National Comprehensive Cancer Network® Adds INQOVI® (decitabine and cedazuridine) Tablets to its Clinical Practice Guidelines in Oncology for Myelodysplastic Syndromes

PRINCETON, N.J., November 23, 2020 – Taiho Oncology, Inc. today announced that the FDA approved hypomethylating agent INQOVI® (decitabine and cedazuridine) 35 mg/100 mg tablets, for oral use, has been included in the latest National Comprehensive Cancer Network® Clinical Practice Guidelines (NCCN Guidelines®) in Oncology for Myelodysplastic Syndromes (MDS). The NCCN Guidelines now include a category 2a recommendation that oral decitabine and cedazuridine (DEC-C) could be considered as a substitution for intravenous decitabine in the treatment of adult patients with MDS.[1]

Specifically, the treatment guidelines allow the substitution of INQOVI for intravenous decitabine in appropriate patients with MDS who are experiencing clinically significant cytopenias or increased marrow blasts, significant anemia or are transplant candidates. The U.S. Food and Drug Administration (FDA) approved INQOVI on July 7, 2020 as the first oral hypomethylating agent for intermediate and high-risk MDS. In September, NCCN, an alliance of 30 leading cancer centers in the U.S., updated the NCCN Guidelines for Myelodysplastic Syndromes.

“The addition of INQOVI to the Clinical Practice Guidelines in Oncology for Myelodysplastic Syndromes will further inform healthcare providers of a new oral treatment option,” said Karin Blakolmer, Senior Vice President and Head of Medical Affairs, Taiho Oncology, Inc. “As the first orally administered hypomethylating agent for MDS, and an important alternative to multiple monthly intravenous infusions, Taiho Oncology believes that INQOVI will help address unmet treatment needs for patients who may currently have limited access to in-office intravenous therapy. We look forward to working with healthcare professionals to bring this therapy to appropriate patients.”

Taiho Oncology previously announced it has assumed commercialization responsibility from Astex Pharmaceuticals, Inc. and its parent company, Otsuka Pharmaceutical Co., Ltd., for INQOVI in the U.S.

The updated NCCN Guidelines are available at www.nccn.org.

About Myelodysplastic Syndromes (MDS)
Myelodysplastic syndromes are a heterogeneous group of hematopoietic stem cell disorders characterized by dysplastic changes in myeloid, erythroid, and megakaryocytic progenitor cells, and are associated with cytopenias affecting one or more of the three lineages. U.S. incidence of MDS is estimated to be 10,000 cases per year, although the condition is thought to be under-diagnosed.[2,3] The prevalence has

been estimated to be from 60,000 to 170,000 in the U.S.[4] MDS may evolve into acute myeloid leukemia (AML) in approximately one-third of patients.[5] The prognosis for MDS patients is poor; patients die from complications associated with cytopenias (infections and bleeding) or from transformation to AML.

About INQOVI (See https://www.inqovi.com)
INQOVI is an orally administered, fixed-dose combination of the approved anti-cancer DNA hypomethylating agent, decitabine, together with cedazuridine,[6] an inhibitor of cytidine deaminase.[7] By inhibiting cytidine deaminase in the gut and the liver, INQOVI is designed to allow for oral delivery of decitabine over five days in a given cycle to achieve comparable systemic exposure to IV decitabine (geometric mean ratio of the 5-day cumulative decitabine area-under-the-curve following 5 consecutive once daily doses of INQOVI compared to that of intravenous decitabine was 99% (90% CI:93, 106).[8] The phase 1 and phase 2 clinical study results have been published in *Lancet Haematology*[9] and *Blood,*[1] respectively. The phase 3 ASCERTAIN study data was presented at the American Society of Hematology (ASH) Meeting in Orlando, Florida, in December 2019 by Dr. Garcia-Manero.[10]

