TAIHO ONCOLOGY TAIHO PHARMA

FDA Approves Taiho's LYTGOBI® (futibatinib) Tablets for Previously Treated, Unresectable, Locally Advanced or Metastatic Intrahepatic Cholangiocarcinoma

- *LYTGOBI (pronounced "light-GOH-bee") delivered an objective response rate of 42% and median duration of response of 9.7 months in the primary analysis of the pivotal clinical trial.*
- *LYTGOBI covalently binds to FGFR2 and inhibits the signaling pathway. The other approved FGFR inhibitors are reversible ATP-competitive inhibitors.*
- *LYTGOBI previously received breakthrough, orphan drug and priority review designations from the FDA.*

PRINCETON, N.J., September 30, 2022 – Taiho Oncology, Inc. and Taiho Pharmaceutical Co., Ltd. announced today that the U.S. Food and Drug Administration (FDA) has approved LYTGOBI® tablets for the treatment of adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma (iCCA) harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements.

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).

"LYTGOBI is an effective, well-tolerated therapy for patients with intrahepatic CCA that can be taken orally," said Tim Whitten, President and CEO of Taiho Oncology, Inc. "This approval is an important milestone for patients and may provide hope for improved outcomes. As someone whose family has been impacted by cholangiocarcinoma, I'm acutely aware of the impact this disease can have on the patient and their loved ones."

As a whole, cholangiocarcinoma is an aggressive cancer of the bile ducts and is diagnosed in approximately 8,000 individuals each year in the U.S.[1] This includes both intrahepatic (inside the liver) and extrahepatic (outside the liver) forms of the disease. Approximately 20% of patients diagnosed with CCA have the intrahepatic form of the disease.[2,3] Within this 20%, approximately 10-16% of patients have FGFR2 gene rearrangements, including fusions, which promote tumor proliferation.[4,5,6,7,8] LYTGOBI covalently binds to FGFR2 and inhibits the signaling pathway.[9] The other approved FGFR inhibitors are reversible ATP-competitive inhibitors.[10,11,12]

"LYTGOBI is a key example of the potential of precision medicine in iCCA and represents another advance in the treatment of this rare and challenging disease," said medical oncologist Lipika Goyal, MD, MPhil, of the Massachusetts General Hospital Cancer Center and lead investigator of the pivotal study that led to the approval of LYTGOBI. "I am encouraged that treatment options continue to expand and evolve for this disease through the dedicated efforts of many over several years."

The approval of LYTGOBI is based on the results of the primary analysis of the FOENIX*-CCA2 trial, a global Phase 2 open-label trial evaluating 103 patients with

unresectable, locally advanced or metastatic iCCA harboring FGFR2 gene rearrangements including fusions. In this trial, patients received LYTGOBI orally once daily at a dose of 20mg until disease progression or unacceptable toxicity.

The trial met its primary endpoint with an objective response rate of 42% as measured by independent central review. The median duration of response (DOR) was 9.7 months, with 72% of responses lasting at least six months. The most common (≥20%) adverse reactions were nail toxicity, musculoskeletal pain, constipation, diarrhea, fatigue, dry mouth, alopecia, stomatitis, dry skin, arthralgia, dysgeusia, abdominal pain, dry eye, nausea, decreased appetite, urinary tract infection, palmar-plantar erythrodysesthesia syndrome, and vomiting.

LYTGOBI was discovered by Taiho Oncology's parent company, Taiho Pharmaceutical, which continues to co-develop this product for other potential tumor types. "The Taiho group is working as one to optimize this agent for the patients who are waiting," said Teruhiro Utsugi, Senior Managing Director at Taiho Pharmaceutical.

About LYTGOBI

INDICATION AND USAGE
LYTGOBI is indicated for the treatment of adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements.

