

cytoTIL15: A novel TIL therapy for melanoma with superior potency and enhanced persistence without IL2 to improve safety and efficacy and expand patient eligibility

Background: Tumor-infiltrating lymphocyte (TIL) therapy is at the cusp of approval for heavily pretreated patients with solid tumor malignancies. TIL therapy currently requires IL2 for *in vivo* maintenance of TILs, significantly limiting its application due to patient safety and eligibility hurdles. cytoTIL15 is a TIL product engineered with regulatable membrane-bound IL15 (mbIL15) designed via our cytoDRiVE® platform technology. Armoring TILs with endogenous mbIL15 has several advantages over systemic IL2. Unlike IL2, IL15 does not increase immunosuppressive regulatory T cells and drives T cell differentiation towards memory phenotypes associated with long-term persistence.

Methods: cytoTIL15 uses cytoDRiVE® platform technology and consists of a carbonic anhydrase 2 (CA2) derived drug responsive domain that enables regulated expression of mbIL15 under control of acetazolamide (ACZ), an FDA-approved orally bioavailable small molecule ligand. We use a proprietary process for high efficiency transduction of TILs with regulatable

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