Johnson&Johnson

Media contact:
Suzanne Frost
sfrost@its.jnj.com

Sarah Freeman
sfreem21@its.jnj.com

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

U.S. Medical Inquiries
+1 800 526-7736

For Immediate Release

RYBREVANT® (amivantamab-vmjw) plus chemotherapy show 49 percent overall response rate in metastatic colorectal cancer

Median duration of response reaches 7.4 months with combination treatment in patients with aggressive form of disease

New results show potential of RYBREVANT® beyond lung cancer

BARCELONA, September 14, 2024 – Johnson & Johnson (NYSE:JNJ) today announced new data from the Phase 1b/2 OrigAMI-1 study, which showed RYBREVANT® (amivantamab-vmjw) combined with chemotherapy (mFOLFOX6 [FOLFOX] or FOLFIRI) demonstrated promising rapid and durable antitumor activity in patients with RAS/BRAF wild-type (WT) metastatic colorectal cancer (mCRC) who have not previously received anti-epidermal growth factor receptor (*EGFR*) therapy. These data were presented in a mini-oral presentation at the European Society of Medical Oncology (ESMO) 2024 Congress.[1]

“OrigAMI-1 is the first study to show RYBREVANT plus chemotherapy may provide clinically meaningful benefits to patients with metastatic colorectal cancer who have not received any *EGFR*-targeted treatments as their first or second line of therapy,” said Filippo Pietrantonio, M.D., medical oncologist at Fondazione IRCCS Istituto Nazionale dei Tumori in Milan, Italy, and presenting author.* “Notably, we saw 21 percent of patients proceed to curative intent surgery, showing the promise of RYBREVANT in patients in this setting.”

In the study, patients receiving RYBREVANT® plus chemotherapy were either in their first (26 percent) or second line (74 percent) of treatment for mCRC and had not been treated with specific anti-*EGFR* therapies. Patients receiving FOLFOX were oxaliplatin-naïve and patients receiving FOLFIRI were irinotecan-naïve. Response was assessed by the investigator per RECIST v1.1.** Forty-three patients were treated with RYBREVANT® along with either FOLFOX (20 patients) or FOLFIRI (23 patients). The median follow-up period was 7.3 months for RYBREVANT® plus FOLFOX and RYBREVANT® plus FOLFIRI.[1]

Patients treated with RYBREVANT® plus chemotherapy achieved an overall response rate (ORR) of 49 percent (95 percent confidence interval [CI], 33-65), median duration of response of 7.4 months (95 percent CI, 5.6-not estimable [NE]) and median progression-free survival of 7.5 months (95 percent CI, 7.4–NE). Disease control was observed in 88 percent of patients (95 percent CI, 75-96). Clinically meaningful intrahepatic antitumor activity was observed among patients with liver metastases treated with RYBREVANT® plus chemotherapy, demonstrating a significant reduction in liver tumors (ORR of 53 percent, disease control rate of 93 percent). Notably, nine (21 percent) patients were able to proceed to curative-intent surgery due to strong antitumor activity.[1]

The safety profile of RYBREVANT® plus FOLFOX/FOLFIRI was manageable and consistent with each of the individual components, without any additive toxicity. No new safety signals were observed. The most frequent treatment-emergent adverse events were neutropenia, rash, stomatitis, infusion-related reactions and diarrhea. All IRRs were Grade 1 or 2 and there were no Grade 3 or higher IRR events reported. Treatment-related discontinuations of RYBREVANT® were 10 percent for RYBREVANT® plus FOLFOX and nine percent for RYBREVANT® plus FOLFIRI.[1]

“Confirmation that RYBREVANT has activity beyond lung cancer, given its unique multi-targeted approach in inhibiting *EGFR* and MET, is a potentially important step forward for patients with *EGFR* inhibitor-naïve metastatic colorectal cancer,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Johnson & Johnson Innovative Medicine. “Colorectal cancer is the third most common cancer globally, representing about 10 percent of all cancer cases and the second leading cause of cancer-related deaths. Our commitment to advancing cancer care drives us to evaluate every possibility to improve patient outcomes, and these findings highlight the potential of RYBREVANT to help even more patients with cancer.”