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).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Ocular Toxicity:** Retinal Pigment Epithelial Detachment (RPED), which may cause symptoms such as blurred vision, occurred in 9% of 318 patients who received LYTGOBI across clinical trials. The median time to first onset of RPED was 40 days. Perform a comprehensive ophthalmological examination, including optical coherence tomography (OCT) of the macula, prior to initiation of therapy, every 2 months for the first 6 months, and every 3 months thereafter. For onset of visual symptoms, refer patients for ophthalmologic evaluation urgently, with follow-up every 3 weeks until resolution or discontinuation of LYTGOBI. Withhold or reduce the dose of LYTGOBI as recommended. Dry Eye/Corneal Keratitis: Among 318 patients who received LYTGOBI across clinical trials, dry eye occurred in 15% of patients. Treat patients with ocular demulcents as needed.
- **Hyperphosphatemia and Soft Tissue Mineralization:** Hyperphosphatemia, which can cause soft tissue mineralization, calcinosis, nonuremic calciphylaxis, and vascular calcification was reported in 88% of 318 patients treated with LYTGOBI across clinical trials with a median time of onset of 5 days (range 3-117).

Phosphate binders were received by 77% of patients who received LYTGOBI. Monitor for hyperphosphatemia throughout treatment. Initiate a low-phosphate diet and phosphate-lowering therapy when serum phosphate level is ≥5.5 mg/dL; initiate or intensify phosphate-lowering therapy when >7 mg/dL; reduce dose, withhold, or permanently discontinue LYTGOBI based on duration and severity of hyperphosphatemia.

- **Embryo-fetal Toxicity:** LYTGOBI can cause fetal harm. Advise pregnant women of the potential risk to the fetus. Advise female patients of reproductive potential, and males with female partners of reproductive potential, to use effective contraception during treatment with LYTGOBI and for 1 week after the last dose.

ADVERSE REACTIONS

- **Serious adverse reactions** occurred in 39% of patients receiving LYTGOBI, and in ≥2% of patients included pyrexia, gastrointestinal hemorrhage, ascites, musculoskeletal pain, and bile duct obstruction.
- **The most common adverse reactions** (≥20%) were nail toxicity, musculoskeletal pain, constipation, diarrhea, fatigue, dry mouth, alopecia, stomatitis, abdominal pain, dry skin, arthralgia, dysgeusia, dry eye, nausea, decreased appetite, urinary tract infection, palmar-plantar erythrodysesthesia syndrome, and vomiting.
- **The most common laboratory abnormalities** (≥20%) were increased phosphate, increased creatinine, decreased hemoglobin, increased glucose, increased calcium, decreased sodium, decreased phosphate, increased alanine aminotransferase, increased alkaline phosphatase, decreased lymphocytes, increased aspartate aminotransferase, decreased platelets, increased activated partial thromboplastin time, decreased leukocytes, decreased albumin, decreased neutrophils, increased creatine kinase, increased bilirubin, decreased glucose, increased prothrombin international normalized ratio, and decreased potassium.

DRUG INTERACTIONS

- **Dual P-gp and Strong CYP3A Inhibitors:** Avoid concomitant use of drugs that are dual P-gp and strong CYP3A inhibitors.
- **Dual P-gp and Strong CYP3A Inducers:** Avoid concomitant use of drugs that are dual P-gp and strong CYP3A inducers.

USE IN SPECIFIC POPULATIONS

- **Lactation:** Because of the potential for serious adverse reactions from LYTGOBI in breastfed children, advise women not to breastfeed during treatment and for 1 week after the last dose.

Please see accompanying full Prescribing Information for complete details.

For more information, visit http://www.LYTGOBI.com

About Taiho Oncology, Inc.
The mission of Taiho Oncology, Inc. is to improve the lives of patients with cancer, their families and their caregivers. The company specializes in the development of orally

administered anti-cancer agents and markets these medicines for a range of tumor types in the U.S. Taiho Oncology's growing pipeline of antimetabolic and selectively targeted anti-cancer agents is led by a world-class clinical development organization. Taiho Oncology is a subsidiary of Taiho Pharmaceutical Co., Ltd. which is part of Otsuka Holdings Co., Ltd. Taiho Oncology is headquartered in Princeton, New Jersey and oversees its parent company's European and Canadian operations, which are located in Zug, Switzerland and Oakville, Ontario, Canada.

