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**Preclinical Studies**

## Abstract 3

# Generation of Myeloid Cells from Cord Blood-Derived CD34+ Cells for Therapeutic Intent

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**Introduction:** Macrophages and monocytes traffic to and infiltrate complex solid tumor microenvironments where conditions can promote an immunosuppressive phenotype in resident tumor-associated macrophages that hinder effective anti-tumor immune responses. Ongoing advances in cell engineering are being adapted to modify monocytes and macrophages into efficacious anti-tumor cell therapies. However, a limiting factor to this promising therapy has been cell numbers, since monocytes obtained from adult peripheral blood mononuclear cells do not expand ex vivo.

**Objective:** We are developing an expanded allogeneic, cryopreserved, off-the-shelf myeloid cell product for the treatment of solid tumors.

**Methods:** CD34+ cells isolated from pooled donor cord blood are the starting material for generation of myeloid cells. The process has three phases: (1) expansion of hematopoietic stem and progenitor cells, (2) continued expansion and differentiation into monocytes, and (3) differentiation of monocytes into mature macrophages. Cells are characterized before and after cryopreservation by immune phenotyping, morphology, and phagocytic capacity.

**Results:** The current culture method produces several thousand HLA-DR+ CD11b+ myeloid cells at both the monocyte and macrophage stage per starting CD34+ cell. These cells make up ~70% of the final cell product along with a potentially beneficial heterogeneous mix of additional myeloid-derived cells. Immunophenotyping demonstrates expression of canonical monocyte/macrophage markers, including CD14, CD86, and CD163. Cell morphology after macrophage differentiation is similar to that of peripheral blood-derived mature adult macrophages. Importantly, the final cell product can be cryopreserved with excellent recovery of viable cells post-thaw that are functional, as demonstrated by maintenance of phagocytic potential when compared with pre-cryopreservation function.

**Discussion:** This proprietary CD34+ cell expansion and directed differentiation platform results in the generation of therapeutically relevant numbers of functional myeloid cells. Furthermore, the ability to cryopreserve these cells, with demonstrated viability and function upon thaw, facilitates their use as an off-the-shelf cell therapy, with potential for faster and less expensive routes to treatments for solid tumors that have proven resistant to other cell therapies. Additional work is being done toward engineering these myeloid cells to express proteins to enhance a patient's anti-tumor immune responses, whether these cells are used alone or in combination with other therapeutics.