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NEWS RELEASE

RYBREVANT® (amivantamab-vmjw) longer-term results show promising and durable responses in difficult-to-treat colorectal cancer

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Over 70 percent of patients in the first-line subgroup responded to amivantamab plus chemotherapy with most responses lasting beyond 16 months

Notable responses were also seen in patients with liver metastases, who often face poorer outcomes with this disease

RARITAN, N.J., Jan. 10, 2026 /PRNewswire/ -- Johnson & Johnson (NYSE:JNJ) today announced new longer follow-up results from the investigational Phase 1b/2 OrigAMI-1 study evaluating amivantamab-vmjw, a bispecific antibody targeting epidermal growth factor receptor (EGFR) and MET, in combination with FOLFOX or FOLFIRI chemotherapy in patients with RAS/BRAF wild-type metastatic colorectal cancer. The encouraging anti-tumor activity, durable responses, and low rates of treatment-related discontinuations observed in this study support further investigation in ongoing Phase 3 studies in first- and second-line colorectal cancer. Results were presented during a poster session at the 2026 American Society of Clinical Oncology Gastrointestinal Cancers (ASCO GI) Symposium (Abstract #166).[1]

"These results show the potential of amivantamab combined with chemotherapy to deliver meaningful and durable benefit for people with advanced colorectal cancer, including for those with liver metastases who have historically faced poorer outcomes," said Dr. Filippo Pietrantonio,* M.D., Head of the Gastrointestinal Oncology Unit, IRCCS Foundation, National Cancer Institute, Milan, Italy. "Seeing patients maintain responses for extended periods, some beyond two years, is a powerful sign of progress in a disease where sustained efficacy has been hard to achieve and speaks to the promise of this treatment approach."

Colorectal cancer is the third most commonly diagnosed cancer worldwide, and a leading cause of cancer-related death.[2] While traditionally seen in older adults, incidence is rising in people under 50.[3] More than half of patients will eventually develop metastatic disease, with liver involvement in roughly 70 percent of cases. In this setting, resistance to current first-line therapies often develops early, shortening the time patients can benefit.[4] For those with RAS/BRAF wild-type metastatic colorectal cancer with disease progression, second-line options remain limited, with historical response rates of 32 to 36 percent and median progression-free survival (PFS) of 5.4 to 6.4 months using EGFR inhibitors and chemotherapy.[5,6,7,8,9,10] Research has shown that MET alterations are a frequent cause of resistance to EGFR-inhibition, highlighting a need for new approaches that target both pathways simultaneously.[11]

Detailed Study Results

Cohorts D and E of the Phase 1b/2 OrigAMI-1 study evaluated intravenous amivantamab as monotherapy or in combination with either FOLFOX or FOLFIRI chemotherapy in patients with RAS/BRAF wild-type metastatic colorectal cancer. Patients were confirmed to be negative for KRAS, NRAS, BRAF and EGFR mutations, and did not have HER2 amplification. They could have received one prior line of systemic therapy in the metastatic setting, and prior treatment with an EGFR inhibitor was not permitted. The primary endpoint was safety, and secondary endpoints included overall response rate (ORR), duration of response (DOR), clinical benefit rate, and PFS. Overall survival was assessed as an exploratory endpoint.[1]

At a median follow-up of 16 months (range, 1.2-29.5), amivantamab plus FOLFOX (n=20) or FOLFIRI (n=23) achieved a confirmed ORR of 51 percent (95 percent confidence interval [CI], 36-67) across the study, with responses observed early and a median time to first response of 8.3 weeks (range, 7.3-20.3), along with a median DOR of 9.3 months (95 percent CI, 5.8-14.7). Median PFS was 9.2 months (95 percent CI, 5.4-12.9), and median overall survival was not estimable (NE) (95 percent CI, 16.2-NE). In the first-line subgroup, ORR was 73 percent (95 percent CI, 53-86), with median DOR not yet reached at the time of data cutoff (95 percent CI, 7.3-NE). Among 11 patients treated in the first-line subgroup, four were able to proceed to curative intent surgery. In the second-line subgroup (n=32), ORR was 44 percent (95 percent CI, 26-62) and median DOR was 7.4 months (95 percent CI, 5.4-14.5). More than one-third of patients treated in the second-line setting remained on therapy for over one year, and three patients have stayed on amivantamab treatment for more than two years. In patients with liver metastases (n=30), the study showed notable activity, with an ORR of 57 percent (95 percent CI, 37-75) and a median PFS of 11.3 months (95 percent CI, 5.9-16.4).[1]

