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Johnson&Johnson

Media contact:
Zayn Qureshi
zqureshi@its.jnj.com
+44 7760 334 666

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

For Immediate Release

European Commission approves RYBREVANT®▼ (amivantamab) in combination with chemotherapy for the treatment of adult patients with advanced EGFR-mutated non-small cell lung cancer after failure of prior therapy

Patients with EGFR ex19del or EGFR L858R mutations, the most common EGFR mutations in NSCLC, have until now faced a poor prognosis and limited treatment options after disease progression on an EGFR TKI[1,2,3,4]

Amivantamab in combination with chemotherapy is the first treatment regimen to show significant improvement in progression-free survival compared to chemotherapy alone in this patient population[5]

BEERSE, BELGIUM (27 August 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved a Type II extension of indication for RYBREVANT®▼ (amivantamab) in combination with chemotherapy (carboplatin and pemetrexed), for the treatment of adults with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) Exon 19 deletions (ex19del) or Exon 21 L858R substitution (L858R) mutations, after failure of prior therapy including an EGFR tyrosine kinase inhibitor (TKI).

“While much progress has been made in the lung cancer treatment landscape over the past decade, resistance to existing therapies continues to pose a major challenge for patients with advanced or metastatic non-small cell lung cancer harbouring EGFR mutations, underscoring the critical need for ongoing innovation,” said Antonio Passaro, M.D., Ph.D., Medical Oncologist, Division of Thoracic Oncology at the European Institute of Oncology in Milan, Italy. “The addition of the bispecific antibody amivantamab to chemotherapy offers an important new treatment option for patients with EGFR ex19del or L858R mutations, progressing on or after osimertinib. In this setting, this combination set the new landmark for overall response rate and reduced the risk of disease progression or death by more than half compared to standard chemotherapy alone. It also demonstrated significant improvements in intracranial progression-free survival.”

“The approval of amivantamab in combination with chemotherapy addresses a major unmet need for those whose disease has progressed following treatment with an EGFR TKI and who, until now, have faced limited treatment options,” said Henar Hevia, Ph.D., Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. “This milestone further reinforces the critical role of precision medicine in driving enhanced outcomes for patients living with lung cancer.”

The expanded indication for amivantamab is based on results from the Phase 3 MARIPOSA-2 study (NCT04988295), evaluating the efficacy and safety profile of amivantamab and chemotherapy in patients with locally-advanced or metastatic EGFR ex19del or L858R substitution NSCLC who had disease progression on or after treatment with osimertinib.[5] The amivantamab plus chemotherapy arm met its primary endpoint, significantly reducing the risk of disease progression or death by 52 percent, compared to chemotherapy alone, with a median progression-free survival (PFS) of 6.3 months, versus 4.2 months (hazard ratio [HR]=0.48; 95 percent confidence interval [CI], 0.36–0.64; $P<0.001$).[5] Additionally, amivantamab plus chemotherapy showed an objective response rate (ORR) of 64 percent, compared to 36 percent with chemotherapy alone.[5]

Data from MARIPOSA-2 study also showed that amivantamab in combination with chemotherapy demonstrates intracranial activity, critical for a disease where nearly 30 percent of patients develop brain metastases.[6,7] Amivantamab plus chemotherapy reduced the risk of intracranial progression or death by 45 percent compared to chemotherapy alone, with a median intracranial progression-free survival of 12.5 versus 8.3 months (HR=0.55; 95 percent CI, 0.38–0.79).[5]

