Johnson&Johnson

NEWS RELEASE

Johnson & Johnson announces U.S. FDA Approval of RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) as First and Only Dual-Targeted Therapy for Advanced Head and Neck Cancer

2026-11-05

- Accelerated approval based on data demonstrating clinically meaningful efficacy, including a 42 percent overall response rate (95 percent confidence interval, 32–52 percent)[1]
- First advancement in the second-line treatment setting for recurrent or metastatic head and neck cancer in a decade, bringing a new subcutaneous option to patients with significant unmet need[2-3]
- Extending its well-established, dual-targeted benefit beyond lung cancer, RYBREVANT FASPRO™ targets both EGFR and MET pathways – two key drivers of tumor progression in head and neck cancer[2]

NEW BRUNSWICK, N.J., Nov. 5, 2026 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) today announced that the U.S. Food and Drug Administration (FDA) granted accelerated approval for RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) (subcutaneous injection, 160 mg/2,000 units per mL) as a single agent for the treatment of adults with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) whose disease has progressed on or after platinum–based chemotherapy and an anti–PD–(L)1 antibody. The indication does not include patients with oropharyngeal squamous cell carcinoma (OPSCC) that is HPV-associated (i.e., by p16 immunohistochemistry). It is the first approval of a dual-targeted therapy in this setting, simultaneously targeting epidermal growth factor receptor (EGFR)- and mesenchymal-epithelial transition (MET).[2-3]

Experience the full interactive Multichannel News Release here: **https://www.multivu.com/johnson-and-johnson/9426351-en-johnson-and-johnson-fda-approval-rybrevant-faspro-hnscc**

Today's approval follows the FDA Breakthrough Therapy Designation (BTD) granted in February 2026 and Priority Review designation in July 2026. This indication was granted accelerated approval based on clinically meaningful and durable tumor response demonstrated in the Phase 1b/2 **OrigAMI-4 trial**.[1]

- Overall Response Rate (ORR): Confirmed ORR was 42 percent (95 percent confidence interval [CI], 32–52 percent), including complete responses in 15 percent of patients, representing one-third of all responders, and partial responses in 28 percent of patients, per blinded independent central review (BICR).
- Duration of Response (DOR): 56 percent of responders maintained a response for more than six months (1.4+, 19.7+), per BICR.

Continued approval may be contingent upon verification and description of clinical benefit in the ongoing confirmatory trial in first-line HNSCC, the Phase 3 OrigAMI-5 study.

RYBREVANT FASPRO™ is contraindicated in patients with known hypersensitivity to hyaluronidase or any of its excipients. Warnings and Precautions include hypersensitivity and administration-related reactions, interstitial lung disease (ILD)/pneumonitis, dermatologic adverse reactions, ocular toxicity and embryo-fetal toxicity.[1] Additional Important Safety Information can be found below.

Expert Perspectives on Improving Outcomes for Patients with Head and Neck Cancer

"For people living with recurrent or metastatic head and neck cancer, the stakes are incredibly high. I've seen firsthand that when the disease progresses, patients often face limited treatment options, while managing symptoms that can affect their ability to eat, speak, swallow and breathe," said Amanda Hollinger, Executive Director, Head and Neck Cancer Alliance. "At a time when treatment advances are urgently needed to improve outcomes for patients, this new option offers renewed hope for patients and their families."

"Outcomes remain poor for patients whose head and neck cancer progresses, and treatment options are limited," said Barbara Burtness, M.D., medical oncologist and professor of medicine at Yale Cancer Center in New Haven, Connecticut.* "The OrigAMI-4 findings represent important progress and highlight the potential of dual EGFR- and MET-targeting with amivantamab as a distinct treatment approach in recurrent or metastatic head and neck cancer, excluding HPV-associated oropharyngeal squamous cell carcinoma. The meaningful responses observed in this study are encouraging for patients who have long faced limited treatment options."

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First Approval for RYBREVANT FASPRO™ Beyond Lung Cancer

EGFR and MET are key drivers of tumor progression, overexpressed in 80 to 90 percent of recurrent and metastatic HNSCC tumors and often associated with poor prognosis.[2] RYBREVANT FASPRO™ addresses this by targeting both the EGFR and MET pathways simultaneously, while activating immune-cell directing activity – delivered via a five-minute subcutaneous injection.[1-2]

This approval marks the first indication beyond non-small cell lung cancer (NSCLC) for RYBREVANT FASPRO™. It reinforces the potential of the EGFR- and MET-targeted mechanism of amivantamab across multiple difficult-to-treat tumors.

"For years, treatment advances in recurrent or metastatic head and neck cancer have been limited by approaches that do not fully address the underlying biology of the disease," said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Head, Oncology, Johnson & Johnson. "RYBREVANT FASPRO delivers a differentiated approach, targeting both EGFR and MET to address the biology that drives this disease. Having redefined outcomes in EGFR+ non-small cell lung cancer, we are unlocking the next chapter of this treatment and bringing meaningful innovation to patients with certain head and neck cancers."

