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For Immediate Release

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

Submission is supported by data from the Phase 3 PALOMA-3 study featured at the American Society of Clinical Oncology (ASCO) Annual Meeting[1]

New formulation showed non-inferiority to intravenous administration in fourth positive Phase 3 amivantamab study[1]

Longer overall survival, progression-free survival and duration of response shown with subcutaneous amivantamab; featured in Best of ASCO 2024[1]

BEERSE, BELGIUM (31 May 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, announced today the submission of an application for the extension of the RYBREVANT®▼(amivantamab) marketing authorisation (line extension) to the European Medicines Agency (EMA). This application seeks 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 non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or L858R mutations, and as a monotherapy in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy.

The application to the EMA is supported by positive data from the Phase 3 PALOMA-3 study (NCT05388669), which demonstrated non-inferior pharmacokinetics and efficacy for SC amivantamab combined with lazertinib compared to intravenous (IV) administration, the currently approved formulation of amivantamab.[1] Administration time for SC amivantamab was reduced to approximately five minutes from five hours for the first IV amivantamab infusion (across two days) and showed a five-fold reduction in infusion-related reactions (IRRs).[1] These late-breaking results, which are the Company's fourth positive Phase 3 readout for the amivantamab clinical programme, were featured for the first time as an oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA8505) taking place in Chicago, Illinois from 31 May – 4 June 2024.[1] These data were also selected for the Best of ASCO 2024 Meetings, which highlight cutting-edge science and reflect leading research in oncology.[1]

"At Johnson & Johnson we constantly strive to transform clinical outcomes for patients and are committed to developing innovative approaches that enhance the treatment experience," said Henar Hevia, Ph.D, Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. "The positive data presented at ASCO show the potential for improved safety outcomes and added convenience for patients treated with the subcutaneous formulation of amivantamab, and we now look forward to working with the EMA to provide this option to patients who may benefit from it, as soon as possible."

The PALOMA-3 study evaluated the pharmacokinetics (PK), efficacy and safety of SC amivantamab (administered via manual injection) compared to IV amivantamab, both in combination with lazertinib, in patients with EGFR-mutated advanced or metastatic NSCLC after progression on osimertinib and chemotherapy.[1] Results showed 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 day 1 to 15).[1]

At a median follow-up of 7 months, the overall response rate 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] SC amivantamab also demonstrated longer duration of response (DoR), progression-

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free survival (PFS) and significant improvement in overall survival (OS) compared to IV administration during this time.[1] Specifically, median duration of response was numerically longer for SC amivantamab combined with lazertinib compared to IV (median, 11.2 vs 8.3 months among confirmed responders) as was PFS (median, 6.1 vs 4.3 months; hazard ratio [HR], 0.84; 95 percent CI, 0.64–1.10; P=0.20).[1] A pre-specified exploratory endpoint showed patients treated with SC amivantamab had significantly longer OS compared with IV (HR, 0.62; 95 percent CI, 0.42–0.92; nominal P=0.02).[1] At 12 months, 65 percent of patients who received SC amivantamab combined with lazertinib were alive compared with 51 percent of those treated with the IV regimen. It is theorised that the efficacy seen with SC amivantamab may be linked to SC absorption, via the lymphatic system, potentially enhancing immune-mediated activity.[1]

“The PALOMA-3 data show that subcutaneous amivantamab offers shorter infusion times and lower rates of administration-related reactions with pharmacokinetics and efficacy comparable to the current IV administration,” said Dr. Natasha B. Leighl*, medical oncologist at the Princess Margaret Cancer Centre in Toronto, Canada, and the presenting author. “I look forward to seeing how these findings can make a meaningful difference in clinical practice by potentially improving the treatment experience for patients with EGFR-mutated non-small cell lung cancer.”

Of particular note, administration time was substantially shorter for SC amivantamab (median less than approximately five minutes) compared to IV administration (up to five hours), with significantly more patients reporting convenience with the SC administration (85 percent with SC amivantamab vs 35 percent with IV administration at end of treatment; P<0.001).[1]

The overall safety profile of SC amivantamab is consistent with the known profile of IV administration. The most common all-Grade adverse events (≥ 20 percent) for SC amivantamab compared to IV were paronychia (54 percent vs 51 percent), hypoalbuminemia (47 percent vs 37 percent) and rash (46 percent vs 43 percent), respectively.[1] The rate of infusion-related reactions for patients treated with SC amivantamab combined with lazertinib was shown to be approximately 5-fold lower than that observed with the IV formulation (13 percent vs 66 percent, respectively).[1] No Grade 4 or 5 IRRs were reported.[1] Preventive blood thinning (prophylactic anticoagulation) was used in most patients and was found to be effective in reducing the rate of venous thromboembolic events (VTE).[1] Patients receiving prophylactic anticoagulation had lower rates of VTE (10 percent) than those without 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 was low among patients receiving anticoagulants in the SC (2 percent) and IV (1 percent) arms.[1]

“We are always exploring innovative approaches to meet the urgent needs of patients living with EGFR-mutated non-small cell lung cancer and these compelling findings reinforce the potential for a new route of administration for amivantamab,” said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Area Head, Oncology, Johnson & Johnson Innovative Medicine. “We look forward to pursuing regulatory submissions for this formulation, as we advance our ambition to transform the first-line treatment of EGFR-mutated NSCLC.”

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About PALOMA-3

PALOMA-3 (NCT05388669), which enrolled 418 patients, is a randomised, open-label Phase 3 study evaluating 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 chemotherapy.[2] The co-primary PK endpoints of the study were trough concentration (Ctrough on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUCD1-D15).[2] Key secondary endpoints were objective response rate and progression-free survival (PFS). Overall survival was a predefined exploratory endpoint. Prophylactic anticoagulation was recommended for the first four months of treatment.[2]

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.[3,4,5,6]

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.[6] Amivantamab is the first approved treatment in the European Economic Area specifically targeting EGFR exon 20 insertion mutations for NSCLC.[6]

In November 2023, a Type II extension of indication application was submitted to the European Medicines Agency (EMA) based on the MARIPOSA-2 study 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.[7]

This was followed, in February 2024, with the submission of a Type II extension of indication application to the EMA based on the MARIPOSA study 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 (L858R) substitution mutations.[8] In April 2024, the 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.[9]

In addition to the PALOMA-3 study, amivantamab is being studied in multiple clinical trials in NSCLC, including:

- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumours including EGFR-mutated NSCLC.[10]
- 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.[11]
- 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.[12]
- 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.[13]
- 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.[14]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating amivantamab in patients with advanced NSCLC.[15]
- 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.[16]
- The Phase 1/2 METalmark (NCT05488314) study assessing amivantamab and capmatinib combination therapy in locally advanced or metastatic NSCLC.[17]
- The Phase 1/2 PolyDamas (NCT05908734) study assessing amivantamab and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[18]
- 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.[19]

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.[6]

▼ 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.[20] NSCLC accounts for 85 percent of all lung cancer cases.[21] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined. [21]

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 controlling cell growth and division.[21,22] 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.[23,24,25,26] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[27] The five-year survival rate for patients with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.[28] Patients with EGFR exon 20 insertion mutations have a real-world five-year overall survival (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.[29] 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.[30,31,32]

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.

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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 materialise, 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 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, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors,"

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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 nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Natasha Leighl has served as a consultant to Johnson & Johnson; she has not been paid for any media work.

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