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Incyte Announces the European Commission Approval of Pemazyre® (pemigatinib) as a Treatment for Adults with Locally Advanced or Metastatic Cholangiocarcinoma with a Fibroblast Growth Factor Receptor 2 (FGFR2) Fusion or Rearrangement

- Pemazyre is the first targeted therapy approved in the EU for this indication

WILMINGTON, Del.--(BUSINESS WIRE)-- Incyte (Nasdaq:INCY) today announced that the European Commission (EC) has approved Pemazyre® (pemigatinib) for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy. The decision follows the positive opinion received from the European Medicines Agency's Committee for Medicinal Products for Human Use in January 2021 recommending the conditional marketing authorization of Pemazyre.

"Pemazyre's approval is a crucial milestone for patients with FGFR2 positive cholangiocarcinoma. It is the first new treatment option to be made available to these patients in the EU in over a decade and has demonstrated a high rate of durable responses in a setting where historically there has been no effective standard of care," said Hervé Hoppenot, Chief Executive Officer, Incyte. "We now look forward to working with individual countries in Europe to ensure eligible patients can access this new treatment as soon as possible."

The EC decision is based on data from the **FIGHT-202 study** evaluating the safety and efficacy of Pemazyre in adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with documented FGF/FGFR status. Interim results from FIGHT-202 demonstrated that in patients harboring FGFR2 fusions or rearrangements (Cohort A [108 patients]), Pemazyre monotherapy resulted in an overall response rate (ORR) of 37 percent (primary endpoint) and a median duration of response (DOR) of 8 months (secondary endpoint) based on an independent central radiographic review. Pemazyre was generally well tolerated. Warnings and precautions for Pemazyre

include high and low levels of phosphate in the blood, vision or eye problems, blood creatinine increase and for women who are pregnant, a risk of harm to the fetus.

“The data from the FIGHT-202 study has demonstrated the potential benefits that pemigatinib may have for eligible patients living with cholangiocarcinoma,” said Eric Van Cutsem, M.D., Ph.D., Professor and Division Head of Digestive Oncology, University of Leuven (KUL) and University Hospitals Gasthuisberg, Leuven, Belgium. “Pemazyre offers a much-needed option to eligible patients that have only had few effective treatment options until today.”

Cholangiocarcinoma is a rare cancer that forms in the bile duct. It is classified based on its origin: intrahepatic cholangiocarcinoma occurs in the bile duct inside the liver and extrahepatic cholangiocarcinoma occurs in the bile duct outside the liver. Patients with cholangiocarcinoma are often diagnosed at a late or advanced stage when the prognosis is poor1,2. In Europe, the incidence of cholangiocarcinoma ranges between 6,000 – 8,0003,4. FGFR2 fusions or rearrangements occur almost exclusively in intrahepatic cholangiocarcinoma, where they are observed in 10-16 percent of patients5,6,7.

“Historically, patients living with advanced cholangiocarcinoma have had very limited treatment options,” said Helen Morement, CEO, AMMF – The Cholangiocarcinoma Charity. “We are encouraged to see new, targeted therapies starting to be approved in Europe, giving hope to those in desperate need of alternatives."

About FIGHT-202

The FIGHT-202 Phase 2, open-label, multicenter study (NCT02924376) is evaluating the safety and efficacy of Pemazyre – a selective fibroblast growth factor receptor (FGFR) inhibitor – in adult (age ≥ 18 years) patients with previously treated, locally advanced or metastatic cholangiocarcinoma with documented FGF/FGFR status.

Patients were enrolled into one of three cohorts – Cohort A (FGFR2 fusions or rearrangements), Cohort B (other FGF/FGFR genetic alterations) or Cohort C (no FGF/FGFR genetic alterations). All patients received 13.5mg Pemazyre orally once daily (QD) on a 21-day cycle (two weeks on/one week off) until radiological disease progression or unacceptable toxicity.

The primary endpoint of FIGHT-202 is overall response rate (ORR) in Cohort A, assessed by independent review per RECIST v1.1. Secondary endpoints include ORR; progression free survival (PFS), overall survival (OS), duration of response (DOR), disease control rate (DCR) and safety in all cohorts.

For more information about FIGHT-202, visit **https://clinicaltrials.gov/ct2/show/NCT02924376**.

About FIGHT

The FIGHT (FIbroblast Growth factor receptor in oncology and Hematology Trials) clinical trial program includes ongoing Phase 2 and 3 studies investigating safety and efficacy of Pemazyre therapy across several FGFR-driven malignancies. Phase 2 monotherapy studies include FIGHT-202, as well as FIGHT-201 investigating Pemazyre in patients with metastatic or surgically unresectable bladder cancer, including with activating FGFR3 mutations or fusions/rearrangements; FIGHT-203 in patients with myeloproliferative neoplasms with activating FGFR1 fusions/rearrangements; FIGHT-207 in patients with previously treated, locally-advanced/metastatic or surgically unresectable solid tumor malignancies harboring activating FGFR mutations or fusions/rearrangements, irrespective of tumor type.

