News Release

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Janssen Submits Supplemental Biologics License Application to the U.S. Food and Drug Administration Seeking Approval of RYBREVANT® (amivantamab-vmjw) in Combination with Chemotherapy for the First-line Treatment of Patients with Locally Advanced or Metastatic EGFR Exon 20 Insertion Mutation-Positive Non-Small Cell Lung Cancer

Application is supported by data from PAPILLON, the first randomized Phase 3 study to show clinically meaningful results in patients with NSCLC with EGFR exon 20 insertion mutations

RARITAN, New Jersey, August 25, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the submission of a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) seeking the expanded approval of RYBREVANT® (amivantamab-vmjw) in combination with chemotherapy (carboplatin-pemetrexed) for the first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations. The sBLA is being reviewed by the FDA through the Real-Time Oncology Review (RTOR) program.*

"PAPILLON is the first randomized Phase 3 study in patients with NSCLC with EGFR exon 20 insertion mutations to show clinically meaningful results. This creates an opportunity to make a significant improvement to the standard of care for this patient population with high unmet medical need," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "We look forward to working with the FDA through the RTOR pathway in pursuit of an approval for RYBREVANT plus chemotherapy as we simultaneously progress the development of this novel bispecific antibody in additional patient populations."

Following Breakthrough Therapy Designation from the U.S. FDA in 2020, RYBREVANT® received accelerated approval in 2021 as the first fully-human, bispecific antibody for the treatment of patients with NSCLC with EGFR exon 20 insertion mutations.[2] The sBLA submission for RYBREVANT® is also intended to satisfy the regulatory requirements of the accelerated approval confirming the clinical benefit observed in the Phase 1 CHRYSALIS study.

The sBLA is supported by data from the Phase 3 PAPILLON (NCT04538664) clinical trial, a randomized, open-label study evaluating the efficacy and safety of RYBREVANT® in combination with chemotherapy as first-line treatment in patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.[1,2] In July, Janssen announced the PAPILLON study met its primary endpoint with a statistically significant and clinically meaningful improvement in PFS (as measured by BICR) in patients receiving RYBREVANT® plus chemotherapy versus chemotherapy alone.[1] The combination of RYBREVANT® and chemotherapy demonstrated a safety profile consistent with the safety profiles of the individual components.[1]

About PAPILLON

PAPILLON (NCT04538664) is a randomized, open-label Phase 3 study evaluating the efficacy and safety of RYBREVANT® in combination with chemotherapy, compared with chemotherapy alone, in newly diagnosed patients with advanced or metastatic NSCLC characterized by EGFR exon 20 insertion mutations.[1] The primary endpoint of the study is PFS (using RECIST v1.1 guidelines**) as assessed by blinded independent central review (BICR). Secondary endpoints include overall response rate (ORR), PFS after first subsequent therapy, time to symptomatic progression and overall survival (OS).[1] Patients who received chemotherapy alone were allowed to receive RYBREVANT® monotherapy in the second-line setting after confirmation of disease progression.[1]

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw) received accelerated approval by the U.S. Food and Drug Administration (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.[2] This indication is approved under accelerated approval based on ORR and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. RYBREVANT® has also received approval from health authorities in Europe, as well as other markets around the world.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer◇ prefer NGS-based strategies over PCR-based approaches for the detection of EGFR exon 20 insertion variants and include amivantamab-vmjw (RYBREVANT®) as a subsequent therapy option with a Category 2A recommendation for patients that have progressed on or after platinum-based chemotherapy with or without immunotherapy and have EGFR exon 20 insertion mutation-positive advanced NSCLC.[9†^]

In addition to the Phase 3 PAPILLON study, RYBREVANT® is being studied in multiple clinical trials in NSCLC, including:

- The Phase 3 MARIPOSA (NCT04487080) study assessing RYBREVANT® in combination with lazertinib, a novel third generation EGFR TKI, versus osimertinib and versus lazertinib alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions (ex19del) or L858R substitution mutations.[10]
- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of RYBREVANT® (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.[11]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating RYBREVANT® in participants with advanced NSCLC.[12]
- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating RYBREVANT® in combination with lazertinib and lazertinib as a monotherapy in patients with advanced NSCLC with EGFR mutations.[13]
- 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.[14]

- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in participants with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[15]
- 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.[16]
- The Phase 1/2 METalmark (NCT05488314) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[17]
- The Phase 1/2 PolyDamas (NCT05908734) study assessing RYBREVANT® 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 RYBREVANT® in combination with lazertinib in relapsed or refractory EGFR-mutated advanced or metastatic NSCLC.[19]

For more information, visit: https://www.RYBREVANT.com.

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is one of the most common cancers, with NSCLC making up 80 to 85 percent of all lung cancer cases.[20,21] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[22] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[23] 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.[22-28] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[29] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[30,31] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[32] 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, who have a real-world five-year OS of 19 percent.[33]

RYBREVANT® IMPORTANT SAFETY INFORMATION[2]

WARNINGS AND PRECAUTIONS

Infusion Related Reactions

RYBREVANT® can cause infusion related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting.

Based on the safety population, IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT® as recommended. Administer RYBREVANT® via a peripheral line on Week 1 and Week 2. Monitor patients for any signs and symptoms of infusion reactions during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.

Interstitial Lung Disease/Pneumonitis

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis. Based on the safety population, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Dermatologic Adverse Reactions

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus and dry skin. Based on the safety population, rash occurred in 74% of patients treated with RYBREVANT®, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days

(range: 1 to 276 days). Rash leading to dose reduction occurred in 5% of patients, and RYBREVANT® was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT®.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT®. Advise patients to wear protective clothing and use broad spectrum UVA/UVB sunscreen. Alcohol free emollient cream is recommended for dry skin.

If skin reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis. Based on the safety population, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients treated with RYBREVANT®. All events were Grade 1-2. Promptly refer patients presenting with eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo Fetal Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the final dose of RYBREVANT®.

Adverse Reactions

The most common adverse reactions (≥20%) were rash (84%), IRR (64%), paronychia (50%), musculoskeletal pain (47%), dyspnea (37%), nausea (36%), fatigue (33%), edema (27%), stomatitis (26%), cough (25%), constipation (23%), and vomiting (22%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased lymphocytes (8%),

decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-glutamyl transferase (4%), and decreased sodium (4%).

Please read the full Prescribing Information for RYBREVANT®.

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. Follow us at @JanssenGlobal and @JanssenUS. Janssen Biotech, Inc. and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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 RYBREVANT® (amivantamab-vmjw). 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., any of the other Janssen Pharmaceutical Companies 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 Research and Development, LLC, Janssen Biotech, Inc., 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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*The Real-Time Oncology Review (RTOR) program aims to provide a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while improving review quality and engaging in early iterative communication with the applicant.[34]

**RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumors, which is a standard way to measure how well solid tumors respond to treatment and is based on whether tumors shrink, stay the same or get bigger.

◇The NCCN Content does not constitute medical advice and should not be used in place of seeking professional medical advice, diagnosis or treatment by licensed practitioners. NCCN makes no representations or warranties and explicitly disclaims the appropriateness or applicability of the NCCN Content to any specific patient's care or treatment.

†See the NCCN Guidelines for detailed recommendations, including other treatment options.

^The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

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