ENROLLMENT COMPLETE: Oral Decitabine and Cedazuridine (ASTX727) Phase 3 Clinical Study

Phase 3 Crossover Study of Oral Decitabine and Cedazuridine (ASTX727) Versus IV Decitabine in Subjects with Myelodysplastic Syndromes (MDS), Chronic Myelomonocytic Leukemia (CMML), or Acute Myeloid Leukemia (AML)

Key Eligibility Criteria*
- MDS, CMML, or AML patients eligible for treatment with IV decitabine
- 1:1 Randomization

Cycle 1: ASTX727 tablet
Cycle 2: IV Decitabine
Cycle ≥3*: ASTX727 tablet

Cycle 1: IV Decitabine
Cycle 2: ASTX727 tablet
Cycle ≥3*: ASTX727 tablet

Treatment, ASTX727 or decitabine, is given daily x5 every 28-day cycle

Except as stated, all compounds presented here are investigational, efficacy and safety have not been established. There is no guarantee that these agents will become commercially available.

Oral decitabine and cedazuridine (ASTX727) is approved in the U.S. for the 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. See full Prescribing Information.

For more information: www.clinicaltrials.gov identifier: NCT03306264 or email: information-request@astx.com

*For a full list of eligibility requirements go to www.clinicaltrials.gov
†Continued dosing with ASTX727 until disease progression, unacceptable toxicity, subject discontinues treatment, or withdraws from study
Phase 1-2 Study of Oral Decitabine and Cedazuridine (ASTX727) Low Dose (LD) Extended Schedule in Subjects with Lower Risk (IPSS Low or Intermediate-1) Myelodysplastic Syndromes (MDS)

NOW ENROLLING - PHASE 2:
ASTX727 LD Phase 1-2 Clinical Study in Lower-Risk MDS

Phase 1-2 Study of Oral Decitabine and Cedazuridine (ASTX727) Low Dose (ASTX727 LD) Extended Schedule in Subjects with Lower Risk (IPSS Low or Intermediate-1) Myelodysplastic Syndromes (MDS)

Except as stated, all compounds presented here are investigational, efficacy and safety have not been established. There is no guarantee that these agents will become commercially available.

Oral decitabine and cedazuridine (ASTX727) is approved in the U.S. for the 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. See full Prescribing Information.

For more information: www.clinicaltrials.gov identifier: NCT03502668 or email: information-request@astx.com
Tolinapant (ASTX660), a cIAP1/2 and XIAP Inhibitor
Phase 1-2 Clinical Study

NOW ENROLLING - PHASE 2 (PTCL):
Tolinapant (ASTX660) Phase 1-2 Study in Solid Tumors and Lymphomas

Phase 1-2 Study of the Safety, Pharmacokinetics, and Preliminary Activity of Tolinapant (ASTX660) in Subjects with Advanced Solid Tumors and Lymphomas

Key Eligibility Criteria*:  
• Relapsed/Refractory T-Cell Lymphoma  
• Evidence of progressive disease  
• Treatment with at least two prior systemic therapies  
• ECOG 0-2

Primary Endpoint: Response Rate

This compound is investigational, and efficacy and safety have not been established. There is no guarantee that this agent will become commercially available.

For more information: www.clinicaltrials.gov identifier: NCT02503423 or email: information-request@astx.com

*For a full list of eligibility requirements go to www.clinicaltrials.gov
†6 Cohorts in study - enrollment completed in: HNSCC, DLBCL, Cervical Carcinoma, & other tumor types
cIAP - cellular inhibitor of apoptosis; XIAP - X-linked inhibitor of apoptosis; ECOG - Eastern Cooperative Oncology Group; HNSCC - head and neck squamous cell carcinoma; DLBCL - diffuse large B-cell lymphoma; PTCL - peripheral T-cell lymphoma; CTCL - cutaneous T-cell lymphoma

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Phase 1-2 Study of the Safety, Pharmacokinetics, and Activity of ASTX029 in Subjects with Advanced Solid Tumors

NOW ENROLLING:
ASTX029 Phase 1-2 Study in Solid Tumors

This compound is investigational, and efficacy and safety have not been established. There is no guarantee that this agent will become commercially available.

