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For Immediate Release

RYBREVANT®▼ (amivantamab) in combination with chemotherapy is the first therapy approved by the European Commission for the first-line treatment of patients with advanced non-small cell lung cancer with activating EGFR exon 20 insertion mutations

Approval is supported by the Phase 3 PAPILLON study, which showed amivantamab plus chemotherapy significantly reduced the risk of disease progression or death by 60 percent compared to chemotherapy alone[1]

BEERSE, BELGIUM (28 June 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, announced today that the European Commission (EC) has approved a Type II variation for 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 epidermal growth factor receptor (EGFR) exon 20 insertion mutations.[1]

"Patients with NSCLC harbouring EGFR exon 20 insertion driver mutations have high unmet needs and urgently require innovative treatment options to tackle the significant disease burden and poor prognosis they may face," 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.* "Treatment with amivantamab has already been established in the second-line setting, and with this approval in the first-line setting, amivantamab combined with chemotherapy has the potential to redefine the standard of care, offering improved patient outcomes both in terms of clinical efficacy and quality of life."

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 eight percent,[2] making the introduction of new targeted therapeutic approaches tailored to address the unique complexities of EGFR exon 20 insertion mutations critical.

"At Johnson & Johnson, we are dedicated to advancing more effective and personalised innovations targeting novel disease pathways, that enable patients diagnosed with lung cancer to receive the treatment that is optimised for their individual characteristics," said Henar Hevia, Ph.D, Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. "Today's approval is an important development for patients with EGFR exon 20 insertion-mutated non-small-cell lung cancer, who may now benefit from amivantamab plus chemotherapy at the start of their treatment journey."

The expanded indication for amivantamab is based on positive results from the Phase 3 PAPILLON study, comparing the efficacy and safety of amivantamab in combination with chemotherapy (n=153) to chemotherapy alone (n=155) in patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.[3] Data from the study were previously published in *The New England Journal of Medicine.*[1]

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).[4] 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).[4]

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 discontinuation with amivantamab (7 percent).[4] The rates of overall adverse events (AEs) and AEs leading to death were comparable between both treatment arms.[4] The rate of Grade ≥3 AEs was higher with amivantamab and chemotherapy, compared to chemotherapy alone (75 percent vs. 54 percent).[4] Serious AEs (SAEs) occurred in 37 percent of patients with amivantamab and chemotherapy, compared to 31 percent with chemotherapy alone.[4] EGFR and MET-related AEs were increased with amivantamab-chemotherapy (primarily Grade 1-2).[4] Chemotherapy-associated haematologic and gastro-intestinal toxicities were comparable, except for the rate of

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neutropenia, which increased with amivantamab-chemotherapy compared to chemotherapy alone, but only occurred transiently.[4] Pneumonitis was reported in three percent of patients in the amivantamab-chemotherapy arm.[4]

As a result of the EC approval, the conditional marketing authorisation (MA) for amivantamab, received in December 2021, has been converted to a standard MA.[5]

“We are committed to advancing the science of EGFR-mutated non-small cell lung cancer for patients, with a focus on precision medicine-based approaches that target earlier stage disease,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumours, Johnson & Johnson Innovative Medicine. “Today’s approval marks another important milestone in our pursuit of transforming care for these patients.”

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About PAPILLON
PAPILLON (NCT04538664) 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 (n=308).[3] The primary endpoint of the study is PFS as assessed by BICR.[4] 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).[4] Patients who received chemotherapy alone were allowed to receive amivantamab monotherapy in the second-line setting after confirmation of disease progression.[4]

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.[6,7,8,9]

The European Commission (EC) granted conditional marketing authorisation of amivantamab in December 2021 for the treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations, after failure of platinum-based therapy.[5] Amivantamab is the first approved treatment in the European Economic Area specifically targeting EGFR exon 20 insertion mutations for NSCLC.[5] In November 2023, a Type II extension of indication application was submitted to the European Medicines Agency (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 NSCLC with common EGFR exon 19 deletions (ex19del) or exon 21 L858R (L858R) substitution mutations.[11] In May 2024, an application for the extension of amivantamab marketing authorisation was submitted seeking approval for the use of a subcutaneous (SC) formulation of amivantamab in combination with lazertinib for the first-line treatment of adult patients with advanced NSCLC with EGFR ex19del or L858R mutations in the first-line treatment setting, and for the use of SC amivantamab in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy.[12]

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.[5]

▼ 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.[13] NSCLC accounts for 85 percent of all lung cancer cases.[14] Lung cancer is Europe’s biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[13]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[14] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[14,15] 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.[16,17,18,19] EGFR ex19del or EGFR L858R mutations are the most

common EGFR mutations.[20] The five-year survival rate for patients with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.[21] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[22] Patients with EGFR exon 20 insertion mutations have a real-world five-year OS of eight 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.

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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-Cilag International NV 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-Cilag International NV nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

*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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