**News Release**

**Media Contacts:**
Noah Reymond
Phone: +31 621 38 5718
Email: NReymond@its.jnj.com

Sarah Jones
Phone: +44 7917 849 211
Email: SJones39@its.jnj.com

**Investor Relations:**
Jessica Moore
Phone: +41 79 395 4823
Email: Jmoore29@its.jnj.com

# Janssen EMEA Receives Conditional Marketing Authorisation for RYBREVANT® ▼ (amivantamab), the First Treatment Approved for Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) with EGFR Exon 20 Insertion Mutations After Failure of Platinum-Based Therapy

*Conditional Marketing Authorisation is based on results from the Phase 1 CHRYSALIS study evaluating amivantamab as a monotherapy in patients after previous treatment with platinum-based therapy*[1,2,3]

**BEERSE, BELGIUM, 10 December, 2021** – The Janssen Pharmaceutical Companies of Johnson & Johnson announced Conditional Marketing Authorisation (CMA) of RYBREVANT® ▼ (amivantamab) for the treatment of adult patients with advanced NSCLC with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations, after failure of platinum-based therapy.[1] Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.[1,2,4]

"Patients with NSCLC harbouring EGFR exon 20 insertion mutations represent a specific population who have been underserved by current treatment options that are limited in both number and efficacy.[5] The decision made by the European Commission represents an important milestone and recognises that amivantamab offers a new treatment specifically targeted for patients with this alteration," said Antonio Passaro, M.D., Ph.D, Medical

Oncologist at the Division of Thoracic Oncology of the European Institute of Oncology in Milan, Italy.[†]

The CMA is based on results from the Phase 1 CHRYSALIS study, a multicentre, open-label, clinical study evaluating amivantamab as a monotherapy in patients after previous treatment with platinum-based therapy, which demonstrated efficacy and a generally well-tolerated safety profile.[‡4,6] The investigator-assessed overall response rate was 37 percent (95 percent CI, 28% - 46%), with a median duration of response of 12.5 months (95 percent CI, 6.5 – 16.1) and 64 percent of patients having a duration of response greater than or equal to 6 months.[4] These results were consistent with those reported by blinded independent central review assessment, which showed an overall response rate of 43 percent (34% – 53%), with a median duration of response of 10.8 months (95 percent CI, 6.9 – 15.0) and 55 percent of patients having a duration of response greater than or equal to 6 months.[4]

Analysis showed the median progression-free survival (time experienced without progression or death) was 8.3 months (95 percent CI, 6.5 – 10.9) and the median overall survival in patients treated with amivantamab was 22.8 months (95 percent CI, 14.6 – not reached).[6]

The most common adverse events (AEs) at all grades included rash (76 percent), infusion-related reactions (67 percent) and nail toxicity (47 percent), and these were predominantly Grade 1-2.[4] Treatment-related discontinuations due to adverse events were seen in three percent of patients.[4] Ninety-nine percent of infusion-related reactions occurred with the first infusions and rarely impacted the ability to continue with subsequent treatments (1.1 percent led to treatment discontinuation).[4]

"This marketing authorisation addresses a high unmet need by bringing a new treatment option to this patient population and their healthcare professionals for the first time in Europe. It is an important step towards our goal to deliver innovative therapies that will transform the trajectory of lung cancer," commented Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC.

Conditional marketing authorisation is the approval of a medicine that addresses unmet medical needs of patients based on less comprehensive data than normally required, where

the benefit of immediate availability of the medicine outweighs the risk, and the applicant is able to provide comprehensive clinical data in the future.[7] This CMA follows other recent approvals for amivantamab, including the U.S. Food and Drug Administration (FDA), who approved the treatment in May 2021 for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, whose disease has progressed on or after platinum-based chemotherapy.[8] Additional regulatory applications have been submitted and are being reviewed by other regulatory bodies worldwide.

"We are committed to changing the face of cancer care," said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, Johnson & Johnson. "At Janssen, we're striving to transform long-term patient outcomes and improve quality of life with the right treatment, for the right patient, at the right time."

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† Dr Passaro has previously provided paid consultancy services for Janssen in relation to research and advisory boards. He has not been compensated for any media work.

