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News Release

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Janssen Submits Application to the European Medicines Agency for RYBREVANT®▼ (amivantamab) in Combination with Chemotherapy for the First-Line Treatment of Adult Patients with Advanced Non-Small Cell Lung Cancer with Activating EGFR Exon 20 Insertion Mutations

Type II Extension of Indication Application is supported by data from PAPHILLON, the first randomised Phase 3 study to read out in patients with NSCLC with EGFR exon 20 insertion mutations¹

BEERSE, BELGIUM, 6 October, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Type II extension of indication application to the European Medicines Agency (EMA) seeking approval of RYBREVANT®▼ (amivantamab) in combination with chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations.

“People living with advanced or metastatic NSCLC with activating EGFR exon 20 insertion mutations generally face a poor survival probability, and new treatment options are urgently needed from the very first line of therapy,” said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. “Today’s submission to the EMA highlights our deep commitment to change the trajectory of lung cancer, through earlier intervention with targeted treatment options for eligible patients.”

Amivantamab was granted a conditional marketing authorisation by the European Commission in [December 2021](#) as the first fully-human, bispecific antibody for the monotherapy treatment of patients with NSCLC with EGFR exon 20 insertion mutations, after failure of platinum-based therapy.^{2,3}

The latest submission to the EMA is supported by data from the Phase 3 PAPILLON clinical study ([NCT04538664](#)), a randomised, open-label study evaluating the efficacy and safety of amivantamab in combination with chemotherapy as first-line treatment in patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.⁴ In July, Janssen [announced](#) that the PAPILLON study had met its primary endpoint with a statistically significant and clinically meaningful improvement in progression-free survival (PFS; as measured by blinded independent central review [BICR]) in patients receiving amivantamab in combination with chemotherapy versus chemotherapy alone.⁵ The combination of amivantamab and chemotherapy demonstrated a safety profile consistent with the safety profiles of the individual components.⁵

“PAPILLON is the first randomised Phase 3 study to read out in patients with NSCLC with EGFR exon 20 insertion mutations. Pending approval, this creates an opportunity to make a significant improvement to the standard of care for this patient population, where high unmet medical needs remain,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. “We look forward to working with the EMA to bring this potential new indication to the lung cancer community as soon as possible.”

The submission to the EMA follows the recent [submission](#) of a supplemental biologics license application (sBLA) to the U.S. Food and Drug Administration (FDA) seeking expanded approval of amivantamab as a first-line combination treatment in patients with advanced or metastatic EGFR exon 20 insertion mutation-positive NSCLC.

#ENDS#

About PAPILLON

PAPILLON ([NCT04538664](#)) is a randomised, open-label Phase 3 study evaluating the efficacy and safety of amivantamab in combination with chemotherapy, compared with chemotherapy alone, in the first-line setting for patients with advanced or metastatic NSCLC characterised by EGFR exon 20 insertion mutations.⁴ The primary endpoint of the study is PFS (using RECIST v1.1 guidelines*) as assessed by BICR. Secondary endpoints include overall response rate

(ORR), PFS after first subsequent therapy, time to symptomatic progression and overall survival (OS).⁴ The patients who received chemotherapy alone could transition to amivantamab monotherapy in a second-line setting after confirmation of disease progression.⁵

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.^{2,6,7,8,9} The European Commission granted Conditional Marketing Authorisation of amivantamab in December 2021 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.² Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.² Amivantamab also received accelerated approval by the U.S. FDA in May 2021 for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.¹⁰

The Phase 3 PAPILLON study is part of an extensive clinical trial programme for amivantamab in NSCLC, which includes:

- The Phase 3 MARIPOSA ([NCT04487080](#)) study assessing amivantamab in combination with lazertinib, a novel third generation EGFR TKI, versus osimertinib and versus lazertinib alone as first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions (ex19del) or L858R substitution mutations.¹¹
- The Phase 3 MARIPOSA-2 ([NCT04988295](#)) study assessing the efficacy of amivantamab (with or without lazertinib) and carboplatin-pemetrexed versus carboplatin-pemetrexed in patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC after disease progression on or after osimertinib.¹²

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](#).²

▼In line with EMA regulations for new medicines and those given conditional approval, amivantamab is subject to additional monitoring.

