Taiho Oncology and Astex Pharmaceuticals Present Overall Survival Data for Oral Decitabine and Cedazuridine (INQOVI®, ASTX727) in Patients With MDS and CMML Harboring TP53 Mutations at 64th ASH Annual Meeting

Patients in Phase 3 ASCERTAIN study with biallelic TP53 mutations achieved median overall survival (mOS) of 13 months; mOS in the overall study population was 32 months

Results indicate potential utility of this oral hypomethylating agent in patients with MDS harboring a TP53 mutation, which is an independent prognostic factor for poor outcomes

PRINCETON, N.J. and PLEASANTON, CA, December 12, 2022 – Taiho Oncology, Inc. and Astex Pharmaceuticals, Inc. today announced preliminary data from the Phase 3 ASCERTAIN trial assessing overall and leukemia-free survival in adults with intermediate and high-risk myelodysplastic syndromes (MDS) including chronic myelomonocytic leukemia (CMML) harboring biallelic TP53 mutations following treatment with oral decitabine and cedazuridine (ASTX727). The data are being presented today as an oral presentation (Abstract #854) at the 64th American Society of Hematology (ASH) Annual Meeting in New Orleans.

This analysis evaluated the impact mutation profile of patients from the ASCERTAIN trial on overall survival (OS) and leukemia-free survival (LFS); this was based on the National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines (NCCN Guidelines®) in Oncology for Myelodysplastic Syndromes (Version 1.2023-September 12, 2022) with a focus on the TP53 mutant population. In the study, the population of patients harboring a TP53 mutation (44 of 125 patients) was characterized by allelic status: 14 patients had biallelic mutations and 30 patients had monoallelic mutations without other chromosomal deletions. The median OS (mOS) in patients treated with ASTX727 with biallelic vs. monoallelic mutations was 13.0 months (95% Confidence Interval [CI]: 5.3, 29.1) vs. 29.2 months (95% CI: 19.8, NE).

“The overall results of this post-hoc analysis from ASCERTAIN studying the patients with mutated TP53 are of interest given the typically poor outcomes in these patients,” said Michael Savona, MD, Director of Hematologic Malignancies Research and Early Therapy Program, and Professor of Internal Medicine and Cancer Biology at Vanderbilt University, and co-principal investigator on the study. “This analysis supports the emerging hypothesis that higher burden of mutant TP53 cells connotes poorer risk, and the fixed-dose combination of oral decitabine and cedazuridine may serve as a reasonable option in these patients.”

More broadly, mOS and median LFS (mLFS) in patients with MDS and CMML harboring a TP53 mutation treated with ASTX727 were 25.5 and 22.1 months, respectively, compared to 33.7 and 31.7 months, respectively, in patients with wild-type TP53 status. The mOS and mLFS in the overall ASCERTAIN population were 32 and 29 months, respectively. Of note, the percentage of patients in the trial harboring a TP53 mutation (35%) was substantially higher than the standard patient population, which is approximately 8-12%.[1]

“There remains a significant unmet need for patients with MDS and CMML, particularly for those with mutations that typically don’t respond well to treatment, which is why we are encouraged by what we see in the ASCERTAIN trial,” said Tim Whitten, President and CEO of Taiho Oncology, Inc. “The results build on the body of evidence supporting the utility of oral decitabine and cedazuridine, and we look forward to additional research to assess this combination as a treatment option for these patients.”

Additional Data Presentations on ASTX727

In a second oral presentation, results of a Phase 1 study (Abstract #461) that explored the optimal dosing schedule of low-dose ASTX727 in patients with lower-risk MDS, were presented. The study found that a dosing schedule of 10 mg decitabine/100 mg cedazuridine daily for five days led to balanced clinical efficacy with an

acceptable and manageable safety profile. Based on the results of the study, this dosing schedule was chosen as the recommended dose for an ongoing Phase 2 study that is comparing this regimen to 35 mg decitabine/100 mg cedazuridine for three days in a 28-day cycle. The data were presented by Guillermo Garcia-Manero, MD, on Sunday, December 11 during the "Myelodysplastic Syndromes – Clinical and Epidemiological II" oral session.

In addition, data from the first real-world study on treatment patterns and characteristics for MDS patients initiating ASTX727 (Abstract #1760) were presented by Amer Zeidan, MD, on Saturday, December 10 during the "Myelodysplastic Syndromes – Clinical and Epidemiological: Poster I" session. Parenteral administration of hypomethylating agents has been associated with additional patient burden. Based on the results of this study, characteristics were similar among patients initiating ASTX727 and parenteral hypomethylating agents. Trends in treatment patterns suggest comparable or improved compliance with oral decitabine and cedazuridine treatment regimen at home compared with parenteral treatment in the clinical setting.

About ASCERTAIN

The Phase 3 ASCERTAIN clinical trial was a multicenter, randomized, open-label, crossover pharmacokinetics (PK) 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 in patients with MDS and CMML. Patients continued to receive oral decitabine and cedazuridine from Cycle 3 onwards. The primary endpoint of the study was total 5-day area-under-the-curve (AUC) equivalence of oral decitabine and cedazuridine and IV decitabine.

For more information about ASCERTAIN, please visit:
https://www.clinicaltrials.gov/ct2/show/NCT03306264?term=cedazuridine&draw=3&rank=19.

INDICATIONS

Decitabine and cedazuridine, marketed under the brand name 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.[2]

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.[2]

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

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 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.[3,4] The prevalence has been estimated to be from 60,000 to 170,000 in the U.S.[5] MDS may evolve into acute myeloid leukemia (AML) in one-third of patients.[6] 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,[7] and CMML may transform into AML in 15% to 30% of patients.[8]

About Decitabine and Cedazuridine Fixed-Dose Combination (ASTX727)
ASTX727 is an orally administered, fixed dose combination of the approved anti-cancer DNA hypomethylating agent, decitabine, together with cedazuridine,[3] an inhibitor of cytidine deaminase.[4] By inhibiting cytidine deaminase in the gut and the liver, the fixed dose combination is designed to allow for oral delivery of decitabine over five days in a given cycle to achieve comparable systemic exposure to IV decitabine administered over five days.

The oral decitabine and cedazuridine fixed-dose combination has been evaluated in a Phase 1/2 pharmacokinetics-guided dose escalation and dose confirmation study, and a Phase 3 exposure equivalence study in patients with myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML) – the ASCERTAIN study.

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 www.taihooncology.com.

About Astex
Astex Pharmaceuticals, Inc. 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 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.

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