Protocol Title: Phase II, Randomized, Biomarker-Driven, Clinical Study in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML) with an Exploratory Arm in Patients with Newly Diagnosed High-Risk AML

Target Population: Acute Myeloid Leukemia (AML)
- Relapsed or Primary Refractory AML
- Newly Diagnosed High-Risk (NDHR) AML

Summary:
- In Stage 1 of the study, all eligible AML patients with demonstrated NOXA BH3 Priming of ≥ 40% will receive treatment with Alvocidib, Cytarabine, and Mitoxantrone [ACM ('FLAM') Regimen].
- In Stage 2, all eligible AML patients with demonstrated NOXA BH3 Priming of ≥ 40% will be randomized 1:1 to receive either treatment with ACM or CM (Cytarabine and Mitoxantrone).
- In the NDHR Exploratory Arm, all eligible patients with Newly Diagnosed High-Risk (NDHR) AML with NOXA BH3 Priming ≥40% will receive treatment with ACM.
- In the NOXA Exploratory Arm, all eligible AML patients with demonstrated NOXA BH3 Priming of ≥ 30-39% will receive treatment with ACM.

Key Inclusion Criteria:
- Be between the ages of ≥ 18 and ≤ 65 Years.
- Have an established, pathologically confirmed diagnoses of AML excluding Acute Promyelocytic Leukemia (APL-M3) with a bone marrow of > 5% Blasts based on histology or flow cytometry.
- Be in first relapse or have Primary Refractory AML or have Newly Diagnosed High-Risk AML as defined in this protocol.
- Demonstrate NOXA BH3 Priming of ≥ 40% by mitochondrial profiling in bone marrow or 30-39% for NOXA Exploratory Arm.
- Have a Left Ventricular Ejection Fraction (LVEF) > 45% by ECHO or Multigated Acquisition Scan (MUGA).

Key Exclusion Criteria:
- Received more than 2 cycles of induction therapy for AML.
  - Investigational agents as part of front-line therapy for AML may be acceptable following discussion with the Medical Monitor.
  - Hydroxyurea is permitted.
- Received any previous treatment with Alvocidib or any other CDK Inhibitor.
- Received a Hematopoietic Stem Cell Transplant within the previous 2 Months.
- Have clinically significant Graft Versus Host Disease (GVHD), or GVHD requiring initiation or escalation of treatment within the last 21 Days.
- Require concomitant chemotherapy, radiation therapy, or immunotherapy.
  - Hydroxyurea is allowed up to the evening before starting (but not within 12 Hours) of starting treatment on either arm.
- Received Anti-Leukemic therapy within the last 3 Weeks.
  - Refractory patients who received therapy within the last 3 Weeks may be eligible with prior approval of the Medical Monitor.
- Diagnosed with Acute Promyelocytic Leukemia (APL, M3).
- Have active central nervous system (CNS) Leukemia.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02520011