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For Immediate Release

European Commission approves subcutaneous RYBREVANT®▼ (amivantamab) for the treatment of patients with advanced EGFR-mutated non-small cell lung cancer

Subcutaneous (SC) amivantamab offers patients greater convenience, reducing administration time from hours to minutes and with a five-fold reduction in infusion-related reactions compared to the IV formulation[1]

European Commission (EC) approval based on positive results from the Phase 3 PALOMA-3 study[1]

BEERSE, BELGIUM (7 April 2025) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved an extension of marketing authorisation for a subcutaneous (SC) formulation of 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, and as a monotherapy for the treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy. For these indications, it is recommended that SC amivantamab is administered weekly from Weeks 1 to 4 (total of four doses), then every two weeks starting at Week 5 onwards.[1]

This approval follows the recent presentation of final overall survival (OS) results from the Phase 3 MARIPOSA study (NCT04487080), at the 2025 European Lung Cancer Congress (ELCC), showing statistically superior OS with intravenous (IV) amivantamab plus lazertinib versus osimertinib monotherapy in the first-line treatment of patients with advanced EGFR ex19del or L858R substitution mutated NSCLC (hazard ratio [HR], 0.75; 95 percent Confidence Interval [CI], 0.61-0.92; P<0.005).[2]

“While great strides have been made in the treatment of EGFR-mutated non-small cell lung cancer, a critical need still exists for treatment approaches that are not only effective but also more convenient for patients, while optimising experience in the clinic,” said Silvia Novello, M.D., Ph.D., Professor of Medical Oncology in the Oncology Department at San Luigi Hospital in Orbassano, University of Turin, Italy.* “The approval of subcutaneous amivantamab will have a meaningful impact on clinical practice, offering patients greater convenience and an improved treatment experience, without compromising on the well-established efficacy of intravenous amivantamab.”

The EC approval is supported by positive results from the Phase 3 PALOMA-3 study (NCT05388669), which evaluated non-inferiority of pharmacokinetics (PK) in addition to efficacy and safety of SC amivantamab (administered via manual injection) compared to IV amivantamab (the already approved route of administration), both in combination with lazertinib, in patients with EGFR-mutated advanced or metastatic NSCLC after disease progression on osimertinib and platinum-based chemotherapy.[1,3] The study demonstrated that SC amivantamab was non-inferior to IV amivantamab, meeting both co-primary PK endpoints as measured by amivantamab levels in the blood (C_{trough} and area under the serum concentration time curve from Cycle 2 day 1 to 15).[1] At a median follow-up of 7 months, the overall response rate (a secondary endpoint) was 30 percent (95 percent confidence interval [CI], 24–37) in the SC arm and 33 percent (95 percent CI, 26–39) for IV (relative risk, 0.92; 95 percent CI, 0.70–1.23; *P*=0.001), meeting the non-inferiority criteria.[1]

Administration time for SC amivantamab was approximately five minutes, and results showed a five-fold reduction in infusion-related reactions (IRRs) compared to IV administration.[1] These results were featured as an oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting and published in the *Journal of Clinical Oncology*.[1,4]

“The approval of subcutaneous amivantamab represents a welcome improvement of the treatment experience for both patients living with EGFR-mutated advanced non-small cell lung cancer and the healthcare professionals who support

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them," said Henar Hevia, PhD., Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. "This advancement presents an important opportunity to reduce the treatment burden, improve quality of life and give patients more time to focus on what truly matters to them."

The rate of IRRs for patients treated with SC amivantamab combined with lazertinib was shown to be approximately five-fold lower than that observed with the IV formulation (13 percent vs 66 percent, respectively).[1] The majority of IRRs were grades 1 and 2, with one patient experiencing a grade 3 IRR in the SC arm.[1] Preventive blood thinning (prophylactic anticoagulation) was used in most patients in the PALOMA-3 study.[1] Patients receiving prophylactic anticoagulation had lower rates of venous thromboembolic events (VTEs) (10 percent) than those who did not receive prophylaxis (21 percent).[1] Furthermore, VTE incidence was numerically lower in the SC arm vs the IV arm (9 percent vs 14 percent) regardless of anticoagulation status.[1] Severe bleeding risk (grade 3 to 4) was low among patients receiving anticoagulants in both the SC (2 percent) and IV (0.6 percent) arms.[1] Otherwise, the overall safety profile of SC amivantamab is consistent with the known profile of IV administration.[1] The most common all-grade adverse events of any cause that occurred for SC amivantamab compared to IV, were paronychia (54 percent vs 51 percent), hypoalbuminaemia (47 percent vs 37 percent) and rash (46 percent vs 43 percent), respectively.[1]

"At Johnson & Johnson, we are dedicated to patient-centered innovation in our mission to address the critical unmet needs in lung cancer treatment and care," said Joshua Bauml, M.D., Vice President, Lung Cancer Disease Area Stronghold Leader, Johnson & Johnson Innovative Medicine. "Our ongoing focus on advancing the clinical development programme for amivantamab reflects our confidence in its potential to become a standard of care for EGFR-and MET-driven lung cancer."