The safety profile remained consistent with prior reports of amivantamab plus chemotherapy in colorectal cancer and with the known safety profiles of the individual agents. Treatment-emergent adverse events were primarily related to EGFR and MET inhibition and known chemotherapy-associated effects. Four patients (9 percent) discontinued therapy due to treatment-related adverse events. The most common Grade 3 or higher event was

neutropenia, and no new safety signals were observed.[1]

"Treatment for metastatic colorectal cancer has remained largely unchanged for many years, underscoring the need for new strategies," said Kiran Patel, M.D., Vice President, Global Head, Solid Tumor Clinical Development and Companion Diagnostics, Johnson & Johnson Innovative Medicine. "We are drawing on our scientific leadership in EGFR-driven lung cancer to evaluate the potential of amivantamab, and its dual-targeting of EGFR and MET, in colorectal cancer and other solid tumors driven by these pathways."

Pivotal Phase 3 studies, including the global, randomized OrigAMI-2 and OrigAMI-3 studies evaluating subcutaneous amivantamab with FOLFOX and FOLFIRI, are underway to further evaluate the potential of amivantamab-based regimens in both first- and second-line colorectal cancer.

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 wild-type (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.[12]

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.[2] 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.[3]

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.[13]

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 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.[14]

RYBREVANT® is approved in the **U.S.**, **Europe** and other 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., Europe** and other markets around the world 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 exon 21 L858R substitution mutations, as detected by an FDA-approved test.

RYBREVANT® is approved in the **U.S.**, **Europe** and other markets around the world in combination with chemotherapy (carboplatin-pemetrexed) for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR TKI.

RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) is approved in the **U.S.**, **Europe** and other markets around the world in combination with LAZCLUZE® for the first-line treatment of adult patients with advanced NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, and as a monotherapy for the treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy.

The National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[§15] include amivantamab-vmjw (RYBREVANT®) across multiple treatment settings, including its recent inclusion as a NCCN Category 1 preferred option when used with lazertinib (LAZCLUZE®) for first-line treatment of people with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations; see the latest NCCN Guidelines® for NSCLC for complete information. [†‡]

The NCCN Guidelines for Central Nervous System Cancers also identify amivantamab-vmjw (RYBREVANT®)-based regimens, including the combination with lazertinib (LAZCLUZE®), as the only NCCN-preferred combination options for patients with EGFR-mutated NSCLC and brain metastases.[†‡]

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 substitution mutations.[16]

