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For Immediate Release

Late-breaking results from PALOMA-2 study of subcutaneous RYBREVANT®▼ (amivantamab) in combination with lazertinib show clinically meaningful antitumour response and improved safety profile in patients with EGFR-mutated non-small cell lung cancer

Significantly lower infusion-related reactions seen with subcutaneous amivantamab compared with intravenous administration in new Phase 2 data[1]

BEERSE, BELGIUM (3 June 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, announced today new data from the Phase 2 PALOMA-2 study evaluating subcutaneous (SC) amivantamab combined with lazertinib as a first-line treatment in patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion (ex19del) or L858R mutations.[1] These data, which were featured in a late-breaking poster presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA8612) taking place in Chicago, Illinois from 31 May - 4 June 2024, showed a comparable response rate in patients treated with SC amivantamab and lazertinib compared to those treated with the intravenous (IV) formulation in the MARIPOSA study.[1] SC amivantamab was associated with significantly lower rates of infusion-related reactions (IRRs, 15 percent all-grades compared to 63 percent), and shorter administration time compared with the IV formulation.[1]

“These encouraging data show similar response rates in patients treated with the subcutaneous administration of amivantamab compared with the IV formulation,” said Professor Nicolas Girard, Head of Medical Oncology, Institut Curie, and Professor of Thoracic Oncology and Respiratory Medicine at the Paris Saclay University, France, and study author.* “With favourable tolerability based on fewer infusion-related reactions, this formulation has the potential to address a current unmet need in the treatment of EGFR-mutant lung cancer.”

In the PALOMA-2 study, Cohorts 1 and 6 enrolled patients with treatment-naïve, EGFR ex19del or L858R-mutated advanced NSCLC, a patient population similar to the MARIPOSA study population.[1] In Cohort 1 prophylactic anticoagulation use was recommended, and in Cohort 6 it was required.[1] As of 6 January, 2024, 68 and 58 patients were enrolled in Cohorts 1 and 6, respectively.[1] At a median follow-up of 8.6 months, across all patients, SC amivantamab combined with lazertinib demonstrated an overall response rate (ORR) of 77 percent (95 percent Confidence Interval [CI], 68-84) as assessed by the investigator per RECIST v1.1** (primary endpoint) and 79 percent (95 percent CI, 70-86) as assessed by blinded independent central review.[1] A similar ORR of 86 percent (95 percent CI, 83-89) was observed with IV amivantamab in combination with lazertinib, as determined by blinded independent central review in the Phase 3 MARIPOSA study.[1] Average administration time was approximately five minutes versus the IV administration of 2-4 hours.[2] Median duration of response was not estimable in both cohorts.[1]

"These promising results for patients with EGFR-mutated lung cancer show that the effectiveness of subcutaneous amivantamab is consistent with the IV formulation and, in addition, could offer a more convenient option for patients and their caregivers," said Henar Hevia, Ph.D, Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. "At J&J, we are directing our focus on areas where we believe we can truly transform cancer care, including optimising treatment experiences for patients."

The pooled analysis from Cohort 1 and Cohort 6 showed the safety profile for SC amivantamab was consistent with previous reports, with no new safety signals identified.[1] The most common treatment-emergent adverse events (AEs) (≥ 20 percent) across all patients were paronychia (71 percent), rash (61 percent) and hypoalbuminemia (48 percent).[1] IRRs were reported in 15 percent of patients across the two cohorts.[1] Discontinuation of all medicines due to treatment-related AEs occurred in approximately nine percent of all patients.[1] Prophylactic anticoagulation was administered to 71 percent of patients in Cohort 1 and 100 percent of those in Cohort 6.[1] Venous thromboembolic events (VTEs) were reported in 18 and seven percent of patients in Cohorts 1 and 6, respectively, with no dose reductions or discontinuations reported due to VTEs.[1] These findings suggest prophylactic anticoagulation can be implemented and reduce the incidence of VTEs with the combination of amivantamab plus lazertinib.[1]

"The safety and tolerability data from the PALOMA-2 study highlight the potential of subcutaneous amivantamab as an important therapy in the first-line treatment of patients with EGFR-mutant lung cancer," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Johnson & Johnson Innovative Medicine. "As we advance our robust pipeline and portfolio for patients with lung cancer, we remain dedicated to developing effective therapies that offer distinct benefits in the treatment of this disease."

