



## Taiho Oncology and Astex Pharmaceuticals To Present Data In Myelodysplastic Syndromes at the 62nd ASH Annual Meeting and Exposition

PRINCETON, N.J. AND PLEASANTON, CA, December 2, 2020 – Taiho Oncology, Inc. and Astex Pharmaceuticals, Inc. today announced that data for oral decitabine and cedazuridine (INQOVI® [decitabine and cedazuridine] 35mg/100mg tablets) in intermediate and high-risk myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML) will be presented during the 62<sup>nd</sup> Annual American Society of Hematology Meeting and Exposition (ASH 2020), taking place virtually from December 5-8, 2020. Key presentations include:

- **Clinical Efficacy and Safety of Oral Decitabine/Cedazuridine in 133 Patients with Myelodysplastic Syndromes (MDS) and Chronic Myelomonocytic Leukemia (CMML):** Michael R. Savona, MD, Chief of Hematology, Cellular Therapy and Stem Cell Transplantation, Associate Director, Division of Hematology/Oncology, Director, Hematology Research and the Early Therapy Program, and Professor of Medicine and Cancer Biology, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine (Abstract 1230). Results will be shared online as a poster presentation on December 5, 2020. The abstract for this presentation is available on the ASH website: <https://ash.confex.com/ash/2020/webprogram/Paper133855.html>
- **The Direct Medical Costs of Treatment Discontinuation Among Higher-Risk Myelodysplastic Syndrome Patients Receiving Hypomethylating Agents:** Namita Joshi, PhD, MS, BPharm, Associate Director, Patient-Centered Outcomes and Real-World Evidence & Data Analytics Centers of Excellence, Pharmerit International (Abstract 1618). Results will be shared online as a poster presentation on December 5, 2020. The abstract for this presentation is available on the ASH website: <https://ash.confex.com/ash/2020/webprogram/Paper139642.html>
- **Under-Use of Hypomethylating Agents in Patients with Higher-Risk Myelodysplastic Syndrome in the United States: A Large Population-Based Analysis:** Shelby Corman, PharmD, MS, BCPS, Executive Director and Head of the Real-World Evidence & Data Analytics Center of Excellence, Pharmerit International (Abstract 2522). Results will be shared online as a poster presentation on December 6, 2020. The abstract for this presentation is available on the ASH website: <https://ash.confex.com/ash/2020/webprogram/Paper139552.html>

Additional information can be found at Taiho Oncology's Medical Booth when the exhibit opens on December 5, 2020.

“We are pleased to present new data for oral decitabine and cedazuridine that adds to the body of evidence supporting treatment for patients living with intermediate and high-risk MDS and CMML,” said Harold Keer, MD, PhD, Chief Medical Officer, Astex Pharmaceuticals, Inc. “INQOVI is emerging as an important treatment option that can be taken at home.”

The U.S. Food and Drug Administration approved INQOVI in July 2020 for the treatment of adults with intermediate and high-risk MDS and CMML. Taiho Oncology Inc. previously announced that it has assumed commercialization responsibility from Astex Pharmaceuticals, Inc. and its parent company, Otsuka Pharmaceutical Co., Ltd., for INQOVI in the U.S.

### **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 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.<sup>1,2</sup> The prevalence has been estimated to be from 60,000 to 170,000 in the U.S.<sup>3</sup> MDS may evolve into acute myeloid leukemia (AML) in approximately one-third of patients.<sup>4</sup> 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,<sup>5</sup> an inhibitor of cytidine deaminase.<sup>6</sup> 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).<sup>7</sup> The phase 1 and phase 2 clinical study results have been published in *Lancet Haematology*<sup>8</sup> and *Blood*,<sup>9</sup> 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.<sup>10</sup>

### **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 ( $\geq 20\%$ ) 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 ( $\geq 50\%$ ) 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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- <sup>2</sup> Ma X, Does M, Raza A, Mayne ST. Myelodysplastic syndromes: Incidence and survival in the United States. *Cancer* 2007;109(8):1536–1542.
- <sup>3</sup> Cogle C. Incidence and burden of the myelodysplastic syndromes. *Curr Hematol Malig Rep* 2015; 10(3): 272-281.
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- <sup>5</sup> Ogenesian A, Redkar S, Taverna P, Choy G, Joshi-Hangal R, Azab M. Preclinical data in cynomolgus (cyn) monkeys of ASTX727, a novel oral hypomethylating agent (HMA) composed of low-dose oral decitabine combined with a novel cytidine deaminase inhibitor (CDAi) E7727 [ASH Abstract]. *Blood* 2013;122(21): Abstract 2526.
- <sup>6</sup> Ferraris D, Duvall B, Delahanty G, Mistry B, Alt, J, Rojas C, et al. Design, synthesis, and pharmacological evaluation of fluorinated tetrahydrouridine derivatives as inhibitors of cytidine deaminase. *J Med Chem* 2014; 57:2582-2588.
- <sup>7</sup> INQOVI Prescribing Information. [www.inqovi.com/pi](http://www.inqovi.com/pi)
- <sup>8</sup> Savona MR, Odenike O, Amrein PC, Steensma DP, DeZern AE, Michaelis LC, et al. An oral fixed-dose combination of decitabine and cedazuridine in myelodysplastic syndromes: a multicentre, open-label, dose-escalation, phase 1 study. *Lancet Haematol* [Internet]. 2019;6(4):e194-e203.
- <sup>9</sup> Garcia-Manero G, Griffiths A, Steensma D, Robgoz G, Wells R, et al. Oral cedazuridine/decitabine for MDS and CMML: a phase 2 pharmacokinetic/pharmacodynamic randomized crossover study. *Blood* 2020; 136(6) 674-683..
- <sup>10</sup> Garcia-Manero G, McCloskey J, Griffiths EA, et al. Pharmacokinetic exposure equivalence and preliminary efficacy and safety from a randomized cross over Phase 3 study (ASCERTAIN study) of an oral hypomethylating agent ASTX727 (cedazuridine/decitabine) compared to IV decitabine. *Blood* 2019; 134 (Supplement\_1).