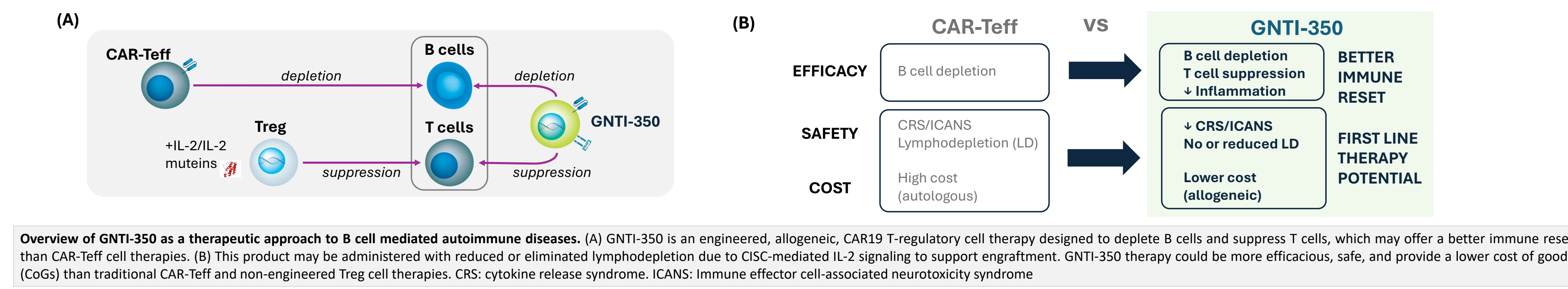


# GNTI-350: A CAR-Treg Therapy Offering Durable Immune Reset with Improved Safety for B Cell-Driven Autoimmune Diseases

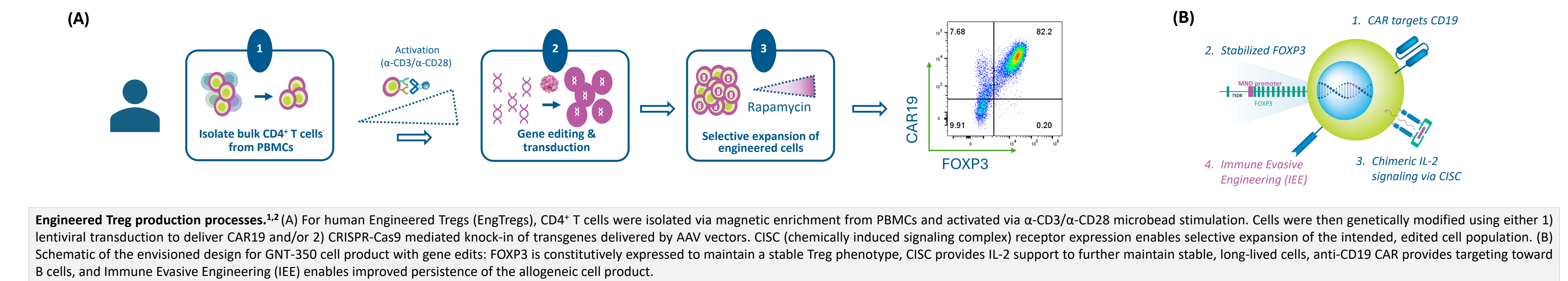