- The Phase 3 MARIPOSA-2 (**NCT04988295**) study assessing the efficacy of RYBREVANT® (with or without LAZCLUZE®) and carboplatin-pemetrexed versus carboplatin-pemetrexed alone in patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or L858R substitution mutations after disease progression on or after osimertinib.[17]
- 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.[18]
- The Phase 3 PALOMA-3 (**NCT05388669**) study assessing LAZCLUZE® with subcutaneous (SC) amivantamab compared to RYBREVANT® in patients with EGFR-mutated advanced or metastatic NSCLC.[19]
- The Phase 2 PALOMA-2 (**NCT05498428**) study assessing SC amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[20]
- The Phase 1 PALOMA (**NCT04606381**) study assessing the feasibility of SC amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for SC amivantamab delivery.[21]
- The Phase 1 CHRYSALIS (**NCT02609776**) study evaluating RYBREVANT® in patients with advanced NSCLC.[22]
- 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.[23]
- The Phase 1/2 METalmark (**NCT05488314**) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[24]
- The Phase 1/2 swalloWTail (**NCT06532032**) study assessing RYBREVANT® and docetaxel combination therapy in patients with metastatic NSCLC.[25]
- The Phase 1/2 PolyDamas (**NCT05908734**) study assessing RYBREVANT® and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[26]
- The Phase 2 SKIPPirr (**NCT05663866**) study 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.[27]
- The Phase 2 COPERNICUS (**NCT06667076**) study combining developments in treatment administration and prophylactic supportive care in representative US patients with common EGFR-mutated NSCLC treated with SC amivantamab in combination with LAZCLUZE® or chemotherapy.[28]
- The Phase 2 COCOON (**NCT06120140**) study assessing the effectiveness of a proactive dermatologic management regimen given with first-line RYBREVANT® and LAZCLUZE® in patients with EGFR-mutated advanced NSCLC.[29]
- The Phase 3 OrigAMI-2 (**NCT06662786**) study assessing subcutaneous amivantamab and mFOLFOX6 or FOLFIRI in patients with KRAS/NRAS and BRAF wild-type unresectable or metastatic left-sided colorectal cancer.[30]

- The Phase 3 OrigAMI-3 (**NCT06750094**) study assessing subcutaneous amivantamab and FOLFIRI in patients with KRAS/NRAS and BRAF wild-type recurrent, unresectable or metastatic colorectal cancer after disease progression on chemotherapy.[31]
- 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.[32]
- The Phase 3 OrigAMI-5 (**NCT07276399**) study assessing SC amivantamab with pembrolizumab and carboplatin in patients with recurrent/metastatic head and neck squamous cell carcinoma.[33]

The legal manufacturer for RYBREVANT® is Janssen Biotech, Inc.

INDICATIONS

RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) and RYBREVANT® (amivantamab-vmjw) are indicated:

- 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 exon 21 L858R substitution mutations, as detected by an FDA-approved test.
- in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- in combination with 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.
- as a single agent 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.

IMPORTANT SAFETY INFORMATION[14,34]

CONTRAINDICATIONS

RYBREVANT FASPRO™ is contraindicated in patients with known hypersensitivity to hyaluronidase or to any of its excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Administration-Related Reactions with RYBREVANT FASPRO™

RYBREVANT FASPRO™ can cause hypersensitivity and administration-related reactions (ARR); signs and symptoms of ARR include dyspnea, flushing, fever, chills, chest discomfort, hypotension, and vomiting. The median time to ARR onset is approximately 2 hours.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3 (n=206), all Grade ARR occurred in 13% of patients, including 0.5% Grade 3. Of the patients who experienced ARR, 89% occurred with the initial dose (Week 1, Day 1).

Premedicate with antihistamines, antipyretics, and glucocorticoids and administer RYBREVANT FASPRO™ as recommended. Monitor patients for any signs and symptoms of administration-related reactions during injection in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt RYBREVANT FASPRO™ injection if ARR is suspected. Resume treatment upon resolution of symptoms or permanently discontinue RYBREVANT FASPRO™ based on severity.

Infusion-Related Reactions with RYBREVANT®

RYBREVANT® can cause infusion-related reactions (IRR) including anaphylaxis; 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®

In MARIPOSA (n=421), IRRs occurred in 63% of patients, including Grade 3 in 5% and Grade 4 in 1% of patients. IRR-related infusion modifications occurred in 54%, dose reduction in 0.7%, and permanent discontinuation of RYBREVANT® in 4.5% of patients.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population (n=281), IRRs occurred in 50% of patients including Grade 3 (3.2%) adverse reactions. IRR-related infusion modifications occurred in 46%, and permanent discontinuation of RYBREVANT® in 2.8% of patients.