FIGHT-302 is a Phase 3 study investigating Pemazyre as a first-line treatment for patients with cholangiocarcinoma with FGFR2 fusions or rearrangements.

About Pemazyre® (pemigatinib)

Pemazyre is a kinase inhibitor indicated in the United States for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test8. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

In Japan, Pemazyre is approved for the treatment of patients with unresectable biliary tract cancer (BTC) with a fibroblast growth factor receptor 2 (FGFR2) fusion gene, worsening after cancer chemotherapy.

In Europe, Pemazyre is approved for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy.

Pemazyre is a potent, selective, oral inhibitor of FGFR isoforms 1, 2 and 3 which, in preclinical studies, has demonstrated selective pharmacologic activity against cancer cells with FGFR alterations.

Pemazyre is marketed by Incyte in the United States, Europe and Japan. Incyte has granted Innovent Biologics, Inc. rights to develop and commercialize pemigatinib in hematology and oncology in Mainland China, Hong Kong, Macau and Taiwan. Incyte has retained all other rights to develop and commercialize pemigatinib outside of the United States.

Pemazyre is a trademark of Incyte Corporation.

Safety Information from the EU Summary of Product Characteristics (SmPC)

Pemazyre may cause serious adverse reactions. The most common serious adverse reactions were hyponatremia and blood creatinine increase.

The most common adverse reactions were hyperphosphatemia, alopecia, diarrhoea, nail toxicity, fatigue, nausea, dysgeusia, stomatitis, constipation, dry mouth, dry eye, arthralgia, hypophosphatemia, dry skin and palmar-plantar erythrodysaesthesia syndrome.

Prolonged hyperphosphatemia can cause precipitation of calcium-phosphate crystals that can lead to hypocalcemia, soft tissue mineralization, anemia, secondary hyperparathyroidism, muscle cramps, seizure activity, QT interval prolongation and arrhythmias. Soft tissue mineralization, including cutaneous calcification and calcinosis, have been observed with Pemazyre treatment. Recommendations for management of hyperphosphatemia include dietary phosphate restriction, administration of phosphate-lowering therapy and dose modification when required.

Pemazyre can cause serous retinal detachment reactions, which may present with symptoms such as blurred vision, visual floaters or photopsia. Ophthalmological examination, including optical coherence tomography (OCT) should be performed prior to initiation of therapy and every 2 months for the first 6 months of treatment, every 3 months afterwards, and urgently at any time for visual symptoms. For serous retinal detachment reactions, the dose modification guidelines should be followed.

Pemazyre should not be used during pregnancy unless the clinical condition of the women requires treatment with Pemazyre. Patients with cancer cells that have spread into the brain or spinal cord should notify their physician before initiating treatment with Pemazyre.

About Incyte

Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit **Incyte.com** and follow **@Incyte**.

Forward Looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding whether or when Pemazyre might provide a successful treatment option for patients with locally advanced or metastatic cholangiocarcinoma, and the FIGHT clinical trial program, contain predictions,

estimates, and other forward-looking statements.

These forward-looking statements are based on the Company's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials and the ability to enroll subjects in accordance with planned schedules; the effects of the COVID-19 pandemic and measures to address the pandemic on the Company's clinical trials, supply chain and other third-party providers and development and discovery operations; determinations made by European regulatory authorities or other regulatory authorities; the Company's dependence on its relationships with its collaboration partners; the efficacy or safety of the Company's products and the products of the Company's collaboration partners; the acceptance of the Company's products and the products of the Company's collaboration partners in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; greater than expected expenses; expenses relating to litigation or strategic activities; and other risks detailed from time to time in the Company's reports filed with the Securities and Exchange Commission, including its Form 10-K for the quarter ending December 31, 2021. The Company disclaims any intent or obligation to update these forward-looking statements.

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1 Banales JM, et al. Nat Rev Gastroenterol Hepatol. 2016;13:261–280.

2 Uhlig J, et al. Ann Surg Oncol. 2019;26:1993–2000.

3 Kirstein MM, Vogel A. Visc Med 2016; 32: 395-400.

4 Countries factored include: UK, Germany, France, Spain, Italy, Switzerland, Denmark, Finland, Poland and Austria

5 Graham RP, et al. Hum Pathol. 2014;45:1630–1638.

6 Ang C. J. Gastroenterol Hepatol. 2015;30:1116–1122.

7 Ross JS et al. The Oncologist. 2014;19:235–242.

8 Pemazyre(pemigatinib) [Package Insert]. Wilmington, DE: Incyte; 2020.

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