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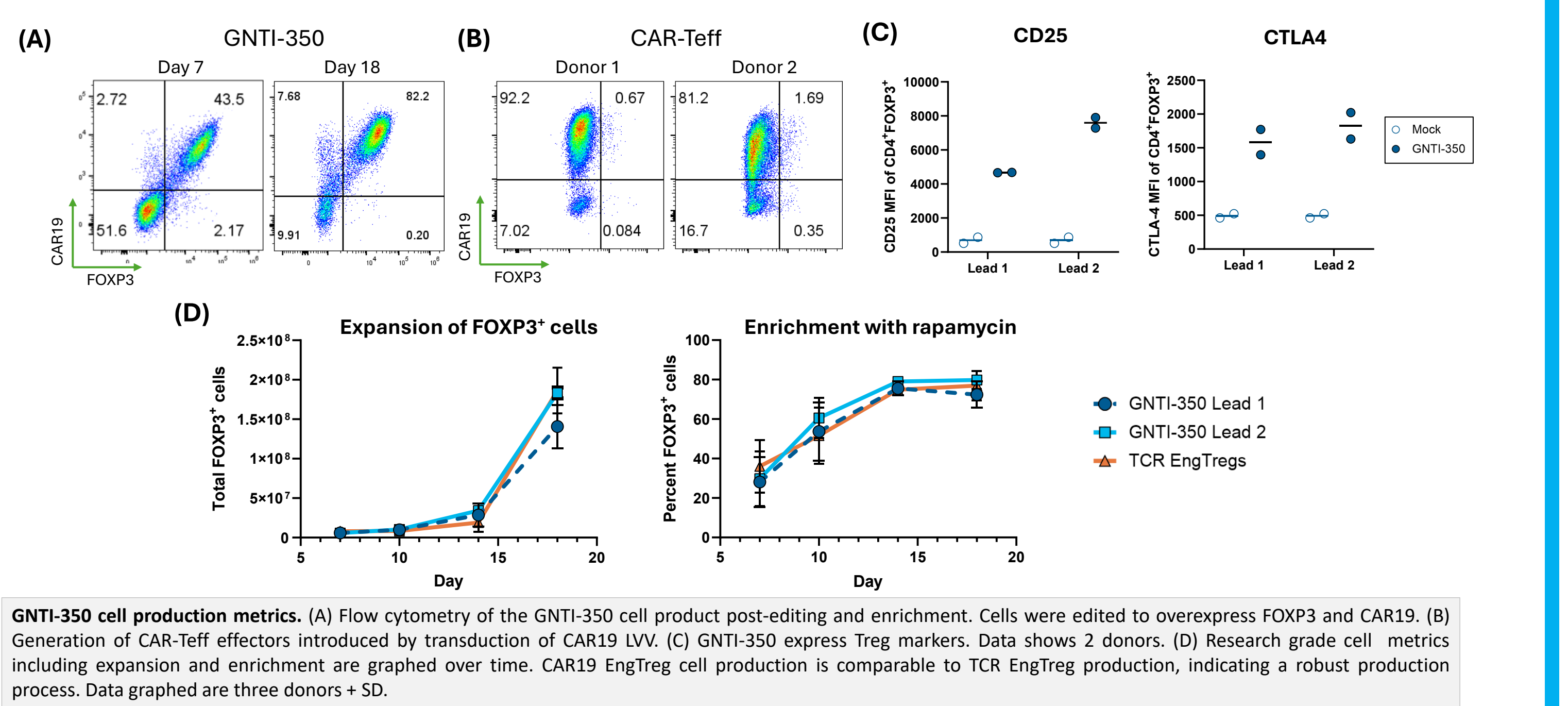
## Premise of GNTI-350: Impacts to B cells & T cells with better efficacy