tumors. Fate Therapeutics is currently using its proprietary induced pluripotent stem cell (iPSC) product platform to generate iPSC-derived CAR T cells and iPSC-derived CAR NK cells that secrete BiTEs for the treatment of solid tumors.

**Ethics Approval**
These studies were approved by Fate Therapeutics Institutional Animal Care and Use Committee and were carried out in accordance with the National Institutes of Health’s Guide for the Care and Use of Laboratory Animals.

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**Abstract 117**

**RAPID POINT-OF-CARE SUBCUTANEOUS CAR-T FROM BLOOD DRAW TO INJECTION IN 4 HOURS WITH MODIFIED LV ENCODING CARS AND SYNTHETIC DRIVER ELEMENTS ENABLES EFFICIENT CAR-T EXPANSION AND TUMOR REGRESSION**

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**Background**
Adoptive cellular therapy with chimeric antigen receptor (CAR)-T cells has demonstrated remarkable clinical activity in a number of hematologic malignancies, but product chain of custody, individualized manufacturing, preparative chemotherapy, and patient management present technical and logistical hurdles to broader implementation.

**Methods**
Lentiviral constructs for CARs (either CD19- or CD22-directed) co-expressed with a synthetic driver domain were identified from a >6 × 10⁶ diversity combinatorial library of proliferative elements, transmembrane domains, leucine zippers, and an EGFR epitope screened for cellular expansion in a lymphoreplete model. Modified serum-free-lentiviral manufacturing process was developed to reduce complexity of CAR-T and to introduce CD3-activating elements into the viral envelope allowing activation and transduction of resting lymphocytes from peripheral blood.

**Results**
Four-hour exposure of as little as 1 ml of blood to the CD3-directed CD19-targeted CAR encoding lentivirus followed by subcutaneous injection in NSG mice bearing CD19+/CD22+ Raji cells resulted in tumor regression (figure 1) and robust CAR-T cell expansion as determined by flow cytometry (figure 2) and qPCR (table 1), with peak levels >10,000 CAR-T cells/ml and less than three CAR copies per genome. In contrast, administration of the same products intravenously failed to support significant CAR-T expansion or control tumor growth (figure 3). Regression of established Raji tumors was also observed in NSG-(KbDb) (IA) animals following SC administration of CD19 or CD22 CARs with driver domains. CAR-T cells contracted in peripheral blood following tumor regression.

Regression of Raji tumor from the initial median volume of 151 mm³ throughout 40 days post subcutaneous administration of the LV transduced (at MOI 1 or 5) CD19-directed CAR T product (1M or 5M cells) in the NSG mice

**Conclusions**
We conclude that through a synthetic subcutaneous lymph node approach with modified lentiviruses and driver domains, rPOC SC may enable CAR-T generation with reduced complexity, while maintaining the ability of CAR-T cells to expand, persist and exert anti-tumor activity.

**Ethics Approval**
All animal studies were IACUC approved.

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**Abstract 119**

**IL-6 IS CRITICAL FOR MEMORY RESPONSES ELICITED BY TH17 CELLS TO TUMORS**

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**Background**
Translation of novel T cell therapies is limited by cost and time-consuming protocols involving long-term T cell