SONATA’S PROPRIETARY INTRINSIC ANTIGEN RELEASE TECHNOLOGY (IART) DRIVES IN SITU GENERATION OF POTENT ANTI-TUMOR IMMUNITY ACROSS WARM AND COLD TUMOR MODELS

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Background Despite considerable progress in immunotherapy, the challenge persists in effectively targeting immunologically ‘cold’ tumors. Cytokine-driven therapy has exhibited promise; however, its integration into clinical practice has been hindered by modest efficacy and adverse effects. Moreover, this strategy is not cytotoxic, limiting antigen availability for uptake and presentation by the immune system. Limited studies have evaluated methods for enhancing the expression and release of intrinsic tumor-associated antigens. Neoantigen-based vaccination can potentially address these limitations but come with their own set of challenges: mainly, they are laborious, costly, and necessitates a highly personalized therapeutic approach. Achieving the right balance of cost, speed of development, and patient accessibility remains a challenge not adequately addressed by the currently available therapeutics.

Methods The efficacy of SNT-3010912, delivered as an mRNA payload was assessed across both warm and cold tumor models. We initiated tumor models by subcutaneously injecting tumors cells into the right flanks of 6–8 weeks old C57BL/6 (B16F10, MC38) or BALB/c mice (CT26). After the tumors reached a palpable size, the mice were randomized into treatment groups. The mRNA therapy, encapsulated in lipid nanoparticles (LNPs), was prepared and administered intratumorally. The control group received LNPs with an irrelevant mRNA payload. Treatment was delivered once daily for a total of four injections.

Results Sonata’s proprietary Intrinsic Antigen Release Technology (iART), SNT-3010912, relies on a single therapeutic that drives antigen release, immunogenicity, and specific T cell priming. Delivered intratumorally, Sonata’s iART demonstrates durable in vivo efficacy, across both warm and cold tumor models, with nearly complete tumor growth inhibition and > 80% complete responses when delivered to warm tumor models (MC38 and CT26). Importantly, when delivered in the cold tumor model, B16F10, iART demonstrates prolonged tumor growth inhibition in the majority of treated mice. Moreover, in B16F10, Sonata’s iART enhances activation of antigen-specific T cells into the tumor microenvironment and demonstrates potent engagement of the adaptive immune system. Together, we demonstrate that mice treated with Sonata’s iART exhibit a considerable survival advantage across a variety of models, highlighting the distinctive capacity of iART to drive protective immunity across a spectrum of tumor immune landscapes.

Conclusions Sonata’s iART induces a state-of-the-art form of enhanced immunogenic antigen release, incorporating an innovative adjuvant, and a novel form of immunogenic cell death, ensuring antigen release, uptake and presentation by recruited APCs. Sonata’s iART demonstrates profound efficacy across a variety of tumor models, representing an exclusive, broadly applicable off-the-shelf therapy for use in oncology.

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