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For Immediate Release

European Commission approves RYBREVANT®▼ (amivantamab) in combination with LAZCLUZE®▼ (lazertinib) for the first-line treatment of patients with EGFR-mutated advanced non-small cell lung cancer

This multitargeted, chemotherapy-free combination demonstrated superiority over osimertinib monotherapy for the first-line treatment of patients with EGFR-mutated NSCLC[1]

In the Phase 3 MARIPOSA study, amivantamab plus lazertinib significantly reduced the risk of disease progression or death by 30 percent versus osimertinib monotherapy[1]

BEERSE, BELGIUM (30 December 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved a Type II variation extension of indication for RYBREVANT®▼ (amivantamab), in combination with LAZCLUZE®▼ (lazertinib), for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or exon 21 L858R substitution mutations.

“For people living with advanced NSCLC harbouring EGFR mutations, new treatment options are urgently needed in the first-line setting,” said Enriqueta Felip, M.D., Ph.D, head of the thoracic cancer unit at Vall d’Hebron University Hospital, Barcelona, Spain*. “The amivantamab and lazertinib combination has shown significant progression-free survival improvements in patients with previously untreated EGFR-mutated advanced NSCLC, including those with brain metastases, compared to osimertinib monotherapy. This approval by the European Commission offers the potential to broaden first-line treatment options and provide a new standard of care for eligible patients.”

Lung cancer is Europe’s biggest cancer killer, with NSCLC accounting for 85 percent of all lung cancer cases.[2,3] EGFR mutation-positive NSCLC refers to a subtype of lung cancer based on specific mutations in the EGFR gene.[4] While there are different types of EGFR mutations, EGFR ex19del and EGFR exon 21 L858R are the most common, accounting for approximately 85-90 percent of mutations.[4] Patients are often treated with targeted therapies known as EGFR tyrosine kinase inhibitors (TKIs).[5] However, treatment resistance or disease reoccurrence remains a significant challenge and there is an urgent need for alternative, novel targeted therapies earlier in the treatment pathway to address resistance and improve survival outcomes.[6,7]

“This approval marks significant progress for those living with the devastating impact of EGFR-mutated non-small cell lung cancer, who too often face a poor prognosis and limited treatment options,” said Henar Hevia, Ph.D., Senior Director, EMEA Therapeutic Area Lead, Oncology. “The combination of amivantamab and lazertinib exemplifies the potential of targeted precision medicine, offering a tailored approach that addresses the underlying genetic drivers of the disease, and avoids or delays the need for chemotherapy.”

The EC approval is supported by results from the Phase 3 MARIPOSA (NCT04487080) study, evaluating amivantamab in combination with lazertinib compared to osimertinib as first-line treatment of patients with

locally advanced or metastatic NSCLC with EGFR ex19del or exon 21 L858R substitution mutations.[1] The study, which was featured during a Presidential Symposium session at the 2023 European Society of Medical Oncology (ESMO) Congress, met its primary endpoint of progression-free survival (PFS), and at median follow-up of 22 months, amivantamab plus lazertinib reduced the risk of disease progression or death by 30 percent compared to osimertinib (median PFS: 23.7 months versus 16.6 months; hazard ratio [HR]=0.70; 95 percent confidence interval [CI], 0.58–0.85; *P*<0.001) as assessed by blinded independent central review (BICR).[1] The median duration of response (DOR) was longer for patients receiving amivantamab plus lazertinib compared to osimertinib, with a nine-month improvement in median DOR (25.8 vs. 16.8 months).[1]

The safety profile of the combination of amivantamab and lazertinib was consistent with previous reports from Phase 1-2 studies, with mostly Grade 1 or 2 adverse events (AEs).[1] Toxicity was largely manageable with dose interruptions and reductions, along with supportive care measures commonly used in the treatment of patients with NSCLC.[1] The most common treatment emergent adverse events (TEAEs) of any grade were paronychia (68 percent), infusion-related reactions (63 percent), and rash (62 percent).[1] Amivantamab plus lazertinib had higher rates of EGFR- and MET-related AEs and venous thromboembolism compared to osimertinib, except diarrhoea, for which rates were higher for osimertinib.[1] The commonest grade 3 or higher TEAEs were rash (15 percent), paronychia (11 percent) and dermatitis acneiform (8 percent).[1] The rate of discontinuation of all study treatments due to treatment-related AEs for the amivantamab combination was 10 percent.[1] The rate of interstitial lung disease (including pneumonitis) was less than three percent in both arms.[1]

