AIM ACT, a Novel Nanoparticle-based Technology, Generates Therapeutic Numbers of Functional Tumor-Specific CD8\(^+\) T Cells with Central, Effector & Stem Cell Memory Phenotype in 14 Days

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**BACKGROUND**

- Single tumor antigen recognition via a genetically modified CAR or TCR T cell has been established as a clinically validated approach for targeting malignant cells.
- Multi-antigen specific Endogenous T cell Therapy (ECT) offers a non-genetically modified approach to generate T cells targeting multiple tumor antigens in a single cellular product.
  - Current ECT technologies depend upon endogenous dendritic cells to activate and expand antigen-specific T cells.
  - Early clinical experience demonstrates both meaningful and durable responses.
- Here we describe the development of a novel Artificial Immune Modulation (AIM\(^\text{TM}\)) platform using nanoparticle-based artificial Antigen Presenting Cells (aAPC) that consistently produce a multi-antigen specific CD8\(^+\) T-cell product with superior in vitro characteristics when compared to other T-cell products.
  - Our proprietary approach leads to direct engagement of naturally selected CD8\(^+\) T cells without requiring antigen processing and presentation by host dendritic cells.
  - aAPCs are designed to drive specific targeting of CD8\(^+\) T-cell receptors on both naive and memory T cells to trigger a desired immune response.
  - AIM-generated T cells are highly antigen-specific, highly polyfunctional and composed of high proportions of Central Memory and Stem Cell Memory phenotypes.
  - When compared to genetically modified T cell therapy, multi-antigen-specific CD8\(^+\) T cells selected from the endogenous repertoire may enhance the magnitude and durability of clinical response while reducing the potential for autoimmune toxicity.

**AIM PLATFORM**

Artificial Antigen Presenting Cell (aAPC)

- Fe+ or PLGA-PEG + Antigenic Peptides
- Synthetic Core Nanoparticle
- Signal 1 HLA-A/GA
- Signal 2 Co-stimulatory Ligand

- HLA-A2 (Class I) dimer fusion protein that can incorporate multiple tumor specific peptide antigens.
- HLA dimer can be readily modified for multiple HLA-subtypes.
- Co-stimulatory or inhibitory ligands provide specific instructions to target T cells (naive and memory) relative to therapeutic goal.
- 80nm core nanoparticle optimized for size, ligand density and ratio, and site-directed orientation.
- Coupling of surface ligands to synthetic core via covalent bonds.
- MOA: direct engagement with target T cells, followed by subsequent activation, suppression, or self-destruction as directed by Signal 2 ligand.

**AIM ACT (Adaptive Cellular Therapy)**

Cellular Expansion System Enables Rapid Antigen-Specific In Vitro T Cell Expansion

- Enrichment and Expansion (E + E) System\(^*\)
- Patient/Donor
- PBMCs
- CDB\(^+\) T Cells + Nano-aAPC
- Enrichment
- Magnetic Column
- Expansion
- Elute and Culture
- Positive Fraction
- Two Weeks Expansion
- AIM ACT T-cell Therapy
- Cancer Patient

- Expansion of therapeutic levels of tumor-specific CD8\(^+\) T cells within 20 WEEKS from the endogenous repertoire.
- Enclosed, automated cellular expansion system provides simple, scalable and cost-efficient manufacturing.
- Consistent generation of tumor-specific CD8\(^+\) T cells using different antigen peptide cocktails (sourced from patient or donor PBMCs).

**A IM ACT: ARTIFICIAL IMMUNE MODULATION ADOPTIVE CELLULAR THERAPY**

T CELL SPECIFICITY

Enriched Antigen-Specific Cell Product

- Total CD8\(^+\)/CD3\(^+\) T Cells (Day 14)
- Fresh PBMCs
- Fresh aAPCs

- MOA: direct engagement

- Clinical Scale: Automated system using PBMC leukopak

**SUMMARY**

- AIM ACT is a proprietary platform using nanoparticle-based artificial Antigen Presenting Cells (aAPC) which directly engage T-cell receptors on naive and memory T cells to trigger an immune response.
- The AIM ACT cellular product:
  - Is composed of multi-antigen specific, CDB\(^+\) restricted, T cells from an endogenous repertoire.
  - Contains from 22% up to 63% of antigen-specific CD8\(^+\) T cells (indication & donor dependent).
  - Comprises more than 90% Central and Effector Memory T Cells.
  - Includes approximately 15% Stem Cell Memory T Cells.
  - Central & Stem Cell Memory T Cells are instrumental in both initial & long-term clinical responses.
- Antigen-specific T cells retain polyfunctionality as assessed by effector cytokine production.
- Generates an immune response driven by diverse TCR repertoire.
- Clinical cellular expansion system with flexible scale-up provides simple, rapid, and cost-effective manufacturing system.
- AIM ACT Phase 1 clinical trials targeting AML and Multiple Myeloma are planned for 2019.

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