RYBREVANT® as a Single Agent

In CHRYSALIS (n=302), IRRs occurred in 66% of patients. IRRs occurred in 65% of patients on Week 1 Day 1, 3.4% on Day 2 infusion, 0.4% with Week 2 infusion, and were cumulatively 1.1% with subsequent infusions. 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. IRR-related infusion modifications occurred in 62%, and permanent discontinuation of RYBREVANT® in 1.3% of patients.

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 IRRs. Monitor patients for signs and symptoms of IRRs 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. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

Interstitial Lung Disease/Pneumonitis

RYBREVANT FASPRO™ and RYBREVANT® can cause severe and fatal interstitial lung disease (ILD)/pneumonitis.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3, ILD/pneumonitis occurred in 6% of patients, including Grade 3 in 1%, Grade 4 in 1.5%, and fatal cases in 1.9% of patients. 5% of patients permanently discontinued RYBREVANT FASPRO™ and LAZCLUZE® due to ILD/pneumonitis.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients, including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case of ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT® and LAZCLUZE® due to ILD/pneumonitis.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% of patients with 1.8% of patients experiencing Grade 3 ILD/pneumonitis. 2.1% discontinued RYBREVANT® due to ILD/pneumonitis.

RYBREVANT® as a Single Agent

In CHRYSALIS, ILD/pneumonitis occurred in 3.3% of patients, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) permanently 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 FASPRO™ or RYBREVANT® and LAZCLUZE® (when applicable) in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use with LAZCLUZE®

RYBREVANT FASPRO™ and RYBREVANT® in combination with LAZCLUZE® can cause serious and fatal venous thromboembolic (VTE) events, including deep vein thrombosis and pulmonary embolism. Without prophylactic anticoagulation, the majority of these events occurred during the first four months of treatment.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3 (n=206), all Grade VTE occurred in 11% of patients and 1.5% were Grade 3. 80% (n=164) of patients received prophylactic anticoagulation at study entry, with an all Grade VTE incidence of 7%. In patients who did not receive prophylactic anticoagulation (n=42), all Grade VTE occurred in 17% of patients. In total, 0.5% of patients had VTE leading to dose reductions of RYBREVANT FASPRO™ and no patients required permanent discontinuation. The median time to onset of VTEs was 95 days (range: 17 to 390).

RYBREVANT® with LAZCLUZE®

In MARIPOSA (n=421), VTEs occurred in 36% of patients 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 FASPRO™ or RYBREVANT® and LAZCLUZE® based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT FASPRO™ or 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 FASPRO™ or RYBREVANT®. Treatment can continue with LAZCLUZE® at the same dose level at the discretion of the healthcare provider. Refer to the LAZCLUZE® Prescribing Information for recommended LAZCLUZE® dosage modification.

Dermatologic Adverse Reactions

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

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3, rash occurred in 80% of patients, including Grade 3 in 17% and Grade 4 in 0.5% of patients. Rash leading to dose reduction occurred in 11% of patients, and RYBREVANT FASPRO™ was permanently discontinued due to rash in 1.5% of patients.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, rash occurred in 86% of patients, 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

Based on the pooled safety population, rash occurred in 82% of patients, including Grade 3 (15%) adverse reactions. Rash leading to dose reductions occurred in 14% of patients, and 2.5% permanently discontinued RYBREVANT® and 3.1% discontinued pemetrexed.

RYBREVANT® as a Single Agent

In CHRYSALIS, rash occurred in 74% of patients, including Grade 3 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% and permanent discontinuation due to rash occurred in 0.7% of patients. Toxic epidermal necrolysis occurred in one patient (0.3%).

When initiating treatment with RYBREVANT FASPRO™ or RYBREVANT® and LAZCLUZE®, prophylactic and concomitant medications are recommended to reduce the risk and severity of dermatologic adverse reactions. Instruct patients to limit sun exposure during and for 2 months after treatment. Advise patients to wear protective clothing and use broad spectrum UVA/UVB sunscreen.

If skin reactions develop, administer supportive care including 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 FASPRO™ or RYBREVANT® in combination with LAZCLUZE®, withhold, reduce the dose, or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT FASPRO™ or RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT FASPRO™ or RYBREVANT® based on severity.