#ENDS#

About the PALOMA-2 Study

PALOMA-2 (NCT05498428) is an open-label Phase 2 study evaluating the efficacy, safety, and pharmacokinetics (PK) of first-line SC amivantamab (administered via manual injection) combined with lazertinib and/or chemotherapy in patients with EGFR-mutated advanced or metastatic NSCLC.[3] Sixty-eight and 58 patients were enrolled in Cohorts 1 and 6, respectively. Prophylactic anticoagulation for the first four months of treatment was recommended in Cohort 1 and mandatory in Cohort 6.[3] The primary endpoint was objective response rate (ORR) as assessed by the investigator per RECIST v1.1.[3]

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.[4,5,6,7,8]

The European Commission (EC) 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.[9] Amivantamab is the first approved treatment in the European Economic Area specifically targeting EGFR exon 20 insertion mutations for NSCLC.[9] In November 2023, a type II extension of indication application was submitted to the European Medicines Agency (EMA) seeking approval of amivantamab in combination with chemotherapy (carboplatin and pemetrexed) for the treatment of adult patients with advanced NSCLC with EGFR ex19del or L858R substitution mutations, after failure of prior therapy including a third-generation EGFR TKI.[10] In February 2024, a type II extension of indication application was submitted to the European Medicines Agency (EMA) for amivantamab, in combination with lazertinib, for the first-line treatment of adult patients with advanced NSCLC with common EGFR exon 19 deletions (ex19del) or exon 21 (L858R) substitution mutations.[11] In April 2024, the Committee for Medicinal Products for Human Use (CHMP) provided a positive opinion for the use of amivantamab in combination with carboplatin and pemetrexed chemotherapy, for the first-line treatment of adult patients with advanced NSCLC with EGFR exon 20 insertion mutations.[12]

On Friday 31 May 2024, Johnson & Johnson announced the submission of an application to the EMA for the extension of the amivantamab marketing authorisation (line extension) 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 exon 19 deletion or L858R mutations, and for the use of SC amivantamab in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy.[13]

In addition to the PALOMA-2 study, amivantamab is being studied in multiple clinical trials in NSCLC, including:

- The Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous administration of amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for amivantamab subcutaneous delivery.[14]
- The Phase 3 PALOMA-3 (NCT05388669) study assessing lazertinib with subcutaneous amivantamab compared to intravenous amivantamab in patients with EGFR-mutated advanced or metastatic NSCLC.[15]
- The Phase 3 PAPILLON (NCT04538664) study assessing amivantamab in combination with carboplatin-pemetrexed versus chemotherapy alone in the first-line treatment of patients with advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.[16]
- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of amivantamab (with or without lazertinib) and carboplatin-pemetrexed versus carboplatin-pemetrexed alone in patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC after disease progression on or after osimertinib.[17]
- The Phase 3 MARIPOSA (NCT04487080) study assessing amivantamab in combination with lazertinib versus osimertinib and versus lazertinib alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R substitution mutations.[18]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating amivantamab in patients with advanced NSCLC.[19]
- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating amivantamab in combination with lazertinib and lazertinib as a monotherapy in patients with advanced NSCLC with EGFR mutations.[20]
- The Phase 1/2 METalmark (NCT05488314) study assessing amivantamab and capmatinib combination therapy in locally advanced or metastatic NSCLC.[21]
- The Phase 1/2 PolyDamas (NCT05908734) study assessing amivantamab and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[22]
- The Phase 2 SKIPPirr study (NCT05663866) exploring how to decrease the incidence and/or severity of first-dose infusion-related reactions with amivantamab in combination with lazertinib in relapsed or refractory EGFR-mutated advanced or metastatic NSCLC.[23]

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.[9]

▼ 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.[24] NSCLC accounts for 85 percent of all lung cancer cases.[25] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[24]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[25] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[25,26] 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.[27,28,29,30] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[31] The five-year survival rate for all patients with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[32,33] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[34] Patients with EGFR ex19del or L858R 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.[35] In addition, it has been demonstrated that approximately 50 percent of patients with NSCLC will develop brain metastases which are a substantial contributor to overall cancer mortality.[36,37,38]

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 www.janssen.com/emea. Follow us at www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen-Cilag International NV is a Johnson & Johnson company.

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 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 materialize, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV and 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 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 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 www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Cilag International NV 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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**Prof. Nicolas Girard has provided consulting, advisory, and speaking services to Janssen-Cilag International NV; he has not been paid for any media work.*

**RECIST (v1.1) 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] Lim S, et al. Subcutaneous amivantamab and lazertinib as first-line treatment in patients with advanced EGFR-mutated, non-small cell lung cancer (NSCLC): Interim results from the phase 2 PALOMA-2 study. 2024 American Society for Clinical Oncology Annual Meeting. June 3, 2024.
[2] Lim S et al. Subcutaneous amivantamab and lazertinib as first-line treatment in patients with advanced *EGFR*-mutated, non-small cell lung cancer (NSCLC): Interim results from the phase 2 PALOMA-2 study. 2024 American Society for Clinical Oncology Annuam Meeting, Abstract submission.
[3] ClinicalTrials.gov. A Study of Amivantamab in Participants With Advanced or Metastatic Solid Tumors Including Epidermal Growth Factor Receptor (EGFR)-Mutated Non-Small Cell Lung Cancer (PALOMA-2). https://clinicaltrials.gov/ct2/show/NCT05498428. Accessed June 2024.
[4] 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://classic.clinicaltrials.gov/ct2/show/NCT04487080. Last accessed: June 2024.
[5] 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.
[6] 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.
[7] 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.

[8] 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.

[9] European Medicines Agency. Amivantamab Summary of Product Characteristics. January 2023. Available at: Rybrevant, INN-amivantamab (europa.eu). Last accessed: June 2024.