Pivotal Study Results

The FDA accelerated approval is supported by data from the multi-cohort Phase 1b/2 OrigAMI-4 trial. Cohort 1 evaluated RYBREVANT FASPRO™ as a single agent in 102 adults with previously treated recurrent or metastatic HNSCC who have received platinum-based chemotherapy and an anti–PD–(L)1 antibody (excluding patients with HPV-positive OPSCC).[1] The pivotal results were presented at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting and published in the **Journal of Clinical Oncology**.

Safety

In the OrigAMI-4 trial, the safety profile of RYBREVANT FASPRO™ was consistent with the well-established safety profile of prior amivantamab experience. No new safety signals were identified, supporting a favorable benefit-risk profile for this advanced patient population. The most common adverse reactions occurring in at least 20 percent of patients were rash (79 percent), fatigue (39 percent), nail toxicity (35 percent), stomatitis (32 percent), and edema (28 percent). Serious adverse reactions occurred in 39 percent of patients. Serious adverse reactions in at least 2 percent of patients included pneumonia (8 percent), hemorrhage (4.9 percent), dysphagia (2.9 percent), pneumothorax (2.9 percent), anemia (2 percent), dyspnea (2 percent), fatigue (2 percent), hepatic enzyme increased (2 percent), and ILD/pneumonitis (2 percent). Fatal adverse reactions occurred in 6 percent of patients who received RYBREVANT FASPRO™, including sudden death (2 percent), myocardial ischemia, tumor hemorrhage, aspiration

pneumonia, and ILD/pneumonitis (1 percent, one patient each).[1]

About the OrigAMI-4 Study

OrigAMI-4 is a multi-cohort, multicenter, open-label, ongoing Phase 1b/2 study evaluating RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) in recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC). The study includes six cohorts exploring RYBREVANT FASPRO™ across different treatment settings and regimens.

Cohort 1 (n=102) evaluated the efficacy and safety of RYBREVANT FASPRO™ as a single agent in patients with previously treated R/M HNSCC whose disease has progressed on or after platinum-based chemotherapy and an anti-PD-(L)1 antibody. Patients with HPV-associated OPSCC were excluded from Cohort 1. Patients received weight-based RYBREVANT FASPRO™ every three weeks at the recommended dose and schedule until disease progression or unacceptable toxicity. The primary endpoint is overall response rate (ORR), and the secondary endpoint is duration of response (DOR), both assessed by blinded independent central review (BICR) using RECIST v1.1.[†,1]

About Head and Neck Squamous Cell Carcinoma

Head and neck squamous cell carcinoma (HNSCC) is the most common form of head and neck cancer, a group of cancers that arise in the mouth, throat, voice box, sinuses, nasal cavity, and salivary glands.[4-5] It represents approximately 4.5 percent of all cancers worldwide and is the seventh most common cancer globally.[4] Major risk factors include tobacco and alcohol use, as well as infection with high-risk human papillomavirus (HPV).[4] Approximately 80 percent of recurrent or metastatic HNSCC are not driven by HPV, and are typically associated with poorer prognosis and reduced response to treatment.[4-5] Despite advances in surgery, radiation, chemotherapy, and immunotherapy, many patients ultimately progress to advanced recurrent or metastatic disease.[5-6]

About RYBREVANT FASPRO™ and RYBREVANT®

RYBREVANT® (amivantamab-vmjw) is a first-in-class, fully-human bispecific antibody targeting EGFR and MET with immune cell-directing activity. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) is approved in the U.S. for the same indications as intravenous RYBREVANT® across multiple markets. RYBREVANT FASPRO™ is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

The FDA accelerated approval RYBREVANT FASPRO™ in head and neck squamous cell carcinoma (HNSCC) is based on objective response rate (ORR) and duration of response (DOR) results from Cohort 1 of the Phase 1b/2 OrigAMI-

4 study. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the ongoing confirmatory trial, the Phase 3 OrigAMI-5 study (**NCT07276399**), which is evaluating subcutaneous amivantamab in combination with carboplatin and pembrolizumab as a first-line treatment for patients with recurrent or metastatic head and neck cancer.[2] For eligible patients with HNSCC, RYBREVANT FASPRO™ may be administered every four weeks or every three weeks, according to the recommended dosing schedule.

Beyond HNSCC, RYBREVANT FASPRO™ is approved in multiple markets worldwide for the treatment of adults with EGFR-mutated non-small cell lung cancer (NSCLC), including those with exon 19 deletions, exon 21 L858R substitution mutations, and exon 20 insertion mutations. It is the only subcutaneous therapy approved for these EGFR-mutated NSCLC populations and may be used as monotherapy or in combination with LAZCLUZE® (lazertinib) or chemotherapy, depending on the specific mutation and treatment setting. For eligible patients with NSCLC, RYBREVANT FASPRO™ offers a once-monthly dosing option following initial weekly dosing.