Ocular Toxicity

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

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3, all Grade ocular toxicity occurred in 13% of patients, including 0.5% Grade 3.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, ocular toxicity occurred in 16%, including Grade 3 or 4 ocular toxicity in 0.7% of patients.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ocular toxicity occurred in 16% of patients. All events were Grade 1 or 2.

RYBREVANT® as a Single Agent

In CHRYSALIS, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients. All events were Grade 1-2.

Promptly refer patients presenting with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT FASPRO™ or RYBREVANT® and continue LAZCLUZE® based on severity.

Embryo-Fetal Toxicity

Based on animal models, RYBREVANT FASPRO™, RYBREVANT® and LAZCLUZE® can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating RYBREVANT FASPRO™ and RYBREVANT®. Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT FASPRO™ or RYBREVANT®, and for 3 weeks after the last dose of LAZCLUZE®.

ADVERSE REACTIONS

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3 (n=206), the most common adverse reactions (≥20%) were rash (80%), nail toxicity (58%), musculoskeletal pain (50%), fatigue (37%), stomatitis (36%), edema (34%), nausea (30%), diarrhea (22%), vomiting (22%), constipation (22%), decreased appetite (22%), and headache (21%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocyte count (6%), decreased sodium (5%), decreased potassium (5%), decreased albumin (4.9%), increased alanine aminotransferase (3.4%), decreased platelet count (2.4%), increased aspartate aminotransferase (2%), increased gamma-glutamyl transferase (2%), and decreased hemoglobin (2%).

Serious adverse reactions occurred in 33% of patients, with those occurring in ≥2% of patients including ILD/pneumonitis (6%); and pneumonia, VTE and fatigue (2.4% each). Death due to adverse reactions occurred in 5% of patients treated with RYBREVANT FASPRO™, including ILD/pneumonitis (1.9%), pneumonia (1.5%), and respiratory failure and sudden death (1% each).

RYBREVANT® with LAZCLUZE®

In MARIPOSA (n=421), the most common adverse reactions (ARs) (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (IRRs) (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%), and nausea (21%). 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 ARs occurred in 49% of patients, with those occurring in ≥2% of patients including VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and IRRs (RYBREVANT®) (2.1% each). Fatal ARs occurred in 7% of patients 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

In MARIPOSA-2 (n=130), the most common ARs (≥20%) were rash (72%), IRRs (59%), fatigue (51%), nail toxicity (45%), nausea (45%), constipation (39%), edema (36%), stomatitis (35%), decreased appetite (31%), musculoskeletal pain (30%), vomiting (25%), and COVID-19 (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased neutrophils (49%), decreased white blood cells (42%), decreased lymphocytes (28%), decreased platelets (17%), decreased hemoglobin (12%), decreased potassium (11%), decreased sodium (11%), increased alanine aminotransferase (3.9%), decreased albumin (3.8%), and increased gamma-glutamyl transferase (3.1%).

In MARIPOSA-2, serious ARs occurred in 32% of patients, with those occurring in >2% of patients including dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and PE (2.3%). Fatal ARs occurred in 2.3% of patients; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

In PAPILLON (n=151), the most common ARs (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), IRRs (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%).

In PAPILLON, serious ARs occurred in 37% of patients, with those occurring in ≥2% of patients including rash, pneumonia, ILD, PE, 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

In CHRYSALIS (n=129), the most common ARs (≥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 ARs occurred in 30% of patients, with those occurring in ≥2% of patients including PE, 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 see full Prescribing Information
for **RYBREVANT FASPRO™**, **RYBREVANT®** and **LAZCLUZE®**.

cp-491009v1

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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 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 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 most recent Annual Report on Form 10-K, 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 **http://www.sec.gov**, **http://www.jnj.com**, or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Filippo Pietrantonio, M.D. has served as a consultant to Johnson & Johnson; he has not been paid for any media work.

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[†]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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