Background: NexImmune’s artificial immune modulation (AIM™) technology is designed to direct T cell function and drive a T cell-mediated response. AIM antigen-specific immunotherapies rely on a nanoparticle-based artificial antigen presenting cell (aAPC) platform. The off-the-shelf injectable nanoparticles (INJ) are developed using biodegradable PLGA-PEG or PLA-PEG core materials and designed to mimic the function of natural APCs. AIM INJ nanoparticles present (i) an antigen-specific recognition signal delivered by an MHC molecule loaded with an antigenic peptide (Signal 1), and (ii) a co-stimulatory signal (anti-CD28, Signal 2) to induce expansion of the T cells activated through Signal 1.

Methods: AIM INJ nanoparticles were synthesized by nanoprecipitation method on the Ignite NanoAssemblr™ microfluidic system. Murine AIM INJ nanoparticles were formulated by conjugating murine protein Signal 1 and 2, and then loading with tumor-specific peptides. Physicochemical characterization, stability, and in vitro functional tests were performed to assess antigen-specific CD8+ T cell proliferation, expansion, and cytokine production upon nanoparticle exposure. In vivo biodistribution and efficacy studies were performed in B16-F10 melanoma model by s.c. injection of AIM INJ nanoparticles. Biodistribution studies were conducted using 89Zr radiolabeled nanoparticles. For the efficacy study, on day 7 after nanoparticle injection, tumor tissues were harvested and stimulated ex vivo to measure the expression of CD107a and cytokines IFN-γ, TNF-α, IL-2 by the tumor infiltrating lymphocytes (TILs).

Results: PLGA-PEG based AIM INJ nanoparticles, with ~100nm diameter, PDI < 0.2, and close-to-neutral surface charge, have round morphology and were stable in liquid formulation over 6-months. The peptide-loaded murine AIM INJ nanoparticles activated CD8+ T cells in antigen-specific manner by promoting cell proliferation, expansion, and poly-functionality. The biodistribution studies showed a significantly higher amount of AIM INJ nanoparticle accumulation in the tumor (24 hours) and draining lymph node (96 hours) compared to naked nanoparticles (no proteins/peptides). In an in vivo treatment study, we demonstrated that the peptide-loaded AIM INJ nanoparticles induced significant amounts of poly-functional CD8+ TILs in a B16-F10 melanoma model. In addition, we will present data from ongoing studies using different sizes and formulations of AIM INJ nanoparticles.

Conclusions: We demonstrated that biodegradable AIM INJ nanoparticles can activate and expand multiple antigen-specific CD8+ T cells in vitro and in vivo to induce anti-tumor activity. These studies along with other in vivo pre-clinical characterization will be used to support multiple INDs and advance AIM INJ into Phase 1 studies for various solid tumors.