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First-In-Class Vorasidenib Among Bumper Crop Of New EU Filings

by Neena Brizmohun

Twelve new drugs are now being reviewed for potential EU marketing approval, including Servier's vorasidenib for IDH-mutant diffuse glioma, which the company says could become the first targeted therapy for the malignant and incurable brain tumor.

Vorasidenib, *Servier*'s investigational targeted therapy for patients with the malignant and incurable brain tumor, IDH-mutant diffuse glioma, is among a raft of new products that the European Medicines Agency has started reviewing for potential pan-EU marketing approval.

The EU marketing authorization application (MAA) for the first-in-class drug is being reviewed under the EMA's accelerated assessment procedure. A filing for US marketing approval has also been accepted for priority review by the Food and Drug Administration.

Vorasidenib, an orphan drug, is among 12 new entries on the EMA's latest monthly list of products for which MAAs are currently under review. The *list*, published on 12 February, contains data extracted on 6 February.

Acoramidis, from *AstraZeneca*/*BridgeBio Pharma*, *J&J Innovative Medicine*'s lazertinib, *Regeneron Pharmaceuticals*' linvoseltamab, *Galderma*/*Chugai Pharmaceutical*'s nemolizumab and *Pfizer*'s tisotumab vedotin are also new entrants on the list, as is AO Pharma's diflunisal.

The remaining new products are biosimilar, generic or hybrid drugs – pegfilgrastim, trastuzumab, trabectedin, and two dimethyl fumarate products.

The EMA began reviewing the MAAs for the 12 products a few weeks ago. While vorasidenib's application is being evaluated under the accelerated assessment pathway, the others are being reviewed under the standard EU centralized drug evaluation timeline, which usually takes around

a year to complete.

Accelerated assessments are reserved for drugs that the agency considers are of potential major public health interest, particularly from the point of view of therapeutic innovation. They can cut months off the standard review timeline.

Regarding the new products on the EMA's list:

- Vorasidenib is Servier's oral, selective, highly brain-penetrant dual inhibitor of mutant IDH1/2 (isocitrate dehydrogenase 1 and 2) enzymes for the treatment of IDH-mutant diffuse glioma. If approved, the drug would be the first targeted therapy in IDH-mutant diffuse glioma, the company said, noting that "in the realm of glioma treatment, innovation has been stagnant for nearly a quarter-century." In clinical studies, vorasidenib has demonstrated strong blood-brain barrier penetration alongside clinically meaningful and statistically significant improvements in progression-free survival and time to next intervention, Servier said. In the US, the FDA is expected to make a decision on whether the drug should be approved on 20 August.

- Acoramidis, an orphan drug, is AstraZeneca/BridgeBio's investigational treatment for patients with transthyretin amyloid cardiomyopathy. It is a next-generation, oral, highly potent small molecule stabilizer of transthyretin, designed to achieve maximal stabilization and preserve native TTR, said AstraZeneca. A marketing application for Acoramidis has also been filed in the US, where the FDA has set an action date of 29 November. Additional global regulatory submissions are planned, including in Japan.

- Lazertinib is J&J's drug for use in combination with the company's Rybrevant (amivantamab) for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with common epidermal growth factor receptor (EGFR) mutations including exon 19 deletions (ex19del) or exon 21 L858R (L858R) substitution mutations. Lazertinib is an oral, third-generation, brain-penetrant EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR. In the US, the company said last December that it had filed an application seeking the approval of lazertinib in combination with Rybrevant for the first-line treatment of EGFR-mutated NSCLC.

- Linvoseltamab is Regeneron's investigational treatment for adult patients with relapsed/refractory multiple myeloma who have progressed after at least three prior therapies. The bispecific antibody is designed to bridge B-cell maturation antigen on multiple myeloma cells with CD3-expressing T cells to facilitate T-cell activation and cancer-cell killing. In the US, a marketing application for linvoseltamab was submitted to the FDA last December.

- Nemolizumab is Galderma/Chugai's subcutaneously administered treatment for prurigo nodularis and for adolescents and adults with moderate to severe atopic dermatitis. The first-in-class monoclonal antibody is being designed to inhibit IL-31 signaling to provide safe and rapid relief from itching, which the company noted was the most burdensome symptom of both skin conditions. In the US, Galderma this month said its marketing application for nemolizumab was under review by the FDA for both indications and that the agency had granted priority review for the prurigo nodularis indication. It added that multiple regulatory submissions were planned in 2024. Nemolizumab was initially developed by Chugai, and subsequently licensed to Galderma in 2016 worldwide, except Japan and Taiwan. In Japan, nemolizumab is approved for the treatment of pruritus associated with atopic dermatitis and is in development for prurigo nodularis.

- Tisotumab vedotin is Pfizer'santibody-drug conjugate (ADC) for treating adult patients with recurrent or metastatic cervical cancer with disease progression on or after first-line therapy. If approved, the drug would be the first ADC granted EU marketing authorization for cervical cancer, the company said. In the US, the FDA granted tisotumab vedotin (brand name Tivdak) accelerated approval in September 2021 for recurrent or metastatic cervical cancer. A supplemental biologics license application seeking to convert the accelerated approval to a full approval was granted priority review by the agency, with an action date of 9 May 2024.

- Diflunisal is AO Pharma's treatment for transthyretin amyloidosis (ATTR). While diflunisal has been used for many years for pain relief, AO Pharma has received orphan drug status to use the drug for ATTR amyloidosis.

- Pegfilgrastim is for the treatment of neutropenia in pediatric patients. The drug is being reviewed under the EMA's pediatric-use marketing authorization (PUMA) pathway, which offers incentives such as eight plus two years of data and market protection for approved products.

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- Trastuzumab is for the treatment of metastatic and early breast cancer.

- Trabectedin is an antineoplastic medicine for soft tissue sarcoma and relapsed platinum-sensitive ovarian cancer.

- The two dimethyl fumarate products are immunosuppressants.