

## **CAR T CELL THERAPY: FIFTEEN YEARS OF ACADEMIC DRIVING**

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We have developed platforms to manufacture T lymphocytes expressing specific chimeric antigen receptors (CARs) that have enabled the successful implementation of multiple phase I/II CAR T cell clinical trials at MSKCC -including 2 multi center trials-. Subjects with leukemia, lymphoma, myeloma, breast cancer, mesothelioma, ovarian cancer and prostate cancer have been enrolled. Over 300 CAR T cell products have been successfully manufactured and more than 200 subjects have been infused across 13 phase I/II clinical trials. In order to support these trials, we established early on a robust platform using magnetic beads coated with agonistic anti-CD3 and anti-CD28 antibodies for the selection and activation of T cells, and the Wave/Xuri bioreactor for CAR T cell expansion. We also established our own process to manufacture replication-defective gammaretroviral vectors encoding CARs. This manufacturing platform consistently allows the generation of clinical doses in less than two weeks. Using this platform, the US Food and Drug Administration granted MSK Breakthrough Therapy Designation and Orphan Drug Designation in late 2014, for its CD19-targeted CAR therapy in patients with relapsed or refractory acute lymphoblastic leukemia yielding more than 85% complete remission. This vast experience provides many insights into addressing the substantial challenges that still remain to be resolved in order to broaden the usage of CAR T cells at the Point of Care and enable the commercialization of this therapeutic modality.