Pierre Fabre Laboratories receives CHMP positive opinion for BRAFTOVI® (encorafenib) in combination with cetuximab and FOLFOX (fluorouracil, leucovorin, and oxaliplatin) for the first-line treatment of adult patients with *BRAF*^{V600E}–mutant metastatic colorectal cancer (mCRC)

- *This positive CHMP opinion is based on results from the Phase 3 BREAKWATER trial, which showed that encorafenib in combination with cetuximab and mFOLFOX6 demonstrated a statistically significant improvement in the dual primary endpoints of objective response rate (ORR) and progression-free survival (PFS), and a significant overall survival (OS) benefit, reducing the risk of death by 51% vs chemotherapy with or without bevacizumab*
- *The European Commission decision is expected later this year. If approved, the regimen will be the first and only combination with BRAF-targeted therapy approved for the first-line treatment of adult patients with BRAF^{V600E}-mutant metastatic colorectal cancer*

Castres, France, May 22, 2026 – Pierre Fabre Laboratories announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending the approval of BRAFTOVI® (encorafenib) in combination with cetuximab and FOLFOX for the first-line treatment of adult patients with *BRAF*^{V600E}–mutant metastatic colorectal cancer (mCRC). The positive opinion will be submitted to the European Commission (EC) with a decision on EU marketing authorisation expected later this year.

Eric Ducournau, Chief Executive Officer, Pierre Fabre Laboratories said: "Today's positive CHMP opinion marks an important step towards a targeted approach for patients with *BRAF*^{V600E}–mutant metastatic colorectal cancer. If approved, it would be the only approved targeted therapy in the EU for this patient population in the first-line setting. This milestone reflects Pierre Fabre Laboratories' commitment to advancing meaningful innovation in oncology and to working in close partnership with the scientific and medical community to address areas of high unmet need."

The CHMP positive opinion is based on results from the Phase 3 BREAKWATER trial which assessed the efficacy and safety of BRAFTOVI® in combination with cetuximab and mFOLFOX6 in patients with previously untreated *BRAF*^{V600E}–mutant mCRC, compared with oxaliplatin-based chemotherapy, with or without bevacizumab.

The regimen of BRAFTOVI® in combination with cetuximab and mFOLFOX6 showed a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared with chemotherapy with or without bevacizumab (median PFS 12.8 vs. 7.1 months; hazard ratio [HR] 0.53; 95% confidence interval [CI], 0.41 to 0.68; P<0.001), and demonstrated a statistically significant improvement in the dual primary endpoint of ORR in

the primary analysis set (60.9% vs. 40.0%; odds ratio 2.44; P<0.001). A confirmed objective response was observed in 65.7% of patients (95% CI, 59.4 to 71.4) compared to 37.4% (95% CI, 31.6 to 43.7) in the chemotherapy with or without bevacizumab group in the overall population. In an interim analysis, the BRAFTOVI® regimen demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS) compared with chemotherapy with or without bevacizumab (median, 30.3 vs. 15.1 months; HR 0.49; 95% CI, 0.38 to 0.63; P<0.001), reducing the risk of death by 51%.[1,2]

The most frequent treatment-related adverse events (TRAEs) in the BRAFTOVI® in combination with cetuximab and mFOLFOX6 group were nausea (53.9%), anemia (46.1%), diarrhea (41.8%), decreased appetite (37.5%), vomiting (36.2%), decreased neutrophil count (34.1%), arthralgia (31.5%), and rash (30.2%). TRAEs of grade 3 or 4 occurred in 81.5%, and grade 5 in 4.3%. Safety profiles were consistent with those known for each agent.[1]

In February 2026, Pfizer Inc. received full approval from the U.S. FDA for BRAFTOVI® in combination with cetuximab and fluorouracil-based chemotherapy, for the treatment of adult patients with mCRC with a *BRAF*^{V600E} mutation, as detected by an FDA authorised test.

BRAFTOVI® in combination with cetuximab was approved by the EC in 2020 for the treatment of adults with *BRAF*^{V600E}–mutated mCRC who had received prior systemic therapy, supported by results from the randomised, active-controlled, open-label, multi-centre Phase III BEACON CRC trial.