Pivotal Phase 3 registration trials evaluating RYBREVANT®-based regimens as first- and second-line treatment in colorectal cancer are planned.

About the OrigAMI-1 Study

OrigAMI-1 (NCT05379595) is an open-label Phase 1b/2 study assessing the efficacy and safety of RYBREVANT® plus mFOLFOX6 or FOLFIRI in anti-*EGFR*-naïve RAS/BRAF WT mCRC. Eligible patients were WT for KRAS, NRAS or BRAF genes based on circulating tumor DNA testing. Additionally, patients were required to have no amplification of the ERBB2/HER2 gene. In the RYBREVANT® and chemotherapy cohorts, patients were either treatment-naïve or had received at least one prior line in the metastatic setting (no *EGFR* inhibitor treatment). The primary endpoint of the combination cohorts was to characterize the safety and confirm the dose of RYBREVANT® plus mFOLFOX6 or FOLFIRI. Response was assessed by the investigator per RECIST v1.1.[2]

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw), a fully-human bispecific antibody targeting *EGFR* and MET with immune cell-directing activity, is approved in the U.S., Europe, and in other markets around the world as monotherapy 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.[3]

RYBREVANT® is approved in the U.S., Europe, and in markets around the world in combination with chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations, as detected by an FDA-approved test.

RYBREVANT® is approved in the U.S. in combination with LAZCLUZE™ (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or L858R substitution mutations, as detected by an FDA-approved test. A marketing authorization application (MAA) and type II extension of indication application were submitted to the European Medicines Agency (EMA) seeking approval of LAZCLUZE™ in combination with RYBREVANT® based on the MARIPOSA study.

In November 2023, Johnson & Johnson submitted a supplemental Biologics License Application (sBLA) to the U.S. FDA for RYBREVANT® in combination with chemotherapy for the treatment of patients with *EGFR*-mutated NSCLC who progressed on or after osimertinib based on the MARIPOSA-2 study. This indication was approved in Europe in August 2024.

In June 2024, Johnson & Johnson submitted a BLA to the U.S. FDA for the subcutaneous formulation of RYBREVANT® in combination with LAZCLUZE™ for all currently approved or submitted indications of intravenous (IV) RYBREVANT® in certain patients with NSCLC. A submission for the extension of the RYBREVANT® marketing authorization (line extension) was also submitted to the EMA seeking approval for this indication.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NSCLC[§] prefer next-generation sequencing–based strategies over polymerase chain reaction–based approaches for the detection of *EGFR* exon 20 insertion variants. The NCCN Guidelines include:

- Amivantamab-vmjw (RYBREVANT®) plus lazertinib (LAZCLUZE™) as a Category 1 recommendation for first-line therapy in patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R mutations.[4 †‡]
- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a Category 1 recommendation for patients with locally advanced or metastatic NCSLC with *EGFR* exon 19 deletions or exon 21 L858R mutations who experienced disease progression after treatment with osimertinib.[4 †‡]
- Amivantamab-vmjw (RYBREVANT®) plus carboplatin and pemetrexed as a Category 1 recommendation for first-line therapy in treatment-naive patients with newly diagnosed advanced or metastatic *EGFR* exon 20 insertion mutation-positive advanced NSCLC, or as 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.[4 †‡]
- Amivantamab-vmjw (RYBREVANT®) as a Category 2A recommendation for patients that have progressed on or after platinum-based chemotherapy with or without an immunotherapy and have *EGFR* exon 20 insertion mutation-positive NSCLC.[4 †‡]

In addition to the Phase 1b/2 OrigAMI-1 study, RYBREVANT® is being studied in multiple clinical trials, including:

