News Release

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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

The submission is supported by data from the Phase 3 MARIPOSA-2 study featured in a Late-Breaking Presidential Symposium session at the 2023 ESMO Congress and simultaneously published in Annals of Oncology[1,2]

Amivantamab plus chemotherapy demonstrated significant improvements in progression-free survival, compared to chemotherapy alone, in patients with EGFR-mutated advanced non-small cell lung cancer following prior osimertinib therapy[1]

BEERSE, BELGIUM, 23 November, 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 treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R substitution mutations, after failure of prior therapy including a third-generation EGFR tyrosine kinase inhibitor (TKI).

"Patients with EGFR-mutated advanced non-small-cell lung cancer treated with osimertinib inevitably develop resistance mechanisms and are faced with poor outcomes on platinum-based chemotherapy alone," said Catherine Taylor, Vice President, EMEA Medical Affairs, Therapy Area Strategy, Janssen-Cilag AG. "Amivantamab is active against a wide range of

EGFR and MET alterations, which are key mechanisms of resistance to osimertinib. The addition of amivantamab to chemotherapy has demonstrated the potential to address post-osimertinib resistance while supporting longer disease control."

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 adult patients with advanced NSCLC with EGFR exon 20 insertion mutations after failure of platinum-based chemotherapy.[3,4]

The latest submission to the EMA is supported by data from the Phase 3 MARIPOSA-2 (NCT04988295) study, evaluating the efficacy and safety of amivantamab and chemotherapy in patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC who had disease progression on or after treatment with osimertinib.[1,5] The amivantamab plus chemotherapy arm met its primary endpoint with a statistically significant and clinically meaningful improvement in progression-free survival (PFS), versus chemotherapy alone, reducing the risk of disease progression or death by 52 percent (Hazard Ratio [HR]= 0.48; 95 percent Confidence Interval [CI], 0.36–0.64; P<0.001).[1,2] The safety profile for amivantamab plus chemotherapy was consistent with that of the individual components and no new safety signals were found for the addition of amivantamab to chemotherapy.[1,2] The most common adverse events (AEs) in the amivantamab-containing arms were haematologic, EGFR, and MET-related.[1,2] Infusion-related reactions in the amivantamab plus chemotherapy arm were 58 percent (all grade).[1,2]

"The encouraging results from the MARIPOSA-2 study are the first to demonstrate a significant benefit in progression-free survival in the post-osimertinib setting. This reinforces the potential of amivantamab plus chemotherapy in this patient population, and our ambition to transform outcomes for patients," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "Pending approval, this amivantamab-based combination has the potential to offer a new standard of care for this patient population, where high unmet medical needs remain."

Results from MARIPOSA-2 were recently presented during a Presidential Symposium at the European Society for Medical Oncology (ESMO) 2023 Congress (Abstract #LBA15) and simultaneously published in the *Annals of Oncology.*[1,2]

#ENDS#

About the MARIPOSA-2 Study

MARIPOSA-2 (NCT04988295), which enrolled 657 patients, is a randomised, open-label Phase 3 study evaluating the efficacy and safety of two combination regimens of amivantamab (with and without lazertinib) and chemotherapy.[1,5] Patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC who had disease progression on or after treatment with osimertinib were randomised to treatment with amivantamab plus chemotherapy, amivantamab plus chemotherapy with lazertinib, or chemotherapy alone.[5] The dual primary endpoint was used to compare the PFS (using RECIST v1.1 guidelines†) as assessed by blinded independent central review (BICR) for each experimental arm to chemotherapy alone.[5] Secondary endpoints included objective response as assessed by BICR, overall survival (OS), duration of response (DOR), time to subsequent therapy, PFS2 and intracranial PFS.[5]

All study participants underwent serial brain imaging to allow for the robust assessment of intracranial endpoints and to assess the CNS activity of amivantamab and doublet chemotherapy with and without lazertinib.[1,2] Because brain metastases can lead to significant burden and poor outcomes for patients, this aspect of the study design provides critical information in an area of high unmet need.[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.[3,7,8,9,10] 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.[3] Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.[3] In October 2023, a type II extension of indication application was submitted to the European Medicines Agency seeking approval for the combination of amivantamab in combination with chemotherapy (carboplatin-pemetrexed) for the first-line treatment of patients with NSCLC with EGFR exon 20 insertion mutations.[11]

In addition to the Phase 3 MARIPOSA-2 study, amivantamab is being studied in multiple clinical trials in NSCLC, including:

- 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. Data for this randomised Phase 3 study were presented at the ESMO 2023 Congress, demonstrating statistically significant and clinically meaningful improvement in PFS in patients receiving amivantamab plus lazertinib versus osimertinib.[12,13]
- The Phase 3 PAPILLON (NCT04538664) study assessing amivantamab in combination with carboplatin-pemetrexed versus carboplatin-pemetrexed in the first-line treatment of patients with advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Data for this randomised Phase 3 study were presented at the ESMO 2023 Congress, demonstrating statistically significant and clinically meaningful improvement in PFS and other key study endpoints in patients receiving amivantamab plus chemotherapy versus chemotherapy alone.[14,15]

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.[3]

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

About Lazertinib

Lazertinib is an oral, third-generation, brain-penetrant EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR. An analysis of the efficacy and safety of lazertinib from the Phase 3 LASER301 study was published in *The Journal of Clinical Oncology* in 2023.[16] In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

About Non-Small Cell Lung Cancer

In Europe, it is estimated that 477,534 patients were diagnosed with lung cancer in 2020.[17] NSCLC accounts for 85 percent of all lung cancer cases.[18] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[17]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[18] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[18,19] 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.[20,21,22,23] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[24] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[25,26] Patients with EGFR ex19del or L858R mutations have a real-world five-year OS of 19 percent.[27]

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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension, and Retina.

Learn more at www.janssen.com/emea. Follow us at www.linkedin.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag AG, Janssen Research & Development, LLC, and Janssen Biotech, Inc. 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 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 Pharmaceutica NV, Janssen Research and Development, LLC, Janssen Biotech, Inc., Janssen-Cilag AG, 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 Research and Development, LLC, Janssen Biotech, Inc., Janssen-Cilag AG, 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 (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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