‡ Results reported in the SmPC are from 114 patients with a median follow up of 12.5 months.[4] Results reported in Park et al are from 81 patients and a median follow up of 9.7 months.[6] Not all efficacy endpoints were reported in the SmPC.[4,6]

**About Amivantamab**

Amivantamab is a fully-human EGFR-MET bispecific antibody with immune cell-directing activity that targets tumours with activating and resistance EGFR mutations and MET mutations and amplifications, approved for patients with advanced non-small cell lung cancer (NSCLC) with EGFR exon 20 insertion mutations after failure of platinum-based therapy.[1,9,10,11,12] Amivantamab is being studied in multiple clinical trials, including:[13]

- the Phase 1/1b, CHRYSALIS-2 (NCT04077463) study assessing the combination of amivantamab and lazertinib in patients who have progressed after treatment with osimertinib and chemotherapy, as well as lazertinib as a monotherapy[14]
- as first-line therapy in the Phase 3 MARIPOSA (NCT04487080) study assessing amivantamab in combination with lazertinib, a novel third-generation EGFR tyrosine kinase inhibitor (TKI), against osimertinib and against lazertinib alone in untreated advanced EGFR-mutated NSCLC[15]

- the Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of lazertinib, amivantamab and carboplatin-pemetrexed vs. with carboplatin-pemetrexed in participants with locally advanced or metastatic EGFR Exon 19del or Exon 21 L858R substitution NSCLC after osimertinib failure[16]
- the Phase 3 PAPILLON (NCT04538664) study assessing amivantamab in combination with carboplatin-pemetrexed vs carboplatin-pemetrexed for patients with advanced or metastatic EGFR-mutated NSCLC with exon 20 insertion mutations[17]
- the Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous (SC) administration of amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for amivantamab SC delivery with the aim to find effective solutions that positively impact patient management.[18]

**About the CHRYSALIS Study**

CHRYSALIS (NCT02609776) is an open-label, multicentre, first-in-human Phase 1 study to evaluate the safety, pharmacokinetics and preliminary efficacy of amivantamab as a monotherapy, in combinations with lazertinib and in combination with platinum-based chemotherapy, in patients with advanced NSCLC with various EGFR mutations.[3] In the study, investigators assessed efficacy using overall response rate per Response Evaluation Criteria in Solid Tumours Version 1.1* (RECIST v1.1), clinical benefit rate, median duration of response and median progression-free survival, as well as the safety profile of amivantamab.[3,19]

The study will enrol 780 patients with advanced NSCLC.[3] The study consists of two parts: the first consists of amivantamab monotherapy and combination dose escalations, and the second consists of amivantamab monotherapy and combination dose expansions.[3]

The first cohort of participants received intravenous infusions of amivantamab as monotherapy.[3]

*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.[3]

**About Non-Small Cell Lung Cancer (NSCLC)**

In Europe, it is estimated that 477,534 patients were diagnosed with lung cancer in 2020, with around 85 percent diagnosed with NSCLC.[20,21] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[20]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[21] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase supporting cell growth and division.[22] EGFR mutations are present in 16 to 19 percent of Caucasian patients with NSCLC and present in 37 to 41 percent of Asian patients who have NSCLC adenocarcinoma.[23] The five-year survival rate for all people with metastatic NSCLC and EGFR mutations who are treated with EGFR TKIs is less than 20 percent.[24] Patients with EGFR exon 20 insertion mutations have a real-world five-year overall survival (OS) of 8 percent in the frontline setting, which is worse than patients with EGFR exon 19 deletions or L858R mutations, who have a real-world five-year OS of 19 percent.[25]

**About the Janssen Pharmaceutical Companies of Johnson & Johnson**

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology and Pulmonary Hypertension.

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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 amivantamab and 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 Research & Development, LLC any of the other Janssen Pharmaceutical Companies, 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 January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies 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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***References:***