For more information: www.clinicaltrials.gov identifier: NCT03520075 or email: information-request@astx.com

ERK 1/2 - Extracellular Signal-Related Protein Kinases 1 and 2; QD - once daily; RP2D - recommended Phase 2 dose; MAPK - mitogen-activated protein kinase

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Phase 1-2 Study of the Safety, Pharmacokinetics, and Preliminary Activity of ASTX295 in Subjects with Wild-Type TP53 Advanced Solid Tumors

This compound is investigational, and efficacy and safety have not been established. There is no guarantee that this agent will become commercially available.

For more information: www.clinicaltrials.gov identifier: NCT03975387 or email information-request@astx.com
NOW ENROLLING:
Tolinapant (ASTX660) Phase 1 Study in R/R AML

Phase 1 Study of the Safety and Tolerability, Pharmacokinetics, and Antileukemic Activity of Tolinapant (ASTX660) as a Single Agent and in Combination with Oral Decitabine and Cedazuridine (ASTX727) in Subjects with Relapsed/Refractory (r/r) Acute Myeloid Leukemia (AML)

Phase 1 - Part 1
Combination Dose Escalation

Tolinapant (ASTX660) + Oral Decitabine/Cedazuridine (ASTX727)

1:1 Randomization

Arm A: Tolinapant (ASTX660)

Arm B: Tolinapant (ASTX660) + Oral Decitabine/Cedazuridine (ASTX727)

Phase 1 - Part 2
Single Agent vs. Combination Dose Escalation

Tolinapant (ASTX660) RDE + Oral Decitabine/Cedazuridine (ASTX727)

Phase 1 - Part 3
Dose Expansion

Except as stated, all compounds presented here are investigational, efficacy and safety have not been established. There is no guarantee that these agents will become commercially available.

Oral decitabine and cedazuridine (ASTX727) is approved in the U.S. for the 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, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups. See full Prescribing Information.

For more information: www.clinicaltrials.gov identifier: NCT04155580 or email information-request@astx.com

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Phase 1-3 Study of Oral ASTX030 (Azacitidine and Cedazuridine given in Combination) Versus Subcutaneous Azacitidine in Subjects with Myelodysplastic Syndromes (MDS), Chronic Myelomonocytic Leukemia (CMML), or Acute Myeloid Leukemia (AML)

**Phase 1**
- **Primary Objective:** Identify ASTX030 dose that achieves target mean azacitidine AUC within 90-110% of SC azacitidine

**Part A (dose escalation)**
- Cycle 1: single doses of oral azacitidine (day -3), SC azacitidine (day 1), oral cedazuridine (day 22); and oral cedazuridine + azacitidine (days 2-7)
- Cycle ≥2: oral ASTX030 (cedazuridine + azacitidine, days 1-7)

**Part B (dose expansion)**
- Oral cedazuridine + azacitidine at RDE as separate tablets

**Phase 2 & 3**
- **Primary Objectives:**
  - Phase 2: Confirm final selected dose of ASTX030
  - Phase 3: Establish azacitidine AUC equivalence with SC azacitidine at final selected dose of ASTX030

**Sequence A**
- Cycle 1: oral ASTX030
- Cycle 2: SC azacitidine
- Cycles ≥3: oral ASTX030

**Sequence B**
- Cycle 1: SC azacitidine
- Cycle 2: oral ASTX030
- Cycles ≥3: oral ASTX030

**RP2D and Regimen**
- 1:1 randomization

This compound is investigational, and efficacy and safety have not been established.
There is no guarantee that this agent will become commercially available.