[10] Janssen EMEA. Janssen Submits Application to the European Medicines Agency for RYBREVANT®▼ (amivantamab) in Combination with Chemotherapy for the Treatment of Adult Patients with Advanced EGFR-Mutated Non-Small Cell Lung Cancer After Failure of Prior Therapy . Available at: https://www.janssen.com/emea/sites/www_janssen_com_emea/files/janssen_mariposa-2_filing_press_release_2023.pdf. Last accessed: June 2024.

[11] Janssen.com/EMEA. Janssen Submits Type II Extension of Indication Application to the European Medicines Agency Seeking Approval of RYBREVANT®▼ (amivantamab), in combination with Lazertinib, for First-Line Treatment of Patients with EGFR-Mutated Non-Small Cell Lung Cancer. Available at: https://www.janssen.com/emea/sites/www_janssen_com_emea/files/amivantamab_mariposa_ema_filing_release_2024_2.pdf Last accessed: June 2024.

[12] Janssen.com/EMEA. Johnson & Johnson receives positive CHMP opinion for RYBREVANT®▼ (amivantamab) in combination with chemotherapy for the first-line treatment of patients with advanced non-small cell lung cancer with activating EGFR exon 20 insertion mutations. Available at: https://www.janssen.com/emea/sites/www_janssen_com_emea/files/papillon_chmp_press_release_2024.pdf. Last accessed: June 2024.

[13] Janssen EMEA. Johnson & Johnson submits application to the European Medicines Agency seeking approval of subcutaneous formulation of RYBREVANT®▼ (amivantamab) for the treatment of patients with EGFR-mutated non-small cell lung cancer. Available at: https://www.globenewswire.com/news-release/2024/05/31/2891769/0/en/Johnson-Johnson-submits-application-to-the-European-Medicines-Agency-seeking-approval-of-subcutaneous-formulation-of-RYBREVANT-amivantamab-for-the-treatment-of-patients-with-EGFR-m.html. Last accessed: June 2024.

[14] ClinicalTrials.gov. A Study of Amivantamab Subcutaneous (SC) Administration for the Treatment of Advanced Solid Malignancies (PALOMA). Available at: https://clinicaltrials.gov/study/NCT04606381. Last accessed: June 2024.

[15] 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. Last accessed: June 2024.

[16] 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. Last acessed: June 2024.

[17] 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://classic.clinicaltrials.gov/ct2/show/study/NCT04988295. Last accessed: June 2024.

[18] 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://classic.clinicaltrials.gov/ct2/show/NCT04487080. Last accessed: June 2024.

[19] ClinicalTrials.gov. A Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants With Advanced Non-Small Cell Lung Cancer (CHRYSALIS). https://clinicaltrials.gov/ct2/show/NCT02609776. Last accessed: June 2024.

[20] ClinicalTrials.gov. A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer (CHRYSALIS-2). https://clinicaltrials.gov/ct2/show/NCT04077463. Last accessed: June 2024.

[21] ClinicalTrials.gov. A Study of Amivantamab and Capmatinib Combination Therapy in Unresectable Metastatic Non-small Cell Lung Cancer (METalmark). https://clinicaltrials.gov/ct2/show/NCT05488314. Last accessed: June 2024.

[22] ClinicalTrials.gov. A Study of Combination Therapy With Amivantamab and Cetrelimab in Participants With Metastatic Non-small Cell Lung Cancer (PolyDamas). https://www.clinicaltrials.gov/study/NCT05908734?term=polydamas&rank=1. Last accessed: June 2024.

[23] ClinicalTrials.gov. Premedication to Reduce Amivantamab Associated Infusion Related Reactions (SKIPPirr). https://classic.clinicaltrials.gov/ct2/show/NCT05663866. Last accessed: June 2024.

[24] Global Cancer Observatory. Cancer Today. Available at: https://gco.iarc.fr/en. Last accessed: June 2024.

[25] Zappa C, et al. Non-small cell lung cancer: current treatment and future advances. Transl Lung Cancer Res 2016;5(3):288–300.

[26] Wee, P & Wang, Z. Cancers 2017. Epidermal Growth Factor Receptor Cell Proliferation Signaling Pathways Volume: 9 Issue: 12 Pages: 52.

[27] 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.* 37:97-104.

[28] 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; 29 January, 2021; Singapore.

[29] 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.

[30] 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.

[31] American Lung Association. EGFR and Lung Cancer. https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/symptoms-diagnosis/biomarker-testing/egfr. Last accessed: June 2024.

[32] Howlader N, et al. SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2016/, based on December 2018 SEER data submission, posted to the SEER web site.
[33] 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.
[34] 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.
[35] 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; 29 January, 2021; Singapore.
[36] Shao J et al. The number of brain metastases predicts the survival of non-small cell lung cancer patients with EGFR mutation status. *Cancer Rep (Hoboken).* 2022;5(9): e1550.
[37] Achrol A et al. Brain metastases. *Nat Rev Dis Primers*. 2019;17(5): 5.
[38] 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.