Rybrevant® (amivantamab-vmjw) – New indication, accelerated approval converted to full approval

- On March 1, 2024, Johnson & Johnson announced the FDA approval of Rybrevant (amivantamab-vmjw), in combination with carboplatin and pemetrexed, for the first-line 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.

- In addition to the new indication, the FDA converted the accelerated approval of Rybrevant as a single agent to a full approval 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.

- The approval of Rybrevant for the new indication was based on PAPILLON, a randomized, open-label study in 308 patients with previously untreated locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Patients were randomized to receive Rybrevant in combination with carboplatin and pemetrexed or carboplatin and pemetrexed. The primary outcome measure was progression-free survival (PFS). Additional outcome measures included overall response rate (ORR), duration of response (DOR) and overall survival (OS).

    - Median PFS was 11.4 months for Rybrevant + carboplatin + pemetrexed and 6.7 months for carboplatin + pemetrexed (hazard ratio 0.40, 95% CI: 0.30, 0.53; $p < 0.0001$).
    - ORR was 67% (95% CI: 59, 75) for Rybrevant + carboplatin + pemetrexed and 36% (95% CI: 29, 44) for carboplatin + pemetrexed.
    - Median DOR was 10.1 months (95% CI: 8.5, 13.9) for Rybrevant + carboplatin + pemetrexed and 5.6 months (95% CI: 4.4, 6.9) for carboplatin + pemetrexed.
    - While OS results were immature at the current analysis, with 44% of pre-specified deaths for the final analysis reported, no trend towards a detriment was observed. Seventy-five (48%) of the treated patients crossed over from the carboplatin and pemetrexed arm after confirmation of disease progression to receive Rybrevant as a single agent.

- The most common adverse reactions (≥ 20%) with Rybrevant use, when used in combination with carboplatin and pemetrexed, were rash, nail toxicity, stomatitis, infusion-related reaction, fatigue, edema, constipation, decreased appetite, nausea, COVID-19, diarrhea, and vomiting.

- The most common grade 3 or 4 laboratory abnormalities (≥ 2%) were decreased albumin, increased alanine aminotransferase, increased gamma-glutamyl transferase, decreased sodium, decreased potassium, decreased magnesium, and decreases in white blood cells, hemoglobin, neutrophils, platelets, and lymphocytes.

- Refer to the Rybrevant drug label for complete dosing and administration recommendations for first-line treatment and previously treated NSCLC.