#ENDS#

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) has approved amivantamab in the following indications:[8]

Intravenous 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.
- 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.

Subcutaneous 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.
- As monotherapy for treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations, after failure of platinum-based therapy.

The recommended dose regimen for SC amivantamab for these indications is 1600 mg (2240 mg for body weight ≥80kg) administered weekly from Weeks 1 to 4 (total of four doses), then every two weeks starting at Week 5 onwards (Q2W).[8] When given in combination with lazertinib, it is recommended to administer SC amivantamab any time after lazertinib when given on the same day.[8]

Subcutaneous amivantamab is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[1]

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.[8]

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

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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.[9] 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.[9]

In January 2025, the European Commission EC approved a marketing authorisation for lazertinib, in combination with amivantamab, for the first-line treatment of adult patients with advanced NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations.[10]

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using lazertinib, please refer to the Summary of Product Characteristics.[11]

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

About PALOMA-3
PALOMA-3 (NCT05388669), which enrolled 418 patients, is a randomised, open-label Phase 3 study evaluating the non-inferiority of pharmacokinetics (PK), efficacy and safety of subcutaneous amivantamab (administered via manual injection) combined with lazertinib compared to IV amivantamab and lazertinib in patients with EGFR-mutated advanced or metastatic NSCLC after progression on osimertinib and platinum-based chemotherapy.[1] The co-primary PK endpoints of the study were trough concentration (C_{trough} on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUCD1-D15).[1] Key secondary endpoints were objective response rate (ORR) and progression-free survival (PFS).[1] Overall survival was a predefined exploratory endpoint.[1] Prophylactic anticoagulation was recommended for the first four months of treatment.[1]

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 exon 21 L858R mutations are the most common EGFR mutations.[19] The five-year survival rate for all 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.[20,21,22,23,24,25,26] EGFR exon 20 insertion (ex20ins) mutations are the third most prevalent activating EGFR mutation.[27] Patients with EGFR ex20ins mutations have a real-world five-year OS of eight percent in the frontline setting, which is worse than patients with EGFR ex19del or L858R mutations, who have a real-world five-year OS of 19 percent.[21]

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 most recent Annual Report on Form 10-K, 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.