- The Phase 3 MARIPOSA (NCT04487080) study assessing RYBREVANT® in combination with LAZCLUZE™ versus osimertinib and versus LAZCLUZE™ alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with *EGFR* ex19del or L858R substitution mutations.[5]
- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of RYBREVANT® (with or without LAZCLUZE™) 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.[6]
- The Phase 3 PAPILLON (NCT04538664) study assessing RYBREVANT® 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.[7]
- The Phase 3 PALOMA-3 (NCT05388669) study assessing LAZCLUZE™ with subcutaneous amivantamab compared to intravenous amivantamab in patients with *EGFR*-mutated advanced or metastatic NSCLC.[8]
- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including *EGFR*-mutated NSCLC.[9]
- 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.[10]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating RYBREVANT® in patients with advanced NSCLC.[11]
- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating RYBREVANT® in combination with LAZCLUZE™ and LAZCLUZE™ as a monotherapy in patients with advanced NSCLC with *EGFR* mutations.[12]
- The Phase 1/2 METalmark (NCT05488314) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[13]
- The Phase 1/2 PolyDamas (NCT05908734) study assessing RYBREVANT® and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[14]
- 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 LAZCLUZE™ in relapsed or refractory *EGFR*-mutated advanced or metastatic NSCLC.[15]

- The Phase 1/2 swalloWTail (NCT06532032) study assessing RYBREVANT® and docetaxel combination therapy in patients with metastatic NSCLC.[16]
- The Phase 1b/2 OrigAMI-4 (NCT06385080) study assessing RYBREVANT® monotherapy and in addition to standard-of-care therapeutic agents in patients with recurrent/metastatic head and neck squamous cell carcinoma.[17]

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

About Colorectal Cancer

Colorectal cancer is the third most common cancer worldwide, accounting for approximately 10 percent of all cancer cases and is the second leading cause of cancer-related deaths worldwide.[18] While it predominantly affects older individuals, recent research suggests that colorectal cancer is now being diagnosed in adults under the age of 50 at record rates.[19]

Left-sided colorectal cancer, which represents approximately 65 percent of cases, often has distinct characteristics that influence treatment strategies. Around half of colorectal cancer patients have mutations in the RAS genes, with KRAS being the most common mutation. While tumors with normal RAS and BRAF genes generally respond better to *EGFR* inhibitors, those with RAS and BRAF mutations – particularly on the left side – are associated with poorer outcomes.[20]

IMPORTANT SAFETY INFORMATION[3,21]

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. The median time to IRR onset is approximately 1 hour.

RYBREVANT® with LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause infusion-related reactions. In MARIPOSA (n=421), IRRs occurred in 63% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 5% and Grade 4 in 1% of patients. The incidence of infusion modifications due to IRR was 54% of patients, and IRRs leading to dose reduction of RYBREVANT® occurred in 0.7% of patients. Infusion-related reactions leading to permanent discontinuation of RYBREVANT® occurred in 4.5% of patients receiving RYBREVANT® in combination with LAZCLUZE™.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON (n=151), infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

RYBREVANT® as a Single Agent

In CHRYSALIS (n=302), 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 to reduce the risk of infusion-related reactions. Monitor patients for 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 severe and fatal interstitial lung disease (ILD)/pneumonitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case (0.2%) of

ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT® and LAZCLUZE™ due to ILD/pneumonitis.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, all patients required permanent discontinuation.

RYBREVANT® as a Single Agent

In CHRYSALIS, 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). For patients receiving RYBREVANT® in combination with LAZCLUZE™, immediately withhold both drugs in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use of RYBREVANT® and LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal venous thromboembolic (VTEs) events, including deep vein thrombosis and pulmonary embolism. The majority of these events occurred during the first four months of therapy.

In MARIPOSA, VTEs occurred in 36% of patients receiving RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 10% and Grade 4 in 0.5% of patients. On-study VTEs occurred in 1.2% of patients (n=5) while receiving anticoagulation therapy. There were two fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose interruptions of RYBREVANT®, and 7% of patients had VTE leading to dose interruptions of LAZCLUZE™; 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 0.5% of patients had VTE leading to dose reductions of LAZCLUZE™; 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT®, and 1.9% of patients had VTE leading to permanent discontinuation of LAZCLUZE™. The median time to onset of VTEs was 84 days (range: 6 to 777).

Administer prophylactic anticoagulation for the first four months of treatment. The use of Vitamin K antagonists is not recommended. Monitor for signs and symptoms of VTE events and treat as medically appropriate.

Withhold RYBREVANT® and LAZCLUZE™ based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level at the discretion of the healthcare provider. In the event of VTE recurrence despite therapeutic anticoagulation, permanently discontinue RYBREVANT® and continue treatment with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider.

