Phase 1 Study of the IDH1m Inhibitor FT-2102 as a Single Agent in Patients with IDH1m Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

Study Objectives

- **Dose Escalation** (n = 19)

- **Dose Expansion** (n = 9)

**Key Study Objectives**

- Determine MTD/RP2D for FT-2102

- Evaluate safety

- Evaluate PK and PD

- Evaluate IDH1m tissue pharmacokinetics

- Determine preliminary anti-leukemia activity of SA and AZA combination (see ASH Poster 1462)

**Key Eligibility Criteria**

- AML or MDS, documented IDH1- or IDH2-mutation by local testing

- Adequate liver and renal function

- Evaluate preliminary anti-leukemia activity of SA and AZA combination

- Baseline IDH1-m inhibitor

**Disease History and Baseline Characteristics**

**Chemokine and Pharmacodynamics**

- FT-2102, with a plasma half-life of ~60 hours, achieved steady-state concentration within 2 weeks of dosing and remained consistent over treatment duration

- At 150 mg BID, steady-state plasma concentrations are above the predicted C_{eff} resulting in a 90% reduction in plasma 2-HG and below FT-2102 levels predicted, in NHP, to pose a Qc proliferation risk

**Study Conclusions**

- FT-2102 demonstrates clinical activity as single agent in a high-risk Phase 1 population of AML/MDS patients with IDH1 mutation.

- 41% CR/CRh/Cri in R/R AML (35% in all AML/MDS)

- Transfusion independence observed in both IWG responders/non-responders

- Likely contributing to rate and depth (CR/CRh) of response

- FT-2102 concentrations < 1,000 ng/mL correspond to early transfusion independence observed in both IWG responders/non-responders

- Median time to CR/Cri: 3.5 months (Range: 1-5 months)

- Significant reduction in bone marrow blast content observed in patients with a CR/CRi response per IWG response

- Transfusion independence (platelets and/or red blood cells) was observed in all response categories in AML patients who were transfusion-dependent at BL

- Patient [1] had an increase of > 60 msec but remained within the normal limits (< 450 msec)

- No AEs of QTcF Prolongation Reported

- No exclusions for concomitant medications

- Adequate liver and renal function

- Baseline ECG ≤ 450 msec (unless history of BBB)