and safety profile than CAR-Teff



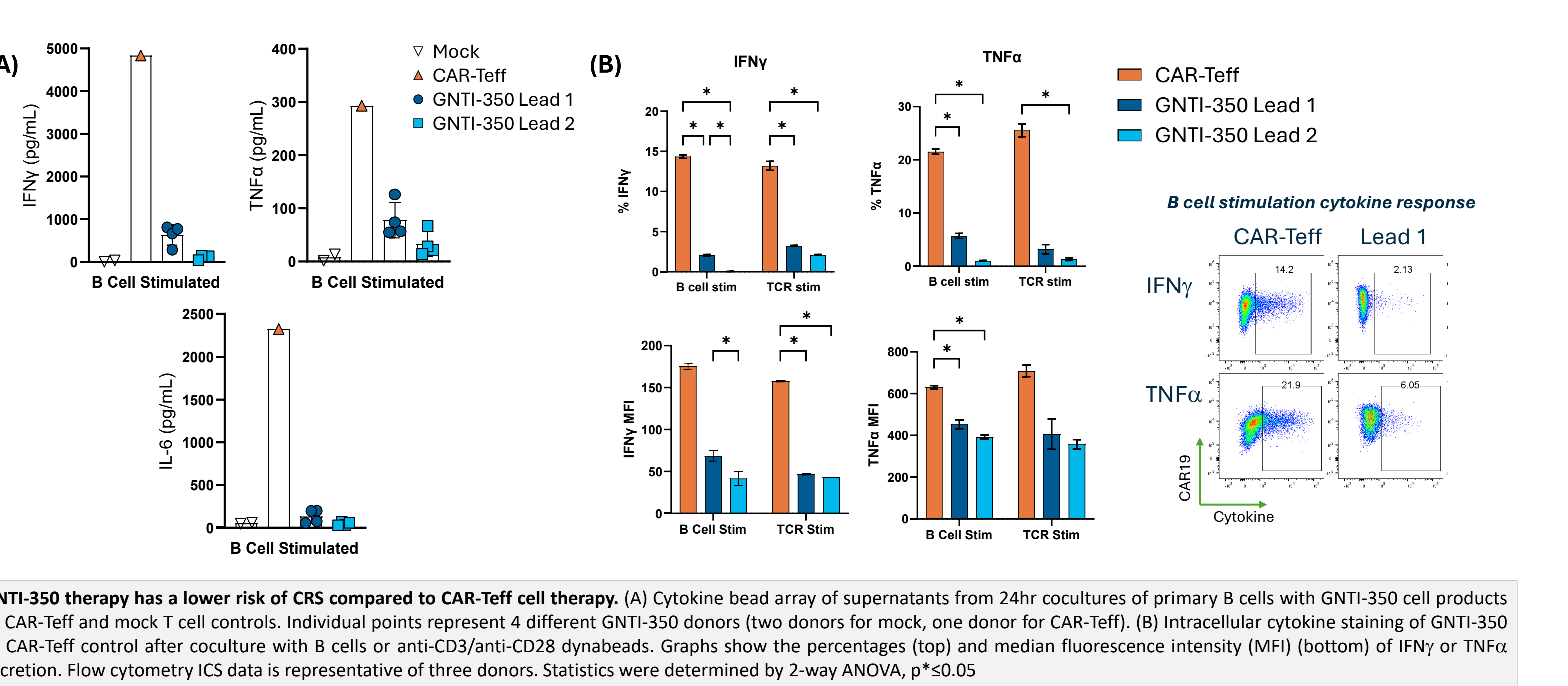
## Generation of GNTI-350: CAR19 EngTregs



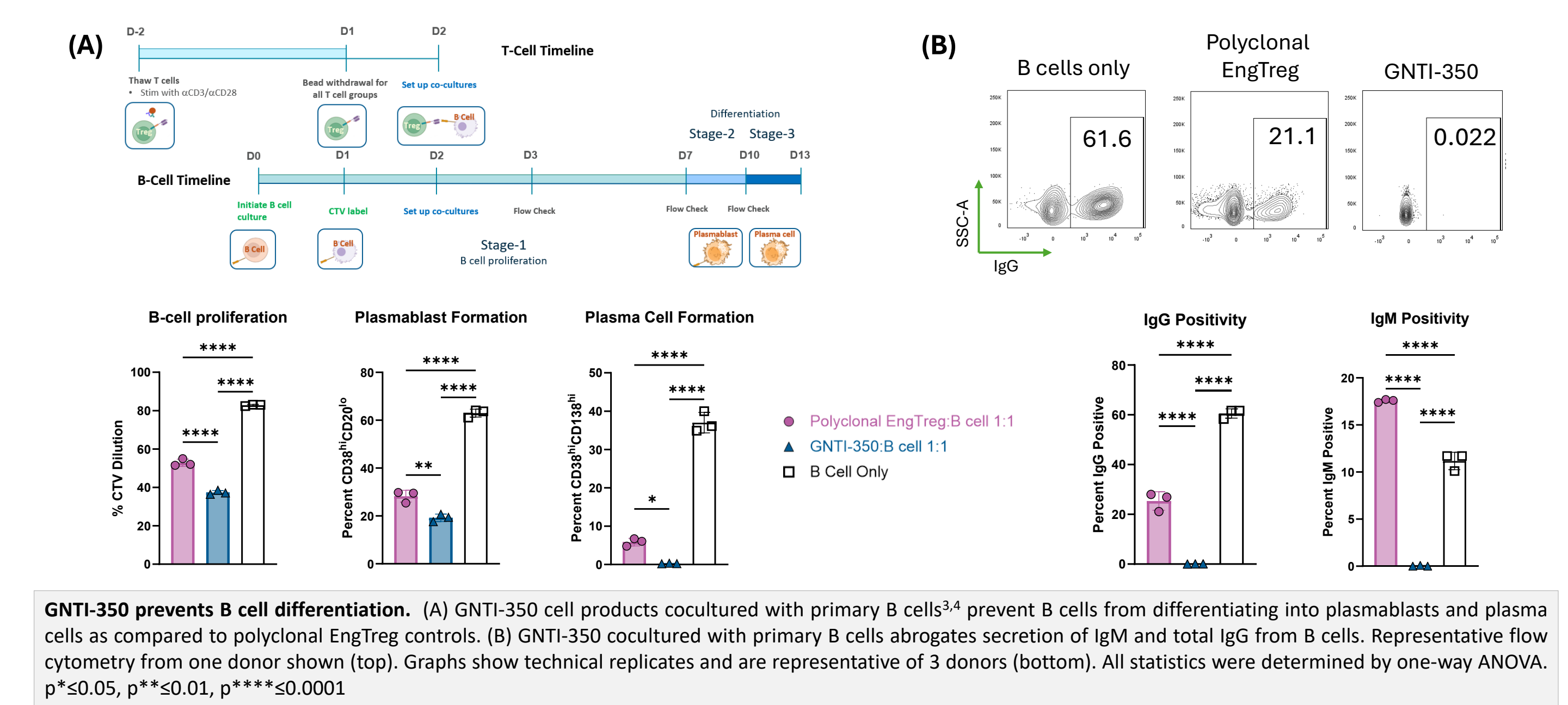