Dermatologic Adverse Reactions

RYBREVANT® can cause severe rash including toxic epidermal necrolysis (TEN), dermatitis acneiform, pruritus, and dry skin.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, rash occurred in 86% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 26% of patients. The median time to onset of rash was 14 days (range: 1 to 556 days). Rash leading to dose interruptions occurred in 37% of patients for RYBREVANT® and 30% for LAZCLUZE™, rash leading to dose reductions occurred in 23% of patients for RYBREVANT® and 19% for LAZCLUZE™, and rash leading to permanent discontinuation occurred in 5% of patients for RYBREVANT® and 1.7% for LAZCLUZE™.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) adverse reactions. Rash leading to dose reductions occurred in 19% of patients, and 2% permanently discontinued RYBREVANT® and 1.3% discontinued pemetrexed.

RYBREVANT® as a Single Agent

In CHRYSALIS, rash occurred in 74% of patients treated with RYBREVANT® as a single agent, 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® as a single agent.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT® or LAZCLUZE™ in combination with RYBREVANT®. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen. Alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream is recommended for dry skin.

When initiating RYBREVANT® treatment with or without LAZCLUZE™, administer alcohol-free emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (e.g. use of oral antibiotics) to reduce the risk of dermatologic reactions. 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. For patients receiving RYBREVANT® in combination with LAZCLUZE™, withhold, dose reduce or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus, and uveitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 or 4 ocular toxicity in 0.7% of patients. Withhold, reduce the dose, or permanently discontinue RYBREVANT® and continue LAZCLUZE™ based on severity.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus occurred in 9%. All events were Grade 1-2.

RYBREVANT® as a Single Agent

In CHRYSALIS, 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 with new or worsening 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® and LAZCLUZE™ 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 last dose of RYBREVANT®.

Advise females of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose.

Adverse Reactions

RYBREVANT® with LAZCLUZE™

For the 421 patients in the MARIPOSA clinical trial who received RYBREVANT® in combination with LAZCLUZE™, the most common adverse reactions (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (RYBREVANT®, 63%), musculoskeletal pain (47%), stomatitis (43%), edema (43%), VTE (36%), paresthesia (35%), fatigue (32%), diarrhea (31%), constipation (29%), COVID-19 (26%), hemorrhage (25%), dry skin (25%), decreased appetite (24%), pruritus (24%), nausea (21%), and ocular toxicity (16%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased albumin (8%), decreased sodium (7%), increased ALT (7%), decreased potassium (5%), decreased hemoglobin (3.8%), increased AST (3.8%), increased GGT (2.6%), and increased magnesium (2.6%).

Serious adverse reactions occurred in 49% of patients who received RYBREVANT® in combination with LAZCLUZE™. Serious adverse reactions occurring in ≥2% of patients included VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and infusion-related reaction (RYBREVANT®) (2.1% each). Fatal adverse reactions occurred in 7% of patients who received RYBREVANT® in combination with LAZCLUZE™ due to death not otherwise specified (1.2%); sepsis

and respiratory failure (1% each); pneumonia, myocardial infarction, and sudden death (0.7% each); cerebral infarction, pulmonary embolism (PE), and COVID-19 infection (0.5% each); and ILD/pneumonitis, acute respiratory distress syndrome (ARDS), and cardiopulmonary arrest (0.2% each).

RYBREVANT® with Carboplatin and Pemetrexed

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), infusion-related reaction (42%), fatigue (42%), edema (40%), constipation (40%), decreased appetite (36%), nausea (36%), COVID-19 (24%), diarrhea (21%), and vomiting (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased albumin (7%), increased alanine aminotransferase (4%), increased gamma-glutamyl transferase (4%), decreased sodium (7%), decreased potassium (11%), decreased magnesium (2%), and decreases in white blood cells (17%), hemoglobin (11%), neutrophils (36%), platelets (10%), and lymphocytes (11%).

Serious adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting, and COVID-19. Fatal adverse reactions occurred in 7 patients (4.6%) due to pneumonia, cerebrovascular accident, cardio-respiratory arrest, COVID-19, sepsis, and death not otherwise specified.

RYBREVANT® as a Single Agent

For the 129 patients in the CHRYSALIS clinical trial who received RYBREVANT® as a single agent, 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%).