For more information, visit http://www.taihooncology.com

About Taiho Pharmaceutical Co., Ltd.
Taiho Pharmaceutical, a subsidiary of Otsuka Holdings Co., Ltd., is an R&D-driven specialty pharma company with a focus on oncology. Taiho Pharmaceutical also has development programs in allergy and immunology, urology and consumer healthcare products. Our corporate philosophy is simple: "We strive to improve human health and contribute to a society enriched by smiles."

For more information about Taiho Pharmaceutical Co., Ltd., please visit:
https://www.taiho.co.jp/en/

LYTGOBI® is a registered trademark of Taiho Pharmaceutical Co., Ltd.

*FGFR Oral SElective Novel Inhibitor X [across] tumors

###

Taiho Oncology Media Contact:
Judy Kay Moore
Taiho Oncology, Inc.
574-526-2369
jumoore@taihooncology.com
www.taihooncology.com

[1] American Cancer Society. Key statistics for bile duct cancer. https://www.cancer.org/cancer/bile-duct-cancer/about/key-statistics.html#:~:text=Bile%20duct%20cancer%20(cholangiocarcinoma)%20is,diagnosed%20with%20it%20each%20year. Accessed July 2022.
[2] Valle JW et al. Biliary Tract Cancer. Lancet. 2021;397:428-444.
[3] Banales JM et al. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. Nat Rev Gastroenterol Hepatol. 2020;17:557-588.
[4] Arai Y, Totoki Y, Hosoda F, et al. Fibroblast growth factor receptor 2 tyrosine kinase fusions define a unique molecular subtype of cholangiocarcinoma. *Hepatology*. Apr 2014;59(4):1427-34.10.1002/hep.26890.
[5] Javle M, Bekaii-Saab T, Jain A, et al. Biliary cancer: Utility of next-generation sequencing for clinical management. *Cancer*. Dec 15 2016;122(24):3838-3847.10.1002/cncr.30254.
[6] Sia D, Losic B, Moeini A, et al. Massive parallel sequencing uncovers actionable FGFR2-PPHLN1 fusion and ARAF mutations in intrahepatic cholangiocarcinoma. *Nat Commun*. Jan 22 2015;6:6087.10.1038/ncomms7087.

[7] Silverman IM, Murugesan K, Lihou CF, et al. Comprehensive genomic profiling in FIGHT-202 reveals the landscape of actionable alterations in advanced cholangiocarcinoma. *Journal of Clinical Oncology*. 2019;37(15_suppl):4080-4080.10.1200/JCO.2019.37.15_suppl.4080.
[8] Javle MM, Murugesan K, Shroff RT, et al. Profiling of 3,634 cholangiocarcinomas (CCA) to identify genomic alterations (GA), tumor mutational burden (TMB), and genomic loss of heterozygosity (gLOH). *Journal of Clinical Oncology*. 2019;37(15_suppl):4087-4087.10.1200/JCO.2019.37.15_suppl.4087.
[9] LYTGOBI [package insert]. Princeton, NJ: Taiho Oncology, Inc.; 2022.
[10] Sootome H, et al. Futibatinib is a novel irreversible FGFR 1-4 inhibitor that shows selective antitumor activity against FGFR-deregulated tumors. Cancer Res 2020;80(22):4986-97.
[11] Janssen Pharmaceutical Companies. Balversa (erdafitinib) [prescribing information]. Horsham, PA: Janssen Pharmaceutical Companies; 2020.
[12] Incyte Corporation. Pemazyre (pemigatinib) [prescribing information]. Wilmington, DE: Incyte Corporation; 2020.