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**News Release**

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# New Data from Phase 3 PAPILLON Study Show RYBREVANT®▼ (amivantamab) Plus Chemotherapy Resulted in 60 Percent Reduction in Risk of Disease Progression or Death in Patients with Previously Untreated EGFR Exon 20 Insertion Mutation-Positive Non-Small Cell Lung Cancer

*Data show the potential impact of amivantamab and chemotherapy combination as first-line treatment for patients with advanced non-small cell lung cancer (NSCLC) with EGFR exon 20 insertion mutations*[1]

*Late-breaking data presented in a Presidential Symposium at 2023 ESMO Congress and simultaneously published in The New England Journal of Medicine*[1,2]

**BEERSE, BELGIUM, October 21, 2023** – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new data from the Phase 3 PAPILLON study showing first-line treatment with RYBREVANT®▼ (amivantamab) in combination with chemotherapy (carboplatin-pemetrexed) resulted in a 60 percent reduction in the risk of disease progression or death (Hazard Ratio [HR]=0.395; 95 percent Confidence Interval [CI], 0.30–0.53; *P*<0.0001) in patients with previously untreated advanced or metastatic NSCLC with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, compared to chemotherapy alone.[1] Results also showed treatment with amivantamab plus chemotherapy significantly improved objective response rate (ORR) and progression-free survival (PFS) after first subsequent therapy (PFS2).[1] These data were presented in a Presidential Symposium at the European Society of Medical Oncology (ESMO) 2023 Congress taking place 20-24 October,

2023 in Madrid, Spain (Abstract #LBA5) and simultaneously published in *The New England Journal of Medicine*.[1,2]

"We have seen promising outcomes with amivantamab in the second-line setting for patients with EGFR exon 20 insertion mutations following platinum-based chemotherapy. However, targeted therapy is generally used as a first-line treatment in other settings to address disease progression earlier and achieve optimal treatment outcomes for patients," said Nicolas Girard* M.D., Professor of Respiratory Medicine at Versailles Saint Quentin University and Chair of Medical Oncology Department at Institut Curie in Paris, and presenting author. "The significant improvement in progression-free survival and in other efficacy results observed in the PAPILLON study support amivantamab plus chemotherapy as a potential future first-line regimen for these patients."

Treatment with amivantamab plus chemotherapy resulted in longer PFS (using RECIST v1.1 guidelines†) as assessed by blinded independent central review (BICR) compared with chemotherapy alone.[1] At a median follow-up of 14.9 months, PFS was significantly prolonged for patients who received amivantamab plus chemotherapy than for those who received chemotherapy alone (median, 11.4 months and 6.7 months, respectively; HR for disease progression or death=0.395; 95 percent CI, 0.30–0.53; *P*<0.0001).[1] At 18 months, 31 percent of patients receiving amivantamab plus chemotherapy remained alive and progression-free compared to 3 percent for patients receiving chemotherapy alone. Treatment with amivantamab plus chemotherapy showed consistent PFS benefit across patient subgroups.[1]

An ORR of 73 percent (95 percent CI: 65–80) was observed for the combination of amivantamab and chemotherapy compared to 47 percent (95 percent CI: 39–55) in patients receiving chemotherapy alone.[1] Median PFS2 was longer with amivantamab plus chemotherapy compared to chemotherapy alone (HR=0.493; 95 percent CI, 0.32–0.76; *P*=0.001), supporting the potential first-line use of amivantamab and chemotherapy.[1] Notably, of those patients receiving chemotherapy alone, 71 of 94 patients (76 percent) received subsequent amivantamab treatment as their second line of therapy.[1] An interim overall survival (OS) analysis showed a favourable trend for patients treated with amivantamab plus chemotherapy compared to those treated with chemotherapy alone (HR=0.675; 95 percent CI, 0.42–1.09; *P*=0.106), with 72 percent and 54 percent alive at two years, respectively.[1]

"EGFR mutations are among the most common driver mutations in NSCLC, with EGFR exon 20 insertion mutations being the third most prevalent. Despite treatment advances, outcomes for people living with Ex20ins advanced EGFR NSCLC are incredibly poor, and new treatment approaches are needed," said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. "At Janssen, our goal is to change the trajectory of lung cancer and we are committed to addressing unmet needs across the disease continuum, including investigating novel treatment combination regimens and sequencing approaches, and identifying patients with these oncogenic driver mutations early on, to help select the most appropriate first-line therapy."

EGFR and MET-related toxicities were observed with amivantamab plus chemotherapy, which were mostly Grade 1 and 2, including paronychia, rash, hypoalbuminemia, and peripheral oedema.[1] Across both study arms, chemotherapy-associated haematologic and gastrointestinal toxicities were comparable except for higher rates of neutropenia for amivantamab plus chemotherapy, which were reversible.[1] Few patients discontinued treatment due to adverse reactions in either study arm.[1] No new safety signals were observed with amivantamab, with the safety profile for the combination of amivantamab plus chemotherapy consistent with the safety profiles of the individual agents.[1]

"Patients with newly diagnosed advanced or metastatic EGFR exon 20 insertion mutation-positive NSCLC are in need of targeted therapies that can be used earlier in the course of their disease, given the tendency for rapid progression and poor outcomes often seen with chemotherapy alone," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "PAPILLON is the first randomised Phase 3 study to show clinically meaningful results for a targeted therapy in combination with

chemotherapy – a regimen with the potential to become a practice-changing first-line treatment for these patients."

Results from the PAPILLON study have been submitted to both the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) for respective review.[3,4]

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**About the PAPILLON Study**

PAPILLON (NCT04538664), which enrolled 308 patients, is a randomised, open-label Phase 3 study evaluating the efficacy and safety of amivantamab in combination with chemotherapy, compared with chemotherapy alone, in newly diagnosed patients with advanced or metastatic NSCLC characterised by EGFR exon 20 insertion mutations.[5] The primary endpoint of the study is PFS as assessed by BICR.[1] Secondary endpoints include ORR, PFS2, duration of response (DOR), time to subsequent therapy (TST) and OS. Patients who received chemotherapy alone were allowed to receive amivantamab monotherapy in the second-line setting after confirmation of disease progression.[1]

**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.[6,7,8,9,10] 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 marketing authorisation 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 PAPILLON 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. Topline data for this randomised Phase 3 study demonstrated statistically significant and clinically meaningful improvement in PFS in patients receiving amivantamab plus lazertinib versus osimertinib.[12,13]

- 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. Topline data for this randomised Phase 3 study demonstrated statistically significant and clinically meaningful improvement in PFS in these patients receiving amivantamab plus chemotherapy with and without lazertinib versus chemotherapy.[14,15]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating amivantamab in participants with advanced NSCLC.[16]
- 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.[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.[18]
- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in participants with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[19]
- The Phase 3 PALOMA-3 (NCT05388669) study assessing lazertinib with subcutaneous amivantamab compared to intravenous amivantamab in participants with EGFR-mutated advanced or metastatic NSCLC.[20]
- The Phase 1/2 METalmark (NCT05488314) study assessing amivantamab and capmatinib combination therapy in locally advanced or metastatic NSCLC.[21]
- 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.[22]

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.[10]

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▼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.[23,24] 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.[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.[27,28,29,30,31] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[32] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[33,34] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[35] Patients with EGFR exon 20 insertion 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.[36]

**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 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 *Research and Development, LLC, Janssen Biotech, Inc*., Jannsen-Cilag GmbH *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 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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*Professor Girard has served as a consultant to the Janssen Pharmaceutical Companies; 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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