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The safety profile of amivantamab plus chemotherapy was demonstrated to be consistent with that of its individual components.[5] Adverse events (AEs) of Grade 3 or higher, mainly due to haematologic toxicities, were reported by 72 percent of patients treated with amivantamab plus chemotherapy, and 48 percent with chemotherapy alone.[5] The most common Grade 3 or higher AEs included neutropenia, thrombocytopenia, anaemia, and leukopenia.[5] Grade 3 or 4 bleeding events were seen in one percent of patients treated with amivantamab plus chemotherapy, and in no patients with chemotherapy.[5] Serious treatment-emergent AEs (TEAEs) were observed in 32 percent of patients treated with amivantamab plus chemotherapy and 20 percent with chemotherapy.[5] Infusion-related reactions in the amivantamab plus chemotherapy arm were 58 percent (all grades).[5] Treatment-related AEs leading to death were infrequent in all arms (2 percent vs. 1 percent) in the amivantamab plus chemotherapy and chemotherapy alone arms respectively.[5]

"Today's approval marks further positive progress in our mission to transform the treatment landscape for people living with lung cancer," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumours, Johnson & Johnson Innovative Medicine. "This latest marketing authorisation for amivantamab underscores our commitment to advancing a robust lung cancer portfolio and redefining standards of care through precision medicine approaches."

Results from MARIPOSA-2 were presented during a Presidential Symposium at the European Society for Medical Oncology (ESMO) 2023 Congress and simultaneously published in the *Annals of Oncology.*[5,8]

About MARIPOSA-2

MARIPOSA-2 (NCT04988295), which enrolled 657 patients, is a randomised, open-label Phase 3 study evaluating the efficacy and safety of two combination regimens of amivantamab (with and without lazertinib) and chemotherapy.[5] Patients with locally-advanced or metastatic EGFR ex19del or L858R substitution NSCLC who had disease progression on or after treatment with osimertinib were randomised to treatment with amivantamab plus chemotherapy, amivantamab plus chemotherapy with lazertinib, or chemotherapy alone.[5] The dual primary endpoint was used to compare the PFS (using RECIST v1.1 guidelines†) as assessed by blinded independent central review (BICR) for each experimental arm to chemotherapy alone.[5] Secondary endpoints included objective response as assessed by BICR, overall survival (OS), duration of response (DOR), time to subsequent therapy, PFS2 and intracranial PFS.[5]

All study participants underwent serial brain imaging to allow for the robust assessment of intracranial endpoints and to assess the CNS activity of amivantamab and platinum doublet chemotherapy with and without lazertinib.[5] Because brain metastases can lead to significant burden and poor outcomes for patients, this aspect of the study design provides critical information in an area of high unmet need.[7]

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.[9,10,11,12]

The European Commission (EC) has granted marketing authorisation of amivantamab in the following indications:[13]

- In combination with carboplatin and pemetrexed, for the first-line treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations
- As monotherapy, for treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations, after failure of platinum-based therapy
- In combination with carboplatin and pemetrexed, for the treatment of adult patients with advanced NSCLC with EGFR exon 19 deletions (ex19del) or L858R substitution mutations, after failure of prior therapy including an EGFR TKI

In February 2024, a Type II extension of indication application was submitted 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 ex19del or L858R substitution mutations.[14] In May 2024, an application for the extension of the 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, and for the use of SC amivantamab monotherapy in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy.[15]

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.[13]

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

About Lazertinib

Lazertinib is an oral, third-generation, brain-penetrant EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR.[16] An analysis of the efficacy and safety of lazertinib from the Phase 3 LASER301 study was published in *The Journal of Clinical Oncology* in 2023.[16] In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

About Non-Small Cell Lung Cancer

In Europe, it is estimated that 484,306 people were diagnosed with lung cancer in 2022.[17] NSCLC accounts for 85 percent of all lung cancer cases.[18] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[17]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[18] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[18,19] 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. [20,21,22,23] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[24] 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.[25]

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 Research & Development, LLC, Janssen Pharmaceutica NV, Janssen-Cilag, S.A. and Janssen-Cilag International NV 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 International NV, Janssen-Cilag, S.A, Janssen Research & Development nor 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 International NV, Janssen-Cilag, S.A, Janssen Research & Development 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 Tumours, 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.

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

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