Aleta Biotherapeutics Presents *In Vivo* Results of a Novel Therapeutic Designed to Reactivate CAR T Cells in Patients Who Relapse After CAR T Therapy

Novel CD19-anti-CD20 bridging protein technology to prevent and reverse relapse presented at ASH 2019

NATICK, Mass., December 7, 2019 – Aleta Biotherapeutics, a privately held immunotherapy company focused on transforming cellular therapeutics to allow a broad spectrum of cancer indications to be targeted, today presented *in vitro* and *in vivo* results demonstrating that Aleta's novel CD19-anti-CD20 bridging protein prevents and reverses CD19-negative relapse from CAR-CD19 T cell treatment.

"FDA-approved CAR-CD19 T cell therapies such as tisagenlecleucel and axicabtagene ciloleucel have demonstrated remarkable success in treating B cell cancers including refractory and relapsed acute lymphoblastic leukemia and non-Hodgkin lymphoma. However, relapse rates of up to 50% have been reported, most occurring within 6 months of CAR-CD19 T cell therapy. Some patients relapse due to the loss of expression of CD19 on tumor cells and other patients relapse because the cell therapy has failed to fully control tumor cell proliferation," said Paul Rennert, Ph.D., President and Chief Scientific Officer, Aleta Biotherapeutics. "The studies we presented today demonstrate that Aleta's CD19-anti-CD20 bridging protein can reactivate CAR-CD19 T cells to prevent and to reverse relapses by redirecting CAR-CD19 T cells to the novel antigen CD20, present on the majority of B cell malignancy tumor cells. Aleta has identified a development candidate for the treatment of B cell malignancy patients relapsing from CAR-CD19 treatment and based on these and other studies, we are advancing this program into development and then into Phase 1 clinical trials."

Results Presented at ASH 2019

A stabilized form of the CD19 extracellular domain (ECD) was cloned in frame with an anti-CD20 antibody fragment and an anti-albumin antibody fragment, to create a monomeric CD19-ECD-anti-CD20 bridging protein with extended circulating half-life characteristics. The protein was purified from a mammalian cell expression system. Protein stability, binding affinities, and cytotoxic activity were analyzed *in vitro*.

The Aleta CD19-anti-CD20 bridging protein was shown to be expressed at high levels, readily purified and highly stable. The purified bridging protein directed CAR19 cytotoxicity against CD19-negative/CD20-positive cells with superb potency (IC_{50} = 0.7 pM = 0.04 ng/ml). CAR-CD19 T cells that were previously activated by a CD19-positive tumor cell could subsequently be activated by a CD19-negative tumor cell in the presence of the Aleta CD19-anti-CD20 bridging protein.

In vitro, CAR19 T cells found and eliminated CD19-negative cells that escaped from CAR-CD19 T cell treatment. *In vivo*, CAR-CD19 T cells, plus the injected Aleta bridging protein, controlled tumor cell growth, preventing escape from therapy, while CAR-CD19 T cells alone did not prevent tumor relapse. The growth of an aggressive mantle-cell-derived tumor cell line was only delayed by therapy with CAR-CD19 T cells alone but was fully eradicated when CAR-CD19 cells were given along with Aleta's CD19-anti-CD20 bridging protein injected systemically. In a parallel set of studies, it was shown that CAR-CD19 T cells modified to secrete the CD19-anti-CD20 bridging protein were as effective as CAR-CD19 T cells given in the presence of the purified bridging protein.

About Aleta Biotherapeutics

Aleta Biotherapeutics is an immunotherapy company focused on transforming cellular therapeutics to allow a broad spectrum of cancer indications to be targeted, including currently intractable solid tumors. The company was founded by Paul Rennert and Roy Lobb, who bring extensive scientific and leadership experience in immunology, oncology and drug development to this new enterprise. Aleta has created a unique portfolio of multi-antigen targeting solutions for cell therapy, designed to address the critical issues of CAR-T persistence, tumor antigen loss leading to patient relapse, and tumor antigen heterogeneity. For more information, visit www.aletabio.com.

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