

# RYBREVANT(TM) (amivantamab-vmjw) Receives FDA Approval as the First Targeted Treatment for Patients with Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations

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United States

RYBREVANT™ is the first fully-human, bispecific antibody approved in lung cancer

Simultaneous FDA approval of a companion diagnostic aids in the identification of exon 20 insertion mutations

May 21, 2021 (HORSHAM, P.A.) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the U.S. Food and Drug Administration (FDA) has granted the accelerated approval of RYBREVANT™ (amivantamab-vmjw) for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.<sup>[1]</sup> RYBREVANT™ is the first fully-human, bispecific antibody approved for the treatment of patients with NSCLC that targets EGFR exon 20 insertion mutations, which are the third most prevalent activating EGFR mutation.<sup>1</sup><sup>[2]</sup> Today's approval follows the FDA's decision to grant Breakthrough Therapy Designation (BTD) in March 2020 and to initiate a Priority Review of the Biologics License Application (BLA) in December 2020. This indication is approved under accelerated approval based on overall response rate and duration of response.<sup>1</sup> Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.<sup>1</sup>

"Today's FDA approval is an important development for people living with non-small cell lung cancer with exon 20 insertion mutations who, until now, have had no approved treatment options to target their disease," said Jill Feldman, co-founder of the EGFR Resisters, an advocacy organization patient group, and a lung cancer patient advocate. "We are excited by the promise this new treatment option brings to people with this particular type of lung cancer and their families."

Lung cancer is the leading cause of cancer death among both men and women, accounting for almost 25 percent of all cancer deaths.<sup>[3]</sup> Currently available targeted treatments, like EGFR tyrosine kinase inhibitors (TKI) are generally insensitive in treating NSCLC driven by EGFR exon 20 insertion mutations and are not FDA-approved for these patients.<sup>[4]</sup><sup>[5]</sup><sup>[6]</sup> In addition, NSCLC driven by this mutation carries a worse prognosis and shorter survival rates compared with lung cancer driven by more common EGFR mutations, such as exon 19 deletions and L858R substitutions.<sup>[7]</sup><sup>[8]</sup> Patients newly diagnosed with metastatic NSCLC with EGFR exon 20 insertion mutations have a real-world median overall survival (OS) of 16.2 months (95 percent confidence interval [CI], 11.0 – 19.4), which is lower than patients with EGFR exon 19 deletions/L858R mutations, who have a real-world median OS of 25.5 months (95 percent CI, 24.5 – 27.0).<sup>[9]</sup>

"Lung cancer is a complex disease, and through the study and deeper understanding of genetic alterations like EGFR exon 20 insertion mutations, we are able to target the disease in new ways and improve treatment outcomes for patients," said Joshua K. Sabari, M.D., New York University Langone's Perlmutter Cancer Center and study investigator, who presented the latest clinical trial results at the International Association for the Study of Lung Cancer's (IASLC WCLC) 2020 World Conference on Lung Cancer Singapore. "Amivantamab-vmjw is an innovative bispecific antibody that brings an important new therapeutic approach to physicians caring for patients with this serious and rare type of lung cancer."

RYBREVANT™ is a fully-human bispecific antibody directed against EGFR and MET receptors.<sup>1</sup> RYBREVANT™ binds extracellularly (outside of the cell) inhibiting tumor growth and leading to tumor cell death.<sup>1</sup> Today's accelerated FDA approval is based on positive results from the Phase 1 CHRYSALIS study, a multicenter, open-label, clinical study evaluating RYBREVANT™ as a monotherapy in patients enrolled in the prior platinum containing chemotherapy cohort.<sup>1</sup><sup>[10]</sup> Initial results from the CHRYSALIS EGFR exon 20 insertion mutation population, which supported the BTD, were [presented](#) at the American Society of Clinical Oncology 2020 Virtual Scientific Program, and updated results were [presented](#) at the IASLC WCLC 2020.

"The approval of RYBREVANT, along with the companion diagnostic test, addresses high unmet need in the treatment of people with genetically defined non-small cell lung cancer," said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. "At Janssen, we are committed to the development of innovative therapies like RYBREVANT and believe that advancing medicines targeting specific pathways can bring the greatest benefits and improve outcomes for patients with tumor alterations such as EGFR and MET."

