Astex Pharmaceuticals Presents Overall Survival Data From ASCERTAIN Phase 3 Study of Oral Hypomethylating Agent INQOVI® (decitabine and cedazuridine) in MDS and CMML at International Congress on Myelodysplastic Syndromes

- **Study achieved median overall survival of 31.7 months**
- **Updated efficacy data demonstrated an overall response rate of 62%, with 22% of patients achieving a complete response**
- **INQOVI is the only oral hypomethylating agent with equivalent exposure to its intravenous (IV) form**

Pleasanton, CA, September 23, 2021. Astex Pharmaceuticals, Inc., a wholly owned subsidiary of Otsuka Pharmaceutical Co. Ltd., based in Tokyo, Japan, today announced updated clinical data, including median overall survival (mOS), from the ASCERTAIN phase 3 trial of INQOVI®, the company's orally administered fixed-dose combination of decitabine and cedazuridine (ASTX727 or DEC-C) in adults with intermediate and high-risk myelodysplastic syndromes (MDS) including chronic myelomonocytic leukemia (CMML). mOS was 31.7 months.

The data were featured in a presentation given today at the 16th International Congress on Myelodysplastic Syndromes in Toronto, Canada, by Michael Savona, MD, Professor of Medicine and Cancer Biology, Department of Internal Medicine at Vanderbilt University School of Medicine, Tenn., on behalf of the study investigators.

The ASCERTAIN clinical trial was designed as a randomized crossover study comparing oral decitabine (35mg) and cedazuridine (100mg) fixed-dose combination tablet given once daily for 5 days on a 28-day cycle to IV decitabine (20mg/m^2) administered as a daily 1-hour IV infusion for 5 days on a 28-day cycle, in the first 2 cycles. Patients continued to receive oral decitabine and cedazuridine from Cycle 3 onwards. The primary endpoint data for the study of total 5-day decitabine area-under-the-curve (AUC) equivalence of oral decitabine and cedazuridine and IV decitabine was previously presented at the American Society of Hematology Annual Meeting in December 2019.[1] The oral/IV decitabine 5-day AUC was 98.9% with a 90% Confidence Interval between 92.7% and 105.6%.

Safety findings from the study were similar to those anticipated with IV decitabine, with incidence of cytopenias slightly higher with INQOVI during Cycle 1 compared to IV decitabine. The most common adverse events (AEs) of thrombocytopenia, neutropenia, and anemia were consistent with expected AEs with parenteral hypomethylating agent treatment.

In the more mature data set used to evaluate overall survival, the complete response (CR) rate for evaluable patients was 22%, with an overall response rate (CR + Partial Response + Marrow CR + Hematological Improvement) of 62%.

"Taken together, the ASCERTAIN phase 3 study data support considerable therapeutic utility of oral decitabine and cedazuridine in the treatment of patients with MDS and CMML," said Co-Principal Investigator of the ASCERTAIN phase 3 study, Michael Savona, MD. "The fixed-dose combination of decitabine and cedazuridine is the only available oral DNA methyltransferase inhibitor / hypomethylating agent that has demonstrated equivalent exposure to an IV form. The median overall survival data from this study makes oral decitabine and cedazuridine an alternative option to parenteral administration of decitabine for patients with these diseases."

Added Timothy Whitten, president and CEO of Taiho Oncology, Inc., Astex's commercialization partner for INQOVI in the United States: "We are encouraged by data from the ASCERTAIN trial that continue to show oral decitabine and cedazuridine is a promising treatment option for patients living with MDS and CMML. Importantly, patients can benefit from the convenience of an at-home hypomethylating agent treatment and potentially reduce the number of office visits and associated travel."

Based on the data from the ASCERTAIN clinical program, INQOVI is being investigated in combination with other agents in hematological malignancies, according to Harold Keer, MD, PhD, chief medical officer of Astex Pharmaceuticals, Inc. "The first of these studies is investigating the all-oral combination of decitabine and cedazuridine with venetoclax for the treatment of AML. We are extremely grateful to all the patients, caregivers, partner research and manufacturing organizations, as well as the healthcare professionals who have contributed to the clinical development program of oral decitabine and cedazuridine."

INQOVI is an orally administered, fixed-dose combination of the approved anti-cancer DNA hypomethylating agent, decitabine, together with cedazuridine,[2] an inhibitor of cytidine deaminase.[3] 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. The phase 1 and phase 2 clinical study results have been published in *Lancet Haematology*[4] and *Blood,*[5] respectively.

INQOVI was approved in July 2020 by the U.S. Food and Drug Administration (FDA) and by Health Canada. INQOVI is the first and only oral hypomethylating agent approved by the FDA and by Health Canada for the treatment of adults with intermediate and high-risk MDS including CMML.[6]

Commercialization of INQOVI in the U.S. and Canada is conducted by Taiho Oncology, Inc. and Taiho Pharma Canada, Inc., respectively. Astex, Otsuka and Taiho are all members of the Otsuka group of companies.

The presentation can be downloaded from the Astex website at: https://astx.com/ASTX727 - International MDS Symposium September 2021

Learn more about INQOVI at https://www.inqovi.com

INDICATIONS

INQOVI (decitabine and cedazuridine) 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.[6]

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 with INQOVI 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, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and transaminase increased. The most common Grade 3 or 4 laboratory abnormalities (>50%) were leukocytes decreased, platelet count decreased, neutrophil count decreased, and hemoglobin decreased.

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 the accompanying Full Prescribing Information.

About Myelodysplastic Syndromes (MDS) and Chronic Myelomonocytic Leukemia (CMML)

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.[7,8] The prevalence has been estimated to be from 60,000 to 170,000 in the U.S.[9] MDS may evolve into acute myeloid leukemia (AML) in one-third of patients.[10] The prognosis for MDS patients is poor; patients die from complications associated with cytopenias (infections and bleeding) or from transformation to AML.

CMML is a clonal hematopoietic malignancy characterized by accumulation of abnormal monocytes in the bone marrow and in blood. The incidence of CMML in the U.S. is approximately 1,100 new cases per year,[11] and CMML may transform into AML in 15% to 30% of patients.[12]

About Astex, Taiho, and Otsuka

Astex Pharmaceuticals, Inc. ("Astex") is committed to the fight against cancer. Astex is developing a proprietary pipeline of novel therapies for the treatment of solid tumors and hematological malignancies. Astex is a member of the Otsuka group of pharmaceutical companies. The group also includes Otsuka Pharmaceutical Co., Ltd., Taiho Pharmaceutical Co., Ltd., and Taiho Oncology, Inc. Subject to regulatory approvals, Astex's products will be commercialized in the U.S. and Canada by Taiho subsidiaries, and in the rest of the world by Otsuka subsidiaries.

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 are 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.

Otsuka Pharmaceutical is a global healthcare company with the corporate philosophy: "Otsuka–people creating new products for better health worldwide." Otsuka researches, develops, manufactures and markets innovative and original products, with a focus on pharmaceutical products for the treatment of diseases and nutraceutical products for the maintenance of everyday health.

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

For more information about Otsuka Pharmaceutical, please visit: https://www.otsuka.co.jp/en/

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

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