About Colorectal Cancer (CRC)

Worldwide, CRC is the third most common type of cancer with an estimated 1.9 million new cases in 2022[3,4]. In 2022, CRC was responsible for approximately 904,000 deaths globally.[5] In Europe, it is the second most common cancer with more than 500,000 European citizens diagnosed every year.[6]

BRAF mutations are estimated to occur in approximately 8–12% of patients with mCRC, with the *BRAF*^{V600E} mutation being the most common. The risk of mortality in CRC patients with the *BRAF*^{V600E} mutation is approximately two times higher than for those with wild-type *BRAF*.[7]

About BREAKWATER

The Phase 3 BREAKWATER trial is an ongoing, open-label, multi-centre, global, randomised trial evaluating BRAFTOVI® plus cetuximab with or without chemotherapy (mFOLFOX6) versus chemotherapy (mFOLFOX6/FOLFOXIRI/CAPOX) with or without bevacizumab, in patients with previously untreated *BRAF*^{V600E}-mutant mCRC (NCT04607421). Pfizer is the sole sponsor of the trial.[8]

Results from BREAKWATER demonstrated the anti-tumour activity of BRAFTOVI® in combination with cetuximab and mFOLFOX6 compared with chemotherapy with or without bevacizumab.

The dual primary endpoints of PFS and objective response rate (ORR) were met, as assessed by blinded independent central review (BICR), as well as OS, a key secondary endpoint.[Erreur ! Signet non défini.,2]

Key eligibility criteria included:[8]

- A histologically or cytologically confirmed diagnosis of stage IV CRC that has a *BRAF*^{V600E} mutation
- Treatment-naïve metastatic patients

About BRAFTOVI® (encorafenib)

BRAFTOVI® is an orally administered kinase inhibitor designed to selectively target the *BRAF*^{V600E} mutation. Dysregulation of the MAPK signalling pathway (RAS-RAF-MEK-ERK) has been implicated in the development of several cancers, including CRC.

In Europe, BRAFTOVI® is approved for use in combination regimens across multiple tumour types driven by *BRAF*^{V600} mutations: in combination with binimetinib for the treatment of adult patients with unresectable or metastatic melanoma; in combination with binimetinib for adult patients with advanced NSCLC with a *BRAF*^{V600E} mutation; and in combination with cetuximab for adult patients with *BRAF*^{V600E}–mutant mCRC who have received prior systemic therapy.[9]

Pfizer holds exclusive commercialisation rights for BRAFTOVI® across the U.S., Canada, Latin America, the Middle East, and Africa. In Japan and South Korea, the product is marketed by Ono Pharmaceutical Co., Ltd. Medison is responsible for commercialisation in Israel, while Pierre Fabre Laboratories oversees availability in Europe, Asia (excluding Japan and South Korea), and other global markets.

About Pierre Fabre Laboratories

Pierre Fabre Laboratories is one of Europe's leading pharmaceutical laboratories and the world's second-largest dermo-cosmetics company. Its Pharma activity covers 5 main therapeutic fields: oncology, dermatology, rare diseases, primary care and family health care. The Dermo-cosmetics & Personal Care portfolio includes international brands such as Eau Thermale,Avène, Ducray, Klorane, A-Derma, René Furterer, Même Cosmetics, Darrow and Elgydium.

For over 40 years, Pierre Fabre Laboratories has established itself as an international player in oncology, mastering the entire value chain from R&D to marketing. Its portfolio of oncology specialties covers colorectal, breast, lung and skin cancers, as well as certain hematologic malignancies and precancerous dermatological conditions such as actinic keratosis. In 2025, Pierre Fabre Laboratories' revenues in oncology came to 565 million euros, 71% of which were generated by international sales, out of a total sales figure of 3.2 billion euros.

Based in southwest France since its creation, Pierre Fabre Laboratories manufactures nearly 90% of its products in France and employs 10,000 people worldwide. In 2025, its R&D budget amounted to 250 million euros, of which 67% is allocated to targeted therapies in oncology with 10 research and development programs underway.

Pierre Fabre Laboratories' majority shareholder (86%) is an eponymous humanitarian Foundation. Employees constitute the company's other shareholder. This capital structure guarantees the company's independence, long-term vision and contribution to the common good. The dividends paid to the Pierre Fabre Foundation contribute to 35 healthcare-access programs deployed in 22 of the least developed countries in the world.

Pierre Fabre Laboratories' CSR policy has been assessed by AFNOR Certification and has been awarded the "Exemplary" level of its CSR label (ISO 26 000 standard for sustainable development).

For more information, visit www.pierre-fabre.com, @Laboratoires Pierre Fabre, @Pierre Fabre Oncology

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