The FDA simultaneously approved Guardant Health's Guardant360® CDx liquid biopsy blood test as a companion diagnostic for use with RYBREVANT™.

Next-generation sequencing tests offer an alternative to polymerase chain reaction (PCR)-based tests which fail to identify 50 percent or more of exon 20 insertion mutations.<sup>[11]</sup> Information on FDA-approved tests for the detection of EGFR genetic alterations in NSCLC is available at: <http://www.fda.gov/CompanionDiagnostics>.

"Today's milestone reflects progress and determination in our mission to develop and deliver transformational therapies to improve the lives of people diagnosed with some of the most devastating and complex diseases of our time," said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, Johnson & Johnson. "The approval of RYBREVANT, the first lung cancer treatment for Johnson & Johnson, strengthens our commitment to harness science, expertise and scale to dramatically alter the trajectory of lung cancer, and reduce the impact of the world's leading cause of cancer mortality."


[Janssen's COVID-19 Vaccine Status >](#)

combination with carboplatin-pemetrexed for people with advanced or metastatic EGFR-mutated NSCLC with exon 20 insertion mutations.<sup>[13]</sup> RYBREVANT™<sup>1</sup> received U.S. FDA BTB in March 2020 and Priority Review Designation following the BLA [announcement](#) in December 2020.<sup>[14]</sup><sup>[15]</sup> Janssen has filed regulatory submissions for RYBREVANT™ with health authorities in [Europe](#) and other markets.

\*\*In 2018, Janssen Biotech, Inc. entered into a license and collaboration agreement with Yuhua Corporation for the development of lazertinib.

#### About the CHRYSALIS Study

CHRYSALIS ([NCT02609776](#)) is a Phase 1 open-label, multicenter, first-in-human study to evaluate the safety, pharmacokinetics and preliminary efficacy of RYBREVANT™ as a monotherapy and in combinations including with lazertinib, a novel third-generation EGFR TKI<sup>[16]</sup>, in adults with advanced NSCLC.<sup>10</sup> The study consists of two parts: RYBREVANT™ monotherapy and combination-dose escalations and RYBREVANT™ monotherapy and combination-dose expansions.<sup>10</sup>

In the ongoing Phase 1 CHRYSALIS study, patients with locally advanced or metastatic NSCLC with EGFR Exon 20 insertion mutations weighing less than 80 kg received RYBREVANT™ 1050 mg and patients weighing at least 80 kg or more received RYBREVANT™ 1400 mg weekly for four weeks, with the initial dose as a split infusion in week 1 on day 1 and day 2, then administered every two weeks thereafter until disease progression or unacceptable toxicity.<sup>1</sup> Disease response using overall response rate (ORR), per Response Evaluation Criteria in Solid Tumors Version 1.1\* (RECIST v1.1) as evaluated by Blinded Independent Central Review (BICR), was the primary endpoint.<sup>1</sup> In the prior-platinum chemotherapy treated cohort (n=81), the confirmed ORR, as assessed by blinded independent central review, was 40 percent (95 percent CI, 29 – 51), with 3.7 percent having complete responses (CR) and 36 percent achieving partial responses (PR).<sup>1</sup>

Permanent discontinuation of RYBREVANT™ due to an adverse reaction (AE) occurred in 11 percent of patients who received RYBREVANT™.<sup>1</sup> AEs resulting in permanent discontinuation of RYBREVANT™ in greater than or equal to one percent of patients were pneumonia, infusion-related reactions (IRR), pneumonitis/interstitial lung disease (ILD) dyspnea, pleural effusion and rash.<sup>1</sup> Dose interruptions of RYBREVANT™ due to AEs occurred in 78 percent of patients.<sup>1</sup> IRR requiring infusions interruptions occurred in 59 percent of patients.<sup>1</sup> Adverse reactions requiring dose interruption in greater than or equal to five percent of patients included dyspnea, nausea, rash, vomiting, fatigue and diarrhea.<sup>1</sup> The most common AEs (greater than or equal to 20 percent) in patients who received RYBREVANT™ were rash (84 percent), IRR (64 percent), paronychia (50 percent), musculoskeletal pain (47 percent), dyspnea (37 percent), nausea (36 percent), fatigue (33 percent), edema (27 percent), stomatitis (26 percent), cough (25 percent), constipation (23 percent) and vomiting (22 percent).<sup>1</sup>

