Astex Pharmaceuticals announces U.S. Food and Drug Administration (FDA) acceptance for review of an NDA for the combination oral hypomethylating agent cedazuridine and decitabine (ASTX727 or oral C-DEC), for the treatment of MDS and CMML

- **NDA is supported by data from the phase 3 ASCERTAIN study of oral C-DEC in adults with intermediate- and high-risk myelodysplastic syndromes (MDS) including chronic myelomonocytic leukemia (CMML)**
- **FDA designated the application for Priority Review**
- **Potential for oral C-DEC to become first approved orally administered hypomethylating agent for MDS and CMML in the U.S.**

Pleasanton, CA, February 11th, 2020. Astex Pharmaceuticals, Inc., a wholly owned subsidiary of Otsuka Pharmaceutical Co. Ltd., based in Japan, today announced that the U.S. FDA has accepted for Priority Review its NDA for oral C-DEC (cedazuridine and decitabine) as a treatment for adults with previously untreated intermediate- and high-risk MDS including CMML. The NDA submission is based on data from the ASCERTAIN phase 3 study which evaluated the 5-day decitabine exposure equivalence of oral C-DEC and IV decitabine.

"We are very pleased that the FDA has accepted our NDA for Priority Review," said Dr Mohammad Azab, MD, president & chief medical officer of Astex Pharmaceuticals, Inc. "Subject to FDA review and regulatory approval, oral C-DEC may offer a new option for patients with MDS and CMML that saves them the burden of 5-day IV infusions every month during their treatment period. We are grateful to all the patients, investigators and other healthcare providers, and partner research and manufacturing organizations, who contributed to the clinical development program of oral C-DEC."

The FDA grants Priority Review to applications for drugs that, if approved, would provide significant improvements in the safety and effectiveness of the treatment, diagnosis or prevention of serious conditions. The Priority Review designation means FDA's goal is to take action on an NDA application within six months (compared to the ten months under standard review).

Oral C-DEC is an investigational compound and is not currently approved in any country.

Astex's parent company, Otsuka Pharmaceutical Co., Ltd., and Taiho Pharmaceutical Co., Ltd. previously announced that, subject to regulatory approvals, commercialization of oral C-DEC in the U.S. and Canada will be conducted by Taiho Oncology, Inc. and Taiho Pharma Canada, Inc. respectively. Astex, Otsuka and Taiho are all members of the Otsuka group of companies.

About C-DEC (Cedazuridine 100 mg and Decitabine 35 mg) Fixed-Dose Combination

C-DEC is a novel, orally administered fixed dose combination of cedazuridine, an inhibitor of cytidine deaminase,[1] with the anti-cancer DNA hypomethylating agent, decitabine.[2] By inhibiting cytidine deaminase in the gut and the liver, C-DEC is designed to allow for oral delivery of the approved DNA hypomethylating agent, decitabine, at exposures which emulate exposures achieved with the approved intravenous form of decitabine administered over 5 days.[3]

C-DEC has been evaluated in a phase 1/2 pharmacokinetics-guided dose escalation and dose confirmation study in patients with MDS and CMML (see https://www.clinicaltrials.gov NCT02103478) and a pivotal phase 3 study (ASCERTAIN) (see https://www.clinicaltrials.gov NCT03306264) conducted at investigator sites in the US and Canada and designed to confirm the results from the phase 1/2 study. The phase 3 study is now being extended to include patients with acute myeloid leukemia (AML) unsuitable to receive intensive induction chemotherapy.

In September 2019 Astex announced that C-DEC had received orphan drug designation for the treatment of MDS and CMML from the U.S. FDA.

The concept of using cedazuridine to block the action of cytidine deaminase is also being evaluated in a low dose formulation of cedazuridine and decitabine for the treatment of lower risk MDS (see https://www.clinicaltrials.gov NCT03502668).

About the Phase 3 ASCERTAIN Study

The study was designed as a randomized crossover study comparing oral C-DEC (cedazuridine 100 mg and decitabine 35 mg fixed-dose combination tablet given once daily for 5 days on a 28-day cycle) to IV decitabine (20 mg/m^2 administered as a daily, 1-hour IV infusion for 5 days on a 28-day cycle) in the first 2 cycles with patients continuing to receive oral C-DEC from Cycle 3 onwards. The data from the ASCERTAIN study was presented at the American Society of Hematology (ASH) Meeting in Orlando, Florida in December 2019 by Dr Guillermo Garcia-Manero, MD, professor and chief of section of myelodysplastic syndromes, Department of Leukemia at The University of Texas MD Anderson Cancer Center, on behalf of the study investigators.[4] The data demonstrated that the ASCERTAIN study met the primary endpoint of total 5-Day decitabine Area-Under-The-Curve (AUC) equivalence of oral C-DEC and IV decitabine. Safety findings from the study were consistent with those anticipated with IV decitabine, with no significant differences in the incidence of most common adverse events between oral C-DEC and IV decitabine in the first 2 randomized cycles. The most common adverse events of any grade >20% regardless of causality in patients in the first 2 randomized cycles who received oral C-DEC were thrombocytopenia (43.8%), neutropenia (35.4%), anemia (36.9%), and fatigue (23.8%). The ASH presentation can be downloaded from the Astex website at https://astx.com/media-center/presentations-and-publications/ASTX727 ASCERTAIN Presentation - ASH - December 2019

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.[5,6] The

prevalence has been estimated to be from 60,000 to 170,000 in the U.S.[7] MDS may evolve into acute myeloid leukemia (AML) in one-third of patients.[8] 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,[9] and CMML may transform into AML in 15% to 30% of patients.[10] The hypomethylating agents decitabine and azacitidine are effective treatment modalities for hematologic cancers and are FDA-approved for the treatment of higher-risk MDS and CMML. These agents are administered by IV infusion, or by large-volume subcutaneous injections.

About Astex Pharmaceuticals, Inc.

Astex is a leader in innovative drug discovery and development, committed to the fight against cancer. Astex is developing a proprietary pipeline of novel therapies and has multiple partnered products in development under collaborations with leading pharmaceutical companies. Astex is a wholly owned subsidiary of Otsuka Pharmaceutical Co. Ltd., based in Tokyo, Japan.

Otsuka 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: http://www.astx.com

For more information about Otsuka Pharmaceutical, please visit: http://www.otsuka.com/en/

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

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