An EC decision on a Marketing Authorisation (MA) for lazertinib for the corresponding combination regimen indication is pending, following a Committee for Medicinal Products for Human Use (CHMP) positive opinion last month.[8]

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Notes to editors

About the MARIPOSA Study
MARIPOSA (NCT04487080), which enrolled 1,074 patients, is a randomised, Phase 3 study evaluating amivantamab in combination with lazertinib versus osimertinib and versus lazertinib alone in first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or exon 21 L858R substitution mutations.[1] The primary endpoint of the study is PFS (using RECIST v1.1 guidelines‡) as assessed by BICR.[1] Secondary endpoints include overall survival (OS), overall response rate (ORR), duration of response (DOR), second progression free survival (PFS2) and intracranial PFS.[1]

The MARIPOSA study required all patients to have serial brain imaging with magnetic resonance imaging (MRI), which is important for a disease where almost 30 percent of patients develop brain metastases.[1,9] The primary endpoint of PFS in MARIPOSA included these central nervous system (CNS) events detected by serial brain MRIs.[1] The median PFS when censoring CNS-only first progressions was 27.5 months for the combination of amivantamab and lazertinib, compared to 18.5 months for osimertinib (HR=0.68; 95 percent CI, 0.56–0.83; *P*<0.001**).[1] Extracranial PFS, which may more closely approximate what would be seen in other trials, was also explored in MARIPOSA.[1]

Longer-term follow-up data presented at the International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer (WCLC) demonstrated a strong favourable overall survival (OS) trend for amivantamab plus lazertinib versus osimertinib. At three years (median follow-up of 31.1 months), 61 percent of patients receiving amivantamab plus lazertinib were alive compared to 53 percent of those treated with osimertinib based on an analysis performed at the request of a health authority*** (median OS not estimable [NE] vs 37.3 months; HR=0.77; 95 percent CI, 0.61-0.96; nominal *P*=0.019).[10]

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.[11,12,13,14]

The European Commission (EC) has granted marketing authorisation of amivantamab in the following indications:[15]

- In combination in with carboplatin and pemetrexed, for the treatment of adult patients with advanced NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, after failure of prior therapy including an EGFR TKI
- 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 first-line treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations

- In combination with lazertinib for the first-line treatment of adult patients with advanced NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations

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.[16]

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.[15]

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

About Lazertinib
In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of 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.[17] An analysis of the efficacy and safety of lazertinib from the Phase 3 study LASER301 was published in *The Journal of Clinical Oncology* in 2023.[17]

▼ In line with EMA regulations for new medicines, lazertinib 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.[2] NSCLC accounts for 85 percent of all lung cancer cases.[3] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[2]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[3] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[3,18] 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.[19,20,21,22] EGFR ex19del or EGFR exon 21 L858R mutations are the most common EGFR mutations.[23] The five-year survival rate for patients with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent and between 25-32 percent of patients receiving the current first-line standard of care, osimertinib, do not survive long enough to reach second-line treatment.[24,25,26]

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://innovativemedicine.jnj.com/emea/. Follow us at http://www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen-Cilag International NV, Janssen Research & Development, LLC, Janssen Biotech, Inc. and Janssen-Cilag, S.A. 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 or lazertinib. 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, Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag, S.A., 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; 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 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, Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag, S.A., nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

* Prof. Felip has served as a consultant to Janssen-Cilag International NV; she has not been paid for any media work.

** Nominal *P*-value; endpoint was exploratory and not part of hierarchical hypothesis testing.

*** This analysis was requested by health authorities and had nominal alpha spend. A P-value of ≤0.00001 was required for statistical significance.

‡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.

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