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

Mithun Khatkar, Rachel Burga, Kyle Pedro, Colleen Foley, Scott Lajoe, Alonso Villasmil Ocando, Jack Tremblay, Dan Thornton, Stanley Tam, Farris Nabulsi, Caroline Vallaster, Sunandan Saha, Gwen Wilmes, Gabriel Helmingjer, Jeremy Tachcha, Dhruv Sethi, Michelle Ols, Gary Vanasse, Shyam Subramanian, Jan ter Meulen
Obsidian Therapeutics, Inc. | 1030 Massachusetts Avenue, Cambridge, MA 02138

**Abstract**

- Background: Tumor infiltrating lymphocytes (TILs) therapy is at the cap of approval for heavily pretreated patients with solid tumors irreparable by conventional TIL therapy currently requires IL2 to improve persistence of TILs in vivo. We engineered IL15-expressing TILs with regulatable and irreversible inhibitors to improve persistence in vivo.
- Methods: cytoTIL15 was engineered to express IL15 and was regulated using a cytoTIL15 by a tunable promoter. Cell lines expressing IL15 alone or with a regulatable inhibitor were generated. The effect of the inhibitor was demonstrated in a 3D tumor spheroid model using an NEO HLA-matched melanoma cell line.
- Results: The cytoTIL15 cell line demonstrated higher expression and persistence compared to conventional TILs treated with cytokine cocktails. The results indicated that a single IL15-expressing cell line may represent a promising strategy for improved persistence of conventional TILs.

**Background and Product Concept**

**Product:** An engineered TIL product that expresses a regulatable mbIL15, making it a more potent and efficacious therapeutic compared to conventional TILs + IL2

**Benefits of IL15-expressing mbIL15 vs. systemic IL2**
- Drive antigen-independent TIL expansion & persistence
- Drive antigen-specific TIL expansion & activity
- Drive phenotype towards CD8+ and memory T cells
- Drive T cell exhaustion and Togu in vivo against degenerate T cell-based therapies
- IL15 expression of cytoTIL15 controlled by acetazolamide (ACZ), via CD8+ T cell & lower Treg frequencies

**Phenotype:** cytoTIL15 have a favorable cytotoxic T cell phenotype

**Persistence:** cytoTIL15 demonstrate improved persistence in vivo compared to conventional TILs + IL2

**Acknowledgements:** The authors wish to acknowledge the Cooperative Human Tissue Network (CHTN) for their supply of human tumor tissue, and the MD Anderson Cancer Center for technical support.

For questions, please reach out to Mithun Khatkar (m.khatkar@obsidianx.com)