Evaluation of Combination Tagraxofusp (SL-401) and Hypomethylating Agent (HMA) Therapy for the Treatment of Chronic Myelomonocytic Leukemia (CMML)

Aishwarya Krishnan1, Bing Li, MD2, Mikhail Roshal M.D3, Maria Pagane3, Erin McGovern, BA4, Zoe Stone-Molloy3, Janice Chen, PhD5, Christopher Brooks, PhD3, Ross L. Levine, MD1 and Raajit K. Rampal, MD, PhD6
1Memorial Sloan Kettering Cancer Center, New York, NY. 2Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Jinan, China 3Memorial Sloan Kettering Cancer Center and Columbia University, New York, 4Center for Hematologic Malignancies, Memorial Sloan Kettering Cancer Center, New York, NY 5Stemline Therapeutics, New York, NY 6Leukemia Service, Department of Medicine, 7Memorial Sloan Kettering Cancer Center

Introduction
Chronic myelomonocytic leukemia (CMML) is a clonal hematopoietic stem cell disorder which often progresses to acute myeloid leukemia (AML). The only known cure for CMML remains allogeneic stem cell transplant. Hypomethylating agents (HMAs) such as Azacitidine (AZA) and Decitabine (DAC) have been utilized to treat CMML patients with variable efficacy, such that complete response only occurs in a minority of patients.

Recent work has identified CD123 (interleukin-3 receptor-α; IL-3Rα) as a potential therapeutic target in myeloid malignancies. CD123 is expressed in a variety of myeloid malignancies, including AML, myelodysplastic syndrome (MDS) and CMML.

Tagraxofusp (Elzonris™, SL-401) is a targeted therapy directed to CD123, comprised of recombinant IL-3 fused to a truncated diphtheria toxin payload. Clinical studies of tagraxofusp are being carried out in CMML. Data from an ongoing Phase I/II trial of tagraxofusp in relapsed/refractory CMML (n=16 patients) demonstrated spleen size reductions in 100% (8/8) patients with baseline splenomegaly and 2 bone marrow complete responses (BMCRs)

Given this activity, and the known activity of HMAs in CMML, we sought to determine if combination HMA and tagraxofusp may provide added therapeutic utility over HMA therapy alone.

Conclusions
Although HMA therapy has demonstrated efficacy in CMML, the effects are often limited in extent and duration. Our preclinical data, including in primary CMML samples, demonstrates a potential therapeutic role for the combination of an HMA and tagraxofusp in CMML. Further studies are ongoing to characterize this combination strategy.