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

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References

[1] Leighl NB et al. Subcutaneous Versus Intravenous Amivantamab, Both in Combination With Lazertinib, in Refractory Epidermal Growth Factor Receptor–Mutated Non–Small Cell Lung Cancer: Primary Results From the Phase III PALOMA-3 Study. *ASCO Journal of Clinical Oncology*. 2024;42(3):3593-3605.
[2] Yang J, et al. Amivantamab Plus Lazertinib vs Osimertinib in First-line (1L) EGFR-mutant (EGFRm) Advanced NSCLC: Final Overall Survival (OS) from the Phase 3 MARIPOSA Study. 2025 European Lung Cancer Congress. March 26, 2025.
[3] ClinicalTrials.gov. A Study of Lazertinib With Subcutaneous Amivantamab Compared With Intravenous Amivantamab in Participants With Epidermal Growth Factor Receptor (EGFR)-Mutated Advanced or Metastatic Non-small Cell Lung Cancer (PALOMA-3). https://clinicaltrials.gov/ct2/show/NCT05388669. Accessed April 2025.
[4] Leighl N, et al. Subcutaneous Amivantamab Plus Lazertinib Vs Intravenous Amivantamab Plus Lazertinib In EGFR-mutated, Advanced Non-small Cell Lung Cancer (NSCLC): PALOMA-3, A Phase 3, Global, Randomized, Controlled Trial. 2024 American Society of Clinical Oncology Annual Meeting. May 31, 2024.
[5] Moores SL, et al. A Novel Bispecific Antibody Targeting EGFR and cMet Is Effective against EGFR Inhibitor-Resistant Lung Tumors. *Cancer Res* 2016;76(13)(suppl 27216193):3942-3953.
[6] Grugan KD, et al. Fc-mediated activity of EGFR x c-Met bispecific antibody JNJ-61186372 enhanced killing of lung cancer cells. *Mabs*. 2017;9(1):114-126.
[7] Yun J, et al. Antitumor Activity of Amivantamab (JNJ-61186372), an EGFR–MET Bispecific Antibody, in Diverse Models of EGFR Exon 20 Insertion–Driven NSCLC. *Cancer Discov*. 2020;10(8):1194-1209.
[8] European Medicines Agency. Amivantamab Summary of Product Characteristics. January 2025. Available at: https://www.ema.europa.eu/en/documents/product-information/rybrevant-epar-product-information_en.pdf. Accessed: April 2025.
[9] Cho, BC, et al. Lazertinib versus gefitinib as first-line treatment in patients with *EGFR*-mutated advanced non-small-cell lung cancer: Results From LASER301. J Clin Oncol. 2023;41(26):4208-4217.
[10] Innovativemedicine.jnj.com/EMEA. 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. Available at: https://www.jnj.com/media-center/press-releases/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. Accessed: April 2025
[11] European Medicines Agency. Lazcluze. January 2025. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/lazcluze. Accessed April 2025.
[12] Global Cancer Observatory. Cancer Today. Available at: https://gco.iarc.fr/en. Accessed April 2025.
[13] Zappa C, et al. Non-small cell lung cancer: current treatment and future advances. *Transl Lung Cancer Res*. 2016;5(3):288–300.
[14] Wee P, Wang Z. Epidermal Growth Factor Receptor Cell Proliferation Signaling Pathways. Cancers. 2017;9(5):52.
[15] Pennell NA, et al. A phase II trial pf adjuvant erlotinib in patients with resected epidermal growth factor receptor-mutant non-small cell lung cancer. *J Clin Oncol*. 2019;37(7);97-104.
[16] Burnett H, et al. Epidemiological and clinical burden of EGFR exon 20 insertion in advanced non-small cell lung cancer: a systematic literature review. Abstract presented at: World Conference on Lung Cancer Annual Meeting; January 29, 2021; Singapore.
[17] Zhang YL, et al. The prevalence of EGFR mutation in patients with non-small cell lung cancer: a systematic review and meta-analysis. *Oncotarget*. 2016;7(48):78985-78993.
[18] Midha A, et al. EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: a systematic review and global map by ethnicity. *Am J Cancer Res*. 2015;5(9):2892-2911.
[19] American Lung Association. EGFR and Lung Cancer. Available at: https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/symptoms-diagnosis/biomarker-testing/egfr. Accessed April 2025.
[20] Lin JJ, et al. Five-Year Survival in EGFR-Mutant Metastatic Lung Adenocarcinoma Treated with EGFR-TKIs. J Thorac Oncol 2016 Apr;11(4):556-65.
[21] Girard N, et al. Comparative clinical outcomes for patients with NSCLC harboring EGFR exon 20 insertion mutations and common EGFR mutations. Abstract presented at: World Conference on Lung Cancer Annual Meeting; January 29, 2021; Singapore.
[22] Shao J et al. The number of brain metastases predicts the survival of non-small cell lung cancer patients with EGFRR mutation status. *Cancer Rep (Hoboken).* 2022;5(9): e1550.
[23] Achrol A et al. Brain metastases. *Nat Rev Dis Primers*. 2019;17(5): 5.
[24] Rangachari D et al. Brain metastases in patients with EGFR-mutated or ALK-rearranged non-small-cell lung cancers. *Lung Cancer*. 2015;88(1): 108-111.
[25] Nieva J, et al. A real-world (rw) observational study of long-term survival (LTS) and treatment patterns after first-line (1L) osimertinib in patients (pts) with epidermal growth factor receptor (EGFR) mutation-positive (m) advanced non-small cell lung cancer (NSCLC). *Ann Oncol*. 2023;34, S774.
[26] Girard N, Leighl NB, Ohe Y, et al. Mortality among EGFR-mutated advanced NSCLC patients after starting frontline osimertinib treatment: a real-world, US attrition analysis. Presented at: the European Lung Cancer Congress; March 29-April 1, 2023; Copenhagen, Denmark. Poster 19P.
[27] Arcila, M. et al. EGFR exon 20 insertion mutations in lung adenocarcinomas: prevalence, molecular heterogeneity, and clinicopathologic characteristics. Mol Cancer Ther. 2013 Feb; 12(2):220-9.