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

Latest topline data from the Phase 3 MARIPOSA study shows amivantamab plus lazertinib is the first regimen to demonstrate superior overall survival benefit compared to the current standard of care osimertinib[1]

Median overall survival improvement is expected to exceed one year[1]

BEERSE, BELGIUM (21 January 2025) - Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved a Marketing Authorisation (MA) for LAZCLUZE®▼(lazertinib), in combination with RYBREVANT®▼(amivantamab), 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 (L858R) substitution mutations.

The EC approval is supported by results from the Phase 3 MARIPOSA (NCT04487080) study, evaluating lazertinib in combination with amivantamab compared to osimertinib as first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or exon 21 L858R substitution mutations.[2] The study met its primary endpoint of progression-free survival (PFS).[2] These data were featured during a Presidential Symposium session at the 2023 European Society of Medical Oncology (ESMO) Congress, with longer-term follow-up data presented at the International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer (WCLC).[3,4]

On 7 January 2025, J&J announced new positive topline overall survival (OS) results showing that amivantamab plus lazertinib met the final pre-specified secondary endpoint of OS and demonstrated clinically meaningful and statistically significant improvement in OS versus the current standard of care, osimertinib monotherapy.[1] Median OS is expected to exceed one year.[1] These landmark OS data will be presented at an upcoming medical meeting.

“This chemotherapy-free regimen has already demonstrated significant progression-free survival improvements, and new topline data suggests it is expected to extend life by a median of one year or more, in patients with untreated EGFR-mutated NSCLC versus the current standard of care, osimertinib,” said Antonio Passaro*, M.D., Ph.D., medical oncologist of the Division of Thoracic Oncology, European Institute of Oncology in Milan, Italy. “These results mark a significant step forward in the treatment of EGFR-mutated NSCLC. Extending life expectancy is a critical indicator of a treatment’s impact. The MARIPOSA study reaffirms the potential of first-line treatment with this combination therapy to redefine the standard of care and offer clinically meaningful improvements in outcomes for patients.”

Previously reported findings from the MARIPOSA study have shown the safety profile of the combination of amivantamab and lazertinib to be consistent with findings from Phase 1-2 studies, with mostly Grade 1 or 2 adverse events (AEs).[2] Toxicity was largely manageable with dose interruptions and reductions, along with supportive care measures commonly used in the treatment of patients with NSCLC.[2] The most common treatment emergent adverse events (TEAEs) of any grade were paronychia (68 percent), infusion-related reactions (63 percent), and rash (62 percent).[2] 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.[2] The commonest grade 3 or higher TEAEs were rash (15 percent), paronychia (11 percent), dermatitis acneiform (8 percent) and pulmonary embolism (8%).[2] The rate of discontinuation of all study treatments due to treatment-related AEs for the amivantamab combination was 10 percent.[2] The rate of interstitial lung disease (including pneumonitis) was three percent in both arms.[2]

“Currently, the five-year survival rate for patients with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors is less than 20 percent,” said Henar Hevia, Ph.D., Senior Director, EMEA Therapeutic Area Lead, Oncology. “Today’s approval marks an important moment in lung cancer care, bringing a new option to patients through a chemotherapy-free regimen, and potentially offering more time with their loved ones.”

This EC decision follows a corresponding EC approval in December 2024 of a Type II variation extension of indication for the bispecific antibody amivantamab, 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.[5]

-ENDS-

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.[2] The primary endpoint of the study is PFS (using RECIST v1.1 guidelines‡) as assessed by BICR.[2] Secondary endpoints include overall survival (OS), overall response rate (ORR), duration of response (DOR), second progression free survival (PFS2) and intracranial PFS.[2]

The study 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).[2] 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).[2]

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.[2,6] The primary endpoint of PFS in MARIPOSA included these central nervous system (CNS) events detected by serial brain MRIs.[2] The median PFS when censoring CNS-only first progressions was 27.5 months for the combination of amivantamab and lazertinib, compared to 18.4 months for osimertinib (HR=0.68; 95 percent CI, 0.55–0.83; *P*<0.001**).[2,4]

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 tyrosine kinase inhibitor (TKI) that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR.[7] 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.[7]

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

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.[8,9,10,11]

The European Commission (EC) has granted marketing authorisation of amivantamab in the following indications:[5,12]

- 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 combination 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.
- 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 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.[13]

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.[12]

▼ 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.[14] NSCLC accounts for 85 percent of all lung cancer cases.[15] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[14]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[15] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[15,16] 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.[17,18,19,20] EGFR ex19del or EGFR exon 21 L858R mutations are the most common EGFR mutations.[21] 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.[22,23,24]

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 https://www.linkedin.com/company/jnj-innovative-medicine-emea/. Janssen-Cilag International NV, 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 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, 2024, 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 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. Passaro has served as a consultant to Janssen-Cilag International NV; he has not been paid for any media work.

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

‡ 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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[1] https://innovativemedicine.jnj.com/. RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) show statistically significant and clinically meaningful improvement in overall survival versus osimertinib. Available at: https://www.jnj.com/media-center/press-

releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-shows-statistically-significant-and-clinically-meaningful-improvement-in-overall-survival-versus-osimertinib. Accessed January 2025

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[5] Innovativemedicine.jnj.com/EMEA. 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. Available at: https://innovativemedicine.jnj.com/emea/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. Accessed January 2025.

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