About Non-Small Cell Lung Cancer

In Europe, it is estimated that 477,534 patients were diagnosed with lung cancer in 2020, with around 85 percent diagnosed with NSCLC.^{13,14} Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.¹³

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 supporting cell growth and division.¹⁶ EGFR mutations are present in 10 to 15 percent of people with NSCLC adenocarcinoma and occur in 40 to 50 percent of Asian patients.^{17,18,19,20,21} EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.²² The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.²³ EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.²⁴ Patients with EGFR exon 20 insertion mutations have a real-world five-year OS of 8 percent in the frontline setting, which is worse than patients with EGFR ex19del or L858R mutations.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 & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com/emea. Follow us at www.linkedin.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag GmbH, and Janssen Research & Development, LLC are Johnson & Johnson companies.

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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 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 materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag GmbH, Janssen Research and Development, LLC, 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior 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 1, 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 www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Pharmaceutica NV, Janssen-Cilag GmbH, Janssen Research and Development, LLC, 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.

References

¹ Results from Clinical Trials.gov website. Available at: [Search of: exon 20 insertion mutations | Non-small Cell Lung Cancer | Phase 3 - List Results - ClinicalTrials.gov](#). Accessed October 2023.

² European Medicines Agency. Amivantamab Summary of Product Characteristics. January 2023. Available at: [Rybrevant, INN-amivantamab \(europa.eu\)](http://europa.eu). Accessed: October 2023.

³ Remon J, et al. EGFR exon 20 insertions in advanced non-small cell lung cancer: A new history begins. *Cancer Treatment Reviews*. 90 (2020).

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- ⁴ 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>. Accessed October 2023.
- ⁵ Pharmaceutical Companies of Johnson and Johnson. (2023 July 17). Treatment with RYBREVANT® (amivantamab-vmjw) Plus Chemotherapy Resulted in Statistically Significant and Clinically Meaningful Improvement in Progression-Free Survival in Patients with Newly Diagnosed EGFR Exon 20 Insertion Mutation-Positive Non-Small Cell Lung Cancer [Press Release].
- ⁶ 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.
- ⁷ 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.
- ⁸ 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.
- ⁹ Vijayaraghavan et al. Amivantamab (JNJ-61186372), an Fc Enhanced EGFR/cMet Bispecific Antibody, Induces Receptor Downmodulation and Antitumor Activity by Monocyte/Macrophage Trophocytosis. *Mol Cancer Ther*. 2020;19(10):2044-2056.
- ¹⁰ JanssenEMEA.com. Janssen Announces New Data Supporting Safety and Efficacy of RYBREVANT® and Lazertinib Combination for Patients with Non-Small Cell Lung Cancer and EGFR Mutations. Available at: https://www.jnj.com/janssen-announces-new-data-supporting-safety-and-efficacy-of-rybrevant-and-lazertinib-combination-for-patients-with-non-small-cell-lung-cancer-and-egfr-mutations#_edn9. Accessed October 2023.
- ¹¹ 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 October 2023.
- ¹² 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 October 2023.
- ¹³ Globocan 2020. Estimated number of incident cases deaths in 2020, Europe, both sexes, all ages. Available at: www.gco.iarc.fr. Accessed October 2023.
- ¹⁴ Zappa C et al. Non-small cell lung cancer: current treatment and future advances. *Transl Lung Cancer Res* 2016;5(3): 288–300.
- ¹⁵ American Cancer Society. What is Lung Cancer? Available at: <https://www.cancer.org/cancer/types/lung-cancer/about/what-is.html> Last accessed: October 2023.
- ¹⁶ Bauml JM, et al. Underdiagnosis of EGFR Exon 20 Insertion Mutation Variants: Estimates from NGS-based Real World Datasets. Abstract presented at: World Conference on Lung Cancer Annual Meeting; January 29, 2021; Singapore.
- ¹⁷ Riess JW, et al. Diverse EGFR exon 20 insertions and co-occurring molecular alterations identified by comprehensive genomic profiling of NSCLC. *J Thorac Oncol*. 2018;13(10):1560-1568. doi:10.1016/j.jtho.2018.06.019
- ¹⁸ Pennell NA, et al. A phase II trial of adjuvant erlotinib in patients with resected epidermal growth factor receptor-mutant non-small cell lung cancer. *J Clin Oncol*. 37:97-104.
- ¹⁹ 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.
- ²⁰ 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.
- ²¹ 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.
- ²² American Lung Association. EGFR and Lung Cancer. <https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/symptoms-diagnosis/biomarker-testing/egfr>. Accessed October 2023.
- ²³ 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.
- ²⁴ Arcila, M. et al. EGFR exon 20 insertion mutations in lung adenocarcinomas: prevalence, molecular heterogeneity, and clinicopathologic characteristics. *Molecular Cancer Therapeutics*. 2013; Feb; 12(2):220-9.
- ²⁵ 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.