INDICATIONS
INQOVI is indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Myelosuppression
Fatal and serious myelosuppression can occur with INQOVI. Based on laboratory values, new or worsening thrombocytopenia occurred in 82% of patients, with Grade 3 or 4 occurring in 76%. Neutropenia occurred in 73% of patients, with Grade 3 or 4 occurring in 71%. Anemia occurred in 71% of patients, with Grade 3 or 4 occurring in 55%. Febrile neutropenia occurred in 33% of patients, with Grade 3 or 4 occurring in 32%. Myelosuppression (thrombocytopenia, neutropenia, anemia, and febrile neutropenia) is the most frequent cause of INQOVI dose reduction or interruption, occurring in 36% of patients. Permanent discontinuation due to myelosuppression (febrile neutropenia) occurred in 1% of patients. Myelosuppression and worsening neutropenia may occur more frequently in the first or second treatment cycles and may not necessarily indicate progression of underlying MDS.

Fatal and serious infectious complications can occur with INQOVI. Pneumonia occurred in 21% of patients, with Grade 3 or 4 occurring in 15%. Sepsis occurred in 14% of

patients, with Grade 3 or 4 occurring in 11%. Fatal pneumonia occurred in 1% of patients, fatal sepsis in 1%, and fatal septic shock in 1%.

Obtain complete blood cell counts prior to initiation of INQOVI, prior to each cycle, and as clinically indicated to monitor response and toxicity. Administer growth factors and anti-infective therapies for treatment or prophylaxis as appropriate. Delay the next cycle and resume at the same or reduced dose as recommended.

Embryo-Fetal Toxicity
INQOVI can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise patients to use effective contraception during treatment and for 6 months (females) or 3 months (males) after last dose.

ADVERSE REACTIONS
Serious adverse reactions in > 5% of patients included febrile neutropenia (30%), pneumonia (14%), and sepsis (13%). Fatal adverse reactions included sepsis (1%), septic shock (1%), pneumonia (1%), respiratory failure (1%), and one case each of cerebral hemorrhage and sudden death.

The most common adverse reactions (≥ 20%) were fatigue (55%), constipation (44%), hemorrhage (43%), myalgia (42%), mucositis (41%), arthralgia (40%), nausea (40%), dyspnea (38%), diarrhea (37%), rash (33%), dizziness (33%), febrile neutropenia (33%), edema (30%), headache (30%), cough (28%), decreased appetite (24%), upper respiratory tract infection (23%), pneumonia (21%), and transaminase increased (21%). The most common Grade 3 or 4 laboratory abnormalities (≥ 50%) were leukocytes decreased (81%), platelet count decreased (76%), neutrophil count decreased (71%), and hemoglobin decreased (55%).

USE IN SPECIFIC POPULATIONS
Lactation
Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with INQOVI and for at least 2 weeks after the last dose.

Renal Impairment
No dosage modification of INQOVI is recommended for patients with mild or moderate renal impairment (creatinine clearance [CLcr] of 30 to 89 mL/min based on Cockcroft-Gault). Due to the potential for increased adverse reactions, monitor patients with moderate renal impairment (CLcr 30 to 59 mL/min) frequently for adverse reactions. INQOVI has not been studied in patients with severe renal impairment (CLcr 15 to 29 mL/min) or end-stage renal disease (ESRD: CLcr <15 mL/min).

Please see full Prescribing Information.

About Taiho Oncology, Inc. (U.S.)

Taiho Oncology, Inc., a subsidiary of Taiho Pharmaceutical Co., Ltd. and Otsuka Holdings Co., Ltd., has established a world class clinical development organization that works urgently to develop innovative cancer treatments and has built a commercial business in the U.S. Taiho Oncology has an oral oncology pipeline consisting of selectively targeted agents. Advanced technology, dedicated researchers, and state of the art facilities are helping us to define the way the world treats cancer. It's our work; it's our passion; it's our legacy.

For more information about Taiho Oncology, please visit:
https://www.taihooncology.com/us

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

For more information about Otsuka Holdings Co., Ltd., please visit:
https://www.otsuka.com/en/

For more information about Astex Pharmaceuticals, Inc. please visit:
https://www.astx.com

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