Serious adverse reactions occurred in 30% of patients who received RYBREVANT®. Serious adverse reactions in ≥2% of patients included pulmonary embolism, pneumonitis/ILD, dyspnea, musculoskeletal pain, pneumonia, and muscular weakness. Fatal adverse reactions occurred in 2 patients (1.5%) due to pneumonia and 1 patient (0.8%) due to sudden death.

LAZCLUZE™ Drug Interactions

Avoid concomitant use of LAZCLUZE™ with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate.

Please read full Prescribing Information for RYBREVANT®.

Please read full Prescribing Information for LAZCLUZE™.

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 https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JanssenUS and @JNJInnovMed. 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 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 & Development, LLC, Janssen Biotech, Inc. 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; 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 Research & Development, LLC, Janssen Biotech, Inc. nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

###

*Dr. Filippo Pietrantonio has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

**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.

†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.

§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 warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Source: Johnson & Johnson

---

[1] Pietrantonio, et al. Amivantamab plus FOLFOX or FOLFIRI in metastatic colorectal cancer: Results from OrigAMI-1, a phase 1b/2 study. 2024 European Society for Medical Oncology. September 14, 2024.
[2] ClinicalTrials.gov. A Study of Amivantamab Monotherapy and in Addition to Standard-of-Care Chemotherapy in Participants With Advanced or Metastatic Colorectal Cancer (OrigAMI-1). https://clinicaltrials.gov/study/NCT05379595?tab=history&a=1. Accessed September 2024.
[3] RYBREVANT® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.
[4] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.9.2024© National Comprehensive Cancer Network, Inc. All rights reserved. To view the most recent and complete version of the guideline, go online to NCCN.org. Accessed September 2024.
[5] ClinicalTrials.gov. A Study of Amivantamab and LAZCLUZE™ Combination Therapy Versus Osimertinib in Locally Advanced or Metastatic Non-Small Cell Lung Cancer (MARIPOSA). Available at: https://www.clinicaltrials.gov/study/NCT04487080. Accessed September 2024.
[6] 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. Accessed September 2024.
[7] 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. Accessed September 2024.
[8] 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. Accessed September 2024.
[9] 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 September 2024.
[10] ClinicalTrials.gov. A Study of Amivantamab Subcutaneous (SC) Administration for the Treatment of Advanced Solid Malignancies (PALOMA). Available at: https://clinicaltrials.gov/study/NCT04606381. Accessed September 2024.
[11] 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. Accessed September 2024.

[12] 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. Accessed August 2024.
[13] 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. Accessed September 2024.
[14] 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. Accessed September 2024.
[15] ClinicalTrials.gov. Premedication to Reduce Amivantamab Associated Infusion Related Reactions (SKIPPirr). https://classic.clinicaltrials.gov/ct2/show/NCT05663866. Accessed September 2024.
[16] ClinicalTrials.gov. A Study of Combination Therapy With Amivantamab and Docetaxel in Participants With Metastatic Non-small Cell Lung Cancer (swalloWTail). https://www.clinicaltrials.gov/study/NCT06532032?term=Swallowtail&intr=amivantamab&rank=1. Accessed September 2024.
[17] ClinicalTrials.gov. A Study of Amivantamab Alone or in Addition to Other Treatment Agents in Participants With Recurrent/ Metastatic Head and Neck Cancer (OrigAMI-4). https://clinicaltrials.gov/study/NCT06385080?term=OrigAMI-4&limit=10&rank=1. Accessed September 2024.
[18] World Health Organization. Colorectal Cancer. 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/colorectal-cancer. Accessed: July 2024
[19] Virostko J, et al. Recent trends in the age at diagnosis of colorectal cancer in the US National Cancer Data Base, 2004-2015. Cancer, 2019;125: 3828-3835. https://doi.org/10.1002/cncr.32347
[20] Christopher H. Lieu et al., Integrating Biomarkers and Targeted Therapy Into Colorectal Cancer Management. Am Soc Clin Oncol Educ Book 39, 207-215(2019). DOI:10.1200/EDBK_240839
[21] LAZCLUZE™ Prescribing Information. Horsham, PA: Janssen Biotech, Inc.