RYBREVANT-based therapies are being investigated across other solid tumors, including colorectal cancers.

The legal manufacturer for RYBREVANT FASPRO™ and RYBREVANT® is Janssen Biotech, Inc. For more information, visit **www.rybrevanthcp.com**.

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.

RYBREVANT FASPRO is also indicated:

- as a single agent for the treatment of adult patients with recurrent or metastatic HNSCC whose disease has progressed on or after platinum–based chemotherapy and an anti–PD–(L)1 antibody.
    - Limitations of use: RYBREVANT FASPRO is not indicated as a treatment for patients with OPSCC that is HPV-associated (i.e., by p16IHC).
    - This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

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 (ARRs); 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).

RYBREVANT FASPRO as a Single Agent

In OrigAMI-4 (n=132), all Grade ARRs occurred in 16% of patients, with 91% of ARR occurring with the initial dose (Week 1, Day 1). All events were Grade 1 or 2.

Premedicate with antihistamines, antipyretics, and glucocorticoids and administer RYBREVANT FASPRO as recommended. Monitor patients for any signs and symptoms of ARR during injection in a setting where cardiopulmonary resuscitation medication and equipment are available. For the first dose, monitor patients for hypersensitivity and ARRs for 2 to 4 hours following the end of injection. Interrupt injection if ARR is suspected. Resume treatment upon resolution of symptoms or permanently discontinue based on severity.

Infusion-Related Reactions with RYBREVANT

RYBREVANT can cause infusion-related reactions (IRRs) 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 FASPRO as a Single Agent

In OrigAMI-4, ILD/pneumonitis occurred in 1.5% of patients, including one fatal case (0.8%). All of these patients permanently discontinued RYBREVANT FASPRO 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 FASPRO as a Single Agent

In OrigAMI-4, rash occurred in 81% of patients, including Grade 3 in 11% and Grade 4 in 0.8%. Rash led to a dose reduction in 11% of patients, and permanent discontinuation in 3% 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, 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 and 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, dose reduce, 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.

Hepatotoxicity

LAZCLUZE in combination with amivantamab can cause severe hepatotoxicity (including increased ALT and AST).

RYBREVANT with LAZCLUZE

In MARIPOSA, based on adverse reaction data, hepatotoxicity occurred in 49% of patients treated with LAZCLUZE, including Grade 3 in 9.3% of patients and Grade 4 in 0.5%. LAZCLUZE was interrupted for an adverse reaction of hepatotoxicity in 8% of patients, the dose was reduced in 1.4% and permanently discontinued in 0.2%.

Perform liver function tests (including ALT, AST, and total bilirubin) before initiation of LAZCLUZE and during treatment, as clinically indicated. Withhold, dose reduce, or permanently discontinue LAZCLUZE and amivantamab 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. Keratitis occurred in one patient (0.5%).

RYBREVANT FASPRO as a Single Agent

In OrigAMI-4, ocular toxicity occurred in 11% of patients, including 0.8% Grade 4. Keratitis occurred in one patient (0.8%).

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 reactions 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 reactions 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

RYBREVANT FASPRO, RYBREVANT and LAZCLUZE can cause fetal harm when administered to a pregnant woman. Verify pregnancy status prior to initiating treatment. Advise pregnant women and females of reproductive potential of the potential risk to the fetus and 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 FASPRO as a Single Agent

In OrigAMI-4 (n=102), the most common adverse reactions (≥20%) were rash (79%), fatigue (39%), nail toxicity (35%), stomatitis (32%), and edema (28%). The most common Grade 3 or 4 laboratory abnormalities (≥ 2%) were

decreased lymphocytes (26%), decreased potassium (9%), decreased hemoglobin (6%), increased alanine aminotransferase (4.9%), decreased albumin (4.9%), decreased sodium (4.9%), increased aspartate aminotransferase (3.9%) and decreased white blood cells (2%).

Serious adverse reactions occurred in 39% of patients. Serious adverse reactions in ≥2% of patients included pneumonia (8%), hemorrhage (4.9%), dysphagia (2.9%), pneumothorax (2.9%), anemia (2%), dyspnea (2%), fatigue (2%), hepatic enzyme increased (2%), and ILD/pneumonitis (2%). Fatal adverse events occurred in 6% of patients who received RYBREVANT FASPRO including sudden death (2%), myocardial ischemia, tumor hemorrhage, aspiration pneumonia, and ILD/pneumonitis (1%, 1 patient each).

RYBREVANT with LAZCLUZE

In MARIPOSA (n=421), the most common adverse reactions (ARs) (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (IRR) (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%).

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%).

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 read full Prescribing Information for **RYBREVANT FASPRO**, **RYBREVANT**, and

LAZCLUZE.

cp-606850v1

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.innovativemedicine.jnj.com**. Follow us at **@JNJInnovMed**.

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-based regimens. 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 **www.sec.gov**, **www.jnj.com**, **www.investor.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.

*Barbara Burtness, M.D. has served as a consultant to Johnson & Johnson; she 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.

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