For more information: www.clinicaltrials.gov identifier: NCT04256317 or email: information-request@astx.com

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TAS1440, a LSD1 Inhibitor
Phase 1 Clinical Study

NOW ENROLLING:
Oral TAS1440 with ATRA in R/R AML

Phase 1 Study of Safety, Pharmacokinetics, and Preliminary Activity of TAS1440, as a Single Agent and in Combination with All-Trans Retinoic Acid (ATRA) in Subjects with Relapsed or Refractory (r/r) Acute Myeloid Leukemia (AML)

Part 1
Monotherapy Dose Escalation
TAS1440 Single agent administered once daily (QD) on specific days during each 28-day cycle

Part 2
Combination Dose Escalation
TAS1440 administered QD on specific days during each 28-day cycle in combination with ATRA twice daily

This compound is investigational, and efficacy and safety have not been established. There is no guarantee that this agent will become commercially available.

For more information: www.clinicaltrials.gov identifier: NCT04282668 or email information-request@astx.com

Taiho Pharmaceutical Co., Ltd. investigational agent being developed in collaboration with Astex Pharmaceuticals, Inc.
Phase 1 Study of Safety, Pharmacokinetics, and Preliminary Activity of TAS1553 in Subjects with Relapsed or Refractory (r/r) Acute Myeloid Leukemia (AML) and Other Myeloid Neoplasms

Part 1
Dose Escalation

- Accelerated Titration
  - Study drug orally QD at specific time points of each 28-day cycle

Part 2
Dose Expansion

- Cohort 1: R/R AML
- Cohort 2: MDS/MPN

Primary Endpoints:
Safety and Tolerability Response Rate

NOW ENROLLING:
TAS1553 Phase 1 Clinical Study in R/R AML

This compound is investigational, and efficacy and safety have not been established. There is no guarantee that this agent will become commercially available.

For more information: www.clinicaltrials.gov identifier: NCT04637009 or email information-request@astx.com

Taiho Pharmaceutical Co., Ltd. investigational agent being developed in collaboration with Astex Pharmaceuticals, Inc.
Oral Decitabine/Cedazuridine (ASTX727) + Venetoclax
Phase 1 Clinical Study

NOW ENROLLING:
Oral Decitabine/Cedazuridine (ASTX727) + Venetoclax

Single-Arm, Open-Label Pharmacokinetic, Safety, and Efficacy Study of ASTX727 in Combination with Venetoclax in Adult Patients with Acute Myeloid Leukemia (AML)

Patient Population
- Newly diagnosed AML
- Projected life expectancy ≥ 3 mo
- Ineligible for intensive induction chemotherapy
- ECOG PS 0–2

Cycle 1 Dosing (28 Day Cycle)
- Day 1: ASTX727 PO* + Venetoclax 100 mg PO (ramp up)
- Day 2: ASTX727 PO* + Venetoclax 200 mg PO (ramp up)
- Days 3–5: ASTX727 PO* + Venetoclax 400 mg PO
- Days 6–28: Venetoclax 400 mg PO

Cycle ≥ 2 Dosing (28 Day Cycle)
- Days 1–5: ASTX727 PO* + Venetoclax 400 mg PO
- Day 6–28: Venetoclax 400 mg PO
- Tx continued until disease progression, unacceptable toxicity or subject withdraws from study

Primary Endpoint:
- PK in Cycle 2 (AUC_0–24, C_{MAX})

Secondary Endpoints:
- Additional PK in Cycle 2, Safety, CR, TTR, DOR, OR

For more information: www.clinicaltrials.gov identifier: NCT04657081 or email information-request@astx.com

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Table fixed-dose combination of 35 mg decitabine and 100 mg cedazuridine

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ECOG PS - Eastern Cooperative Oncology Group performance status; PO - by mouth; mg - milligram;
AUC_0–24 - area under the plasma concentration-time curve over the last 24-h dosing interval; C_{MAX} - maximum observed concentration;
CR - complete response; TTR - time to response; DOR - duration of response; OR - overall response; PK - pharmacokinetic;

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