exon 20 insertion mutations, aiming to substantially improve patient survival and quality of life outcomes.

"Lung cancer remains the leading cause of cancer-related mortality in Europe. As patients living with EGFR exon 20 insertion-mutated NSCLC face a particularly poor prognosis, the need for innovative combinations in the frontline setting is vital," said Henar Hevia, Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. "At Johnson & Johnson, we are dedicated to the development and delivery of novel, targeted therapies aimed to address specific disease pathways, with the ultimate goal of ensuring each patient receives the right treatment at the right time."

The PAPILLON study met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in progression-free survival (PFS; as measured by blinded independent central review [BICR]) in patients receiving amivantamab in combination with chemotherapy, versus chemotherapy alone (hazard ratio [HR]=0.395; 95 percent confidence interval [CI], 0.30–0.53; P<0.0001).[1,3] An interim overall survival (OS) analysis showed a favourable trend for patients treated with amivantamab plus chemotherapy, compared to those treated with chemotherapy alone (HR=0.675; 95 percent CI, 0.42–1.09; P=0.106).[1,3] The combination of amivantamab and chemotherapy demonstrated a safety profile consistent with the safety profiles of the individual agents, with low rates of treatment-related discontinuations (7 percent).[1,3] The rates of overall adverse events (AEs) and AEs leading to death were comparable between both treatment arms.[3] The rate of Grade ≥3 AEs was higher with amivantamab and chemotherapy, compared to chemotherapy alone (75 percent vs. 54 percent).[3] Serious AEs (SAEs) occurred in 37 percent of patients with amivantamab and chemotherapy, compared to 31 percent with chemotherapy alone.[3] EGFR and MET-related AEs were increased with amivantamab-chemotherapy (primarily grade 1-2).[3] Chemotherapy-associated haematologic and gastro-intestinal toxicities were comparable, except for neutropenia, which was transient.[3] Pneumonitis was reported in three percent of patients in the amivantamab-chemotherapy arm.[3]

“Today’s positive opinion represents the culmination of years of work and our team’s commitment to the lung cancer community. We will continue to focus on redefining treatment paradigms, starting from the very first line of therapy, with a goal of improving survival rates and overall patient outcomes.” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumours, Johnson & Johnson Research & Development, LLC. “Through our extensive research and development efforts, we are pioneering novel approaches and targeting key pathways implicated in lung cancer progression, with the ultimate goal of transforming clinical outcomes for patients with EGFR-mutated NSCLC.”

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About PAPILLON
PAPILLON (NCT04538664), which enrolled 308 patients, is a randomised, open-label Phase 3 study evaluating the efficacy and safety of amivantamab in combination with chemotherapy, compared with chemotherapy alone, in newly diagnosed patients with advanced or metastatic NSCLC characterised by EGFR exon 20 insertion mutations.[4] The primary endpoint of the study is PFS as assessed by BICR.[3] Secondary endpoints include overall response rate (ORR), PFS after first subsequent therapy (PFS2), duration of response (DOR), time to subsequent therapy (TTST) and overall survival (OS).[3] Patients who received chemotherapy alone were allowed to receive amivantamab monotherapy in the second-line setting after confirmation of disease progression.[3]

About Amivantamab
Amivantamab 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.[5,6,7,8]

The European Commission (EC) granted conditional marketing authorisation of amivantamab in December 2021 for the treatment of adult patients with advanced NSCLC with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations, after failure of platinum-based therapy.[9] Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.[9] In November 2023, a type II extension of indication application was submitted to the EMA based on the MARIPOSA-2 study seeking approval of amivantamab in combination with chemotherapy (carboplatin and pemetrexed) for the treatment of adult patients with advanced NSCLC with EGFR ex19del or L858R substitution mutations, after failure of prior therapy including a third-generation EGFR TKI.[10] This was recently followed, in February 2024, with the submission of a type II extension of indication application to the EMA based on the MARIPOSA study for amivantamab, in combination with lazertinib, for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with common epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or exon 21 L858R (L858R) substitution mutations.[11] Pending EC approval based on the PAPILLON study, the conditional marketing authorisation will be converted into a standard marketing authorisation.

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using amivantamab, please refer to the Summary of Product Characteristics.[9]

▼ In line with EMA regulations for new medicines, amivantamab is subject to additional monitoring.

About Non-Small Cell Lung Cancer
In Europe, it is estimated that 484,306 people were diagnosed with lung cancer in 2022.[12] NSCLC accounts for 85 percent of all lung cancer cases.[13] Lung cancer is Europe’s biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[12]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[13] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[13,14] EGFR mutations are present in 10 to 15 percent of Western patients with NSCLC with adenocarcinoma histology and occur in 40 to 50 percent of Asian patients.[15,16,17,18] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[19] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.[20] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[21] Patients with EGFR exon 20 insertion mutations have a real-world five-year OS of 8 percent in the frontline setting, which is lower than patients with EGFR ex19del or L858R mutations.[2]

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 www.janssen.com/emea. Follow us at www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen-Cilag International NV and Janssen Research & Development, LLC are Johnson & Johnson companies.

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 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 materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & Development, LLC 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 technological advances, new products and patents attained by competitors; challenges to patents; changes in behaviour 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 http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & Development, LLC 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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‡RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumors, which is a standard way to measure how well solid tumours respond to treatment and is based on whether tumours shrink, stay the same or get bigger.

*Professor Nicolas Girard has served as a consultant to Janssen-Cilag International NV; they have not been paid for any media work.

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