AFM28, a Novel Bispecific Innate Cell Engager (ICE®), Designed to Selectively Re-direct NK Cell Lysis to CD123+ Leukemic Cells in Acute Myeloid Leukemia and Myelodysplastic Syndrome


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BACKGROUND
- Acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) are common hematological malignancies characterized by clonal expansion of myeloid progenitors (blasts) in the bone marrow and peripheral blood.
- Progress in both indications has lagged behind other hematological tumors and novel therapies for patients with relapsed or refractory (R/R) disease and minimal residual disease (MRD) are needed.
- Natural killer (NK) cell-based innate immunotherapy has emerged as a promising treatment option for AML and MDS based on the susceptibility of leukemic blasts for NK cell killing and clinical activity of allogeneic NK cell therapy in R/R disease.
- Depletion of leukemic stem cells (LSCs) alongside leukemic blasts is key to eradicate MRD and prevent relapse; therefore, drugs that effectively target both cell types hold promise in achieving long-term remission in patients with AML/MDS.
- The chimerin-like 3-receptor, CD123, is an attractive target for antibody-based immunotherapeutic approaches to target LSCs and leukemic blasts in AML and MDS, because of its almost universal expression on these cell types.
- Inactivated Cell Engager (ICE®) molecules developed from the Redirected Optimized Cell Killing (ROCK®) platform are designed to bivalently engage CD16A/NK cells and macrophages and induce potent, tumor-directed cytotoxicity via antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).
- AFM28 is a novel, tetravalent, bispecific ICE® designed to bind CD16A and CD123 and induce potent depletion of LSCs and leukemic blasts in AML and MDS.

OBJECTIVES
- Preclinical development of AFM28 and investigation of its mechanism of action as a novel treatment modality for patients with AML or high-risk (HR) MDS.
- Testing of safety, tolerability, and pharmacokinetics profile of AFM28 in a preliminary toxicology model in cynomolgus monkeys.
- Activation of NK cells by AFM28 is target-dependent and does not induce lysis of CD123+ bystander cells.