[1] European Medicines Agency. Rybrevant CMA Approval. December 2021.
[2] Remon, J et al. EGFR exon 20 insertions in advanced non-small cell lung cancer: A new history begins. Cancer Treatment Reviews. 90 (2020).
[3] ClinicalTrials.gov. Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants With Advanced Non-Small Cell Lung Cancer (CHRYSALIS). Available at: https://clinicaltrials.gov/ct2/show/NCT02609776. Accessed November 2021.
[4] European Medicines Agency. Rybrevant Summary of Product Characteristics. December 2021.
[5] Vyse S et al. Targeting EGFR exon 20 insertion mutations in non-small cell lung cancer. Signal Transduct Target Ther 2019; 4: 5. 2, Riess J et al. JTO 2018; 13(10): 1560–1568.
[6] Park et al. Amivantamab in EGFR Exon 20 Insertion–Mutated Non–Small-Cell Lung Cancer Progressing on Platinum Chemotherapy: Initial Results From the CHRYSALIS Phase I Study. Available at https://ascopubs.org/doi/10.1200/JCO.21.00662?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed. Accessed November 2021.
[7] Conditional marketing authorisation. The European Medicines Agency. Available at: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/conditional-marketing-authorisation
[8] Johnson and Johnson. RYBREVANT® (amivantamab-vmjw) Receives FDA Approval as the First Targeted Treatment for Patients with Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations. Available at: https://www.jnj.com/rybrevanttm-amivantamab-vmjw-receives-fda-approval-as-the-first-targeted-treatment-for-patients-with-non-small-cell-lung-cancer-with-egfr-exon-20-insertion-mutations. Accessed November 2021.
[9] Grugan 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.

[10] Moores 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.
[11] Yun 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.
[12] Vijayaraghavan et al. Amivantamab (JNJ-61186372), an Fc Enhanced EGFR/cMet Bispecific Antibody, Induces Receptor Downmodulation and Antitumor Activity by Monocyte/Macrophage Trogocytosis. Mol Cancer Ther. 2020;19(10):2044-2056.
[13] ClinicalTrials.gov. Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants With Advanced Non-Small Cell Lung Cancer. Available at: https://clinicaltrials.gov/ct2/show/NCT02609776. Accessed November 2021
[14] A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer. Available at: https://clinicaltrials.gov/ct2/show/NCT04077463. Accessed November 2021
[15] ClinicalTrials.gov. A Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib in Locally Advanced or Metastatic Non-Small Cell Lung Cancer (MARIPOSA). Available at: https://clinicaltrials.gov/ct2/show/NCT04487080. Accessed November 2021
[16] ClinicalTrials.gov. A Study of Amivantamab and Lazertinib in Combination With Platinum-Based Chemotherapy Compared With Platinum-Based Chemotherapy in Patients With Epidermal Growth Factor Receptor (EGFR)-Mutated Locally Advanced or Metastatic Non- Small Cell Lung Cancer After Osimertinib Failure (MARIPOSA-2). Available at https://clinicaltrials.gov/ct2/show/NCT04988295 Accessed November 2021
[17] ClinicalTrials.gov. A Study of Combination Amivantamab and Carboplatin-Pemetrexed Therapy, Compared With Carboplatin-Pemetrexed, in Participants With Advanced or Metastatic Non-Small Cell Lung Cancer Characterized by Epidermal Growth Factor Receptor (EGFR) Exon 20 Insertions (PAPILLON). Available at: https://clinicaltrials.gov/ct2/show/NCT04538664?term=PAPILLON&cond=NSCLC&draw=2&rank=1. Accessed November 2021.
[18] ClinicalTrials.gov. A Study of Amivantamab Subcutaneous (SC) Administration for the Treatment of Advanced Solid Malignancies. Available at: https://clinicaltrials.gov/ct2/show/NCT04606381. Accessed November 2021.
[19] Park et al, Amivantamab (JNJ-61186372), an anti-EGFR-MET bispecific antibody, in patients with EGFR exon 20 insertion (exon20ins)-mutated non-small cell lung cancer (NSCLC). Available at https://ascopubs.org/doi/abs/10.1200/JCO.2020.38.15_suppl.9512. Accessed November 2021.
[20] Globocan 2020. Estimated number of incident cases deaths in 2020, Europe, both sexes, all ages. Available at: www.gco.iarc.fr. Accessed November 2021.
[21] Zappa C et al. Non-small cell lung cancer: current treatment and future advances. Transl Lung Cancer Res 2016; 5(3): 288–300.
[22] Wee,P, Wang, Z. Epidermal Growth Factor Receptor Cell Proliferation Signaling Pathways. Cancers (Basel). 2017 May; 9(5): 52.
[23] Zhang 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.
[24] Lin JJ, Cardarella S, Lydon CA, Dahlberg SE, Jackman DM, Jänne PA, et al. Five-Year Survival in EGFR-Mutant Metastatic Lung Adenocarcinoma Treated with EGFR-TKIs. J Thorac Oncol. 2016 Apr;11(4):556-65.
[25] Girard N, BazhenovaL, MinchomA, OuSI, GadgeelSM, Trigo J, 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.