\*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.<sup>[17]</sup>

#### Access to RYBREVANT™ (amivantamab-vmjw)

Janssen offers comprehensive access and support information and resources to assist patients in gaining access to RYBREVANT™. Janssen will work closely with payers and providers to ensure RYBREVANT™ is broadly accessible and affordable for people with NSCLC with EGFR exon 20 insertion mutations. Our comprehensive patient support program, Janssen CarePath, helps patients get started on RYBREVANT™ and stay on track. Janssen CarePath helps verify insurance coverage for patients, provides reimbursement information, helps find financial assistance options for eligible patients and provides ongoing support to help patients start and stay on RYBREVANT™. If patients have commercial or private health insurance and need help paying for RYBREVANT™, the Janssen CarePath Savings Program may be able to help. For more information, visit [Rybrevant.JanssenCarePathSavings.com](#). If patients don't have commercial or private health insurance, Janssen CarePath can provide information about other resources that may help with out-of-pocket medication costs. Learn more at [JanssenCarePath.com/Rybrevant](#) or call a Janssen CarePath Care Coordinator at 833-RYBREVANT (833-792-7382).

#### About Non-Small Cell Lung Cancer (NSCLC)

Worldwide, lung cancer is one of the most common cancers, and NSCLC makes up 80 to 85 percent of all lung cancers.<sup>[18]</sup><sup>[19]</sup> The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.<sup>19</sup> Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor [tyrosine kinase](#) supporting cell growth and division.<sup>8</sup> EGFR mutations are present in 10 to 15 percent<sup>8,11</sup><sup>[20]</sup><sup>[21]</sup><sup>[22]</sup> of people with NSCLC adenocarcinoma and occur in 40 to 50 percent of Asians.<sup>[23]</sup><sup>[24]</sup> The five-year survival rate for all people with metastatic NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.<sup>[25]</sup><sup>[26]</sup> EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.<sup>2</sup> Patients with EGFR exon 20 insertion mutations have a real-world five-year OS of 8 percent in the frontline setting, which is worse than patients with EGFR exon 19 deletions or L858R mutations, who have a real-world five-year OS of 19 percent.<sup>9</sup>

#### RYBREVANT™ IMPORTANT SAFETY INFORMATION<sup>1</sup>

##### WARNINGS AND PRECAUTIONS

##### Infusion Related Reactions<sup>1</sup>

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

Based on the safety population, IRR occurred in 66% of patients treated with RYBREVANT™. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR,

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Week 2. Monitor patients for any signs and symptoms of infusion reactions during RYBREVANT™ infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT™ based on severity.

#### Interstitial Lung Disease/Pneumonitis<sup>1</sup>

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

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

#### Dermatologic Adverse Reactions<sup>1</sup>

RYBREVANT™ can cause rash (including dermatitis acneiform), pruritus and dry skin. Based on the safety population, rash occurred in 74% of patients treated with RYBREVANT™, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose reduction occurred in 5% of patients, and RYBREVANT™ was permanently discontinued due to rash in 0.7% of patients.

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

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

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

#### Ocular Toxicity<sup>1</sup>

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

#### Embryo Fetal Toxicity<sup>1</sup>

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

#### Adverse Reactions<sup>1</sup>

The most common adverse reactions (≥20%) were rash, IRR, paronychia, musculoskeletal pain, dyspnea, nausea, fatigue, edema, stomatitis, cough, constipation, and vomiting. The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased albumin, decreased phosphate, decreased potassium, increased alkaline phosphatase, increased glucose, increased gamma-glutamyl transferase, and decreased sodium.

Please read full [Prescribing Information](#) for RYBREVANT™.

#### About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology and Pulmonary Hypertension.

Learn more at [www.janssen.com](http://www.janssen.com). Follow us at [www.twitter.com/JanssenGlobal](https://www.twitter.com/JanssenGlobal) and [www.twitter.com/JanssenUS](https://www.twitter.com/JanssenUS). Janssen Biotech, Inc. and Janssen Research & Development LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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\*Dr. Sabari has served as a consultant to Janssen; he has not been paid for any media work.

*Cautions Concerning Forward-Looking Statements*

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 January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at [www.sec.gov](http://www.sec.gov), [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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