Astex Pharmaceuticals expands clinical evaluation of oral decitabine and cedazuridine tablets through new Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute (NCI)

- **NCI has announced availability to investigators of oral decitabine and cedazuridine tablets for clinical and nonclinical study proposals under the CRADA**
- **The collaboration is intended to study oral decitabine and cedazuridine tablets in a range of tumor types**

Pleasanton, CA, - October 28, 2020. -- Astex Pharmaceuticals, Inc., a wholly owned subsidiary of Otsuka Pharmaceutical Co., Ltd., based in Tokyo, Japan, today announces it has entered into a Cooperative Research and Development Agreement with the U.S. National Cancer Institute, part of National Institutes of Health. The agreement calls for a range of new clinical and translational studies of oral decitabine and cedazuridine tablets as an anticancer agent to be conducted in collaboration with Astex. The NCI's Cancer Therapy Evaluation Program (CTEP) has announced they are accepting Letters of Intent for evaluation of oral decitabine and cedazuridine tablets in hematological malignancies and solid tumors, including in combination with other investigational agents. Study proposals will be reviewed by CTEP and by Astex.

On July 7th, 2020, Astex's hypomethylating agent INQOVI® (decitabine and cedazuridine) 35mg/100mg tablets, for oral use, was approved simultaneously by the U.S. FDA and by Health Canada for the treatment of intermediate- and high-risk myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML) patients in the U.S. and Canada, respectively.

"Oral decitabine and cedazuridine tablets offer a new treatment option for patients with MDS and CMML," said Mohammad Azab, president and chief medical officer of Astex. "We are delighted to be entering into this collaboration with NCI to investigate and broaden the evaluation of the clinical potential of oral decitabine and cedazuridine. We look forward to working with investigators to study how oral targeted therapies might work in combination to treat patients with leukemia and solid tumors."

The initial study being conducted under the CRADA will investigate the combination of oral decitabine and cedazuridine tablets with venetoclax in the treatment of acute myeloid leukemia. The CRADA will also include oral decitabine and cedazuridine tablets in the NCI myeloMATCH master trial aimed at evaluating therapies for the treatment of myeloid malignancies. Astex will provide funding, study drug, and personnel to support the proposed studies.

About INQOVI (decitabine and cedazuridine) 35mg/100mg tablets
Indications and Important Safety Information

INDICATIONS
In the U.S. and Canada, 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.

INQOVI is being commercialized by Taiho Oncology, Inc. and Taiho Pharma Canada, Inc. in the U.S. and Canada, respectively. INQOVI is not approved in any other market worldwide. Taiho and Astex are members of the Otsuka group of companies. INQOVI® is a registered trademark of Otsuka Pharmaceutical Co., Ltd.

About Astex Pharmaceuticals, Otsuka Pharmaceutical and Taiho Oncology

Astex Pharmaceuticals, Inc. 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 Pharmaceutical Co., Ltd. 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.

Taiho Oncology, Inc., is a subsidiary of Taiho Pharmaceutical Co., Ltd. and an indirect subsidiary of Otsuka Holdings Co., Ltd. Taiho 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 has an oral oncology pipeline consisting of both novel antimetabolic agents and selectively targeted agents.

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 Pharmaceutical, please visit: https://www.taihooncology.com/

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