Tempest Receives Orphan Drug Designation from the European Medicines Agency for Amezalpat for the Treatment of Patients with HCC

June 5, 2025

- *EMA Orphan Drug Designation (ODD) builds on U.S. Food & Drug Administration (FDA) ODD and Fast Track Designation, underscoring the urgent need for new treatment options*
- *The multiple regulatory designations were granted following strong positive results from a global randomized Phase 1b/2 study in first-line HCC demonstrating superior outcomes for amezalpat combination therapy across multiple study endpoints, including overall survival in both the entire population and key subpopulations, when compared to standard of care alone*

BRISBANE, Calif., June 05, 2025 (GLOBE NEWSWIRE) -- Tempest Therapeutics, Inc. (Nasdaq: TPST), a clinical-stage biotechnology company with a pipeline of first-in-class[1] targeted and immune-mediated therapeutics to fight cancer, today announced that the European Medicines Agency (EMA) has granted Orphan Drug Designation (ODD) to amezalpat (TPST-1120), an oral, small molecule, selective PPARα antagonist for the treatment of patients with hepatocellular carcinoma (HCC).

“We’re incredibly pleased to receive Orphan Drug Designation from the EMA, building on the momentum of regulatory support we've already received from the FDA,” said Stephen Brady, president and chief executive officer of Tempest. “These designations reflect the significant unmet need in liver cancer and reinforce our belief in the potential of amezalpat to make a meaningful difference for patients and families affected by this devastating disease.”

The company announced earlier this year that the FDA had granted both ODD and Fast Track Designation (FTD) to amezalpat to treat patients with HCC. These three designations follow positive data across multiple key study efficacy and safety endpoints from a global, randomized Phase 1b/2 clinical study evaluating amezalpat plus standard-of-care atezolizumab and bevacizumab versus atezolizumab and bevacizumab alone in the first-line treatment of patients with unresectable or metastatic HCC. Notable positive outcomes of the randomized comparison include a six-month improvement in median overall survival (OS) with a hazard ratio (HR) of 0.65 for patients receiving the amezalpat combination therapy. In addition, a survival benefit from patients receiving amezalpat was preserved in key sub-populations including PD-L1 negative disease, which is consistent with amezalpat’s proposed mechanism of action to target both the tumor cells directly and the patient’s immune system.

About Hepatocellular Carcinoma

HCC is an aggressive cancer with rising mortality and is projected to become the third leading cause of cancer death by 2030.[2] Every year, more than 900,000 people worldwide are diagnosed with HCC.[3] Incidence and mortality are highest in East Asia and are increasing in parts of Europe and the US.[4] In the US, HCC represents the fastest-rising cause of cancer-related death.[3]

Nine out of ten cases of HCC are caused by chronic liver disease, which includes chronic hepatitis B and C infection, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), alcohol-related liver disease (ALD) and cirrhosis resulting from these conditions.[5]

Even if diagnosed in the early stage, an estimated 70-80% of people with early-stage HCC experience disease recurrence following surgery.[6] Early recurrence is associated with poorer prognosis and shorter survival.[5,7] Tumor size, number of tumors, and portal vein invasion are associated with an increased risk of recurrence.[6]

About Amezalpat

Amezalpat is an oral, small molecule, selective PPARα antagonist. Data suggest that amezalpat treats cancer by targeting tumor cells directly and by modulating immune suppressive cells and angiogenesis in the tumor microenvironment. In a global randomized Phase 1b/2 study of amezalpat in combination with atezolizumab and bevacizumab in first-line patients with advanced HCC, the amezalpat arm showed clinical superiority across multiple study endpoints, including overall survival in both the entire population and key subpopulations, when compared to atezolizumab and bevacizumab alone, the standard of care. These randomized data were supported by additional positive results observed in the Phase 1 clinical trial in patients with heavily pretreated advanced solid tumors, including renal cell carcinoma and cholangiocarcinoma.

About Orphan Drug Designation

Orphan Designation is granted to therapies intended for the treatment, prevention, or diagnosis of life-threatening or chronically debilitating diseases that affect no more than two in 10,000 people in the European Union (EU) and for which no satisfactory therapy is available. The treatment must also provide significant benefit to those affected by the condition. EMA orphan drug designation provides certain benefits, including the potential for 10 years of market exclusivity following regulatory approval in the EU, reduction in regulatory fees and a centralized EU approval process.[8]

About Tempest Therapeutics

Tempest Therapeutics is a clinical-stage biotechnology company advancing a diverse portfolio of small molecule product candidates containing tumor-targeted and/or immune-mediated mechanisms with the potential to treat a wide range of tumors. The company’s novel programs range from early research to later-stage investigation in a randomized global study in first-line cancer patients. Tempest is headquartered in Brisbane, California. More

information about Tempest can be found on the company's website at www.tempesttx.com.

Investor & Media Contacts:

Sylvia Wheeler
Wheelhouse Life Science Advisors
swheeler@wheelhouselsa.com

Aljanae Reynolds
Wheelhouse Life Science Advisors
areynolds@wheelhouselsa.com

---

[1] If approved by the FDA

[2] Rahib, L. et al. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. *Cancer Res.* 74, 2913-2921 (2014).

[3] World Health Organization. Liver Cancer Factsheet. Globocan. 2020. Available at: https://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf. Last accessed: April 2023.

[4] Llovet, J. M., Kelley, R. K., Villanueva, A., et al. Hepatocellular carcinoma. Nature Reviews Disease Primers. 2021, 7(1), 6.

[5] Office for Health Improvement & Disparities. Liver disease profiles: November 2021 update. Available at: https://www.gov.uk/government/statistics/liver-disease-profiles-november-2021-update/liver-disease-profiles-november-2021-update. Last accessed: April 2023.

[6] Hack SP, Spahn J, Chen M et al. IMbrave 050: a Phase III trial of atezolizumab plus bevacizumab in high-risk hepatocellular carcinoma after curative resection or ablation. Future Oncology. 2020 May;16(15):975-989.

[7] Saito A, Toyoda H, Kobayashi M et al. Prediction of early recurrence of hepatocellular carcinoma after resection using digital pathology images assessed by machine learning. Modern Pathology. 2021. 34, 417-425.

[8] European Medicines Agency, "Orphan Designation." https://www.ema.europa.eu/en/human-regulatory-overview/orphan-designation-overview