Phase 3 AML (M15-656): Study Design and Endpoints

A phase 3 randomized, double-blind, placebo controlled study of venetoclax in combination with azacitidine versus azacitidine in treatment naive subjects with acute myeloid leukemia who are ineligible for standard induction therapy.

Key Inclusion Criteria
- Previously untreated AML
- ≥ 18 yrs of age
- Ineligible for standard induction therapy
- ECOG PS 0–2 for subjects ≥ 75 yrs of age; 0–3 for subjects 18–74 yrs of age

Key Exclusion Criteria
- Prior HMA and/or any chemotherapeutic agent for MDS, CAR T-cell therapy, or other experimental therapies
- Favorable risk cytogenetics such as t(8;21), inv(16), or t(15;17)
- History of MPN, APL, CNS involvement

Endpoints
- Primary: OS, Composite Complete Remission Rate (CR + CRi)
- Secondary: EFS, CCRR by initiation of Cycle 2, fatigue reduction based on PROMIS F-SF 7a and EORTC QLQ-C30
- Exploratory: Predictive biomarker analysis, MRD negativity, remaining EORTC QLQ-C30, EQ-5D-5L

Dosing
- Cycle 1: Venetoclax D1 (100mg); D2 (200 mg); D3-28 (400 mg) PO QD
  Azacitidine 75 mg/m² SQ on days 1-7 (28 day cycle)
- Venetoclax (400 mg) PO QD on days 1-28 plus azacitidine 75 mg/m² SQ on days 1-7 (28 day cycle)
- Placebo QD on days 1-28 plus azacitidine 75 mg/m² SQ QD on days 1-10 (28 day cycle)

Venetoclax is being investigated for indications that have not been approved by Regulatory Agencies. Safety and Efficacy have not been established in unapproved indications.