## Figure 1: GNTI-350 can be engineered and enriched with rapamycin



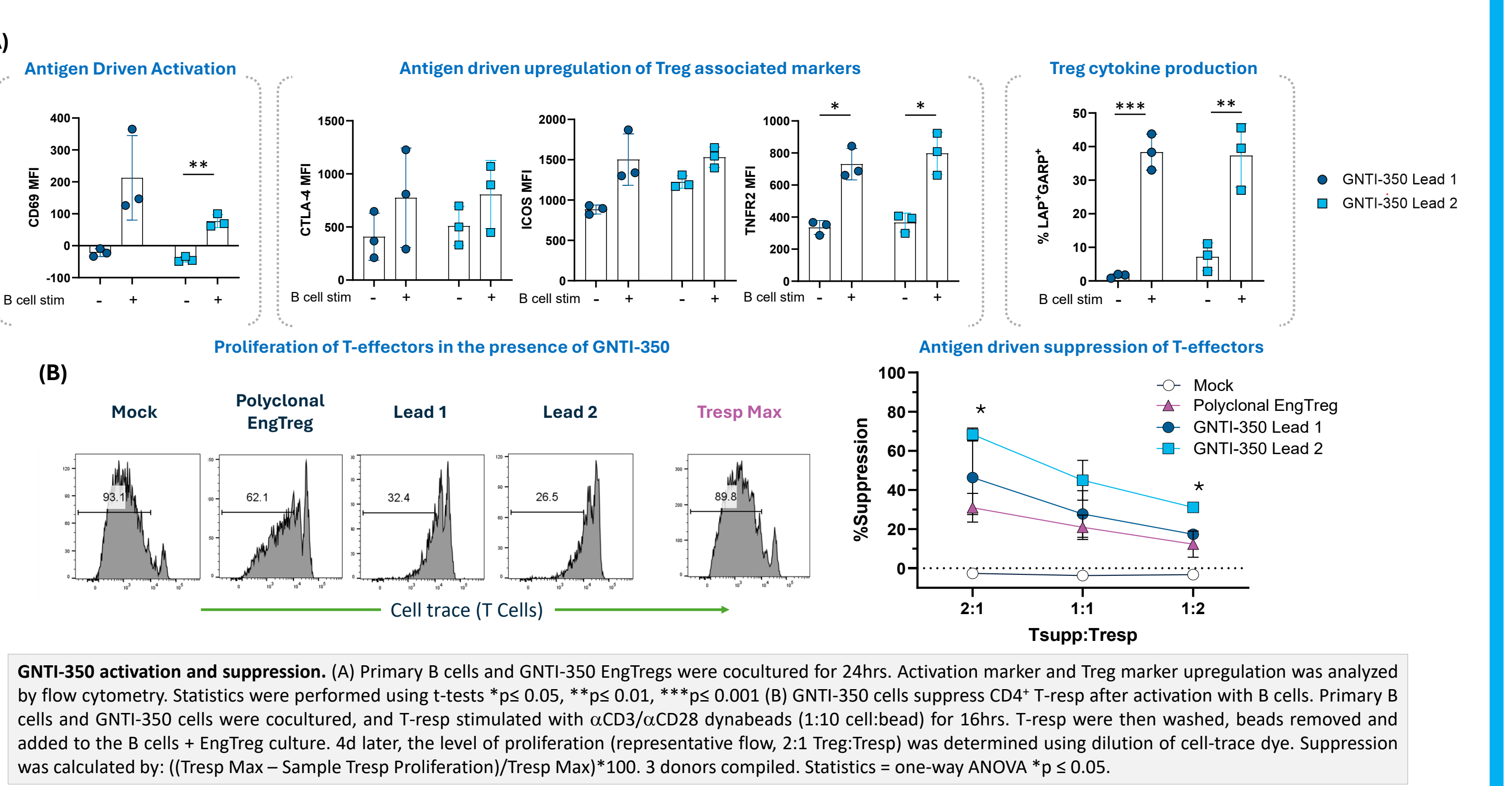
## Figure 2: GNTI-350 express lower levels of CRS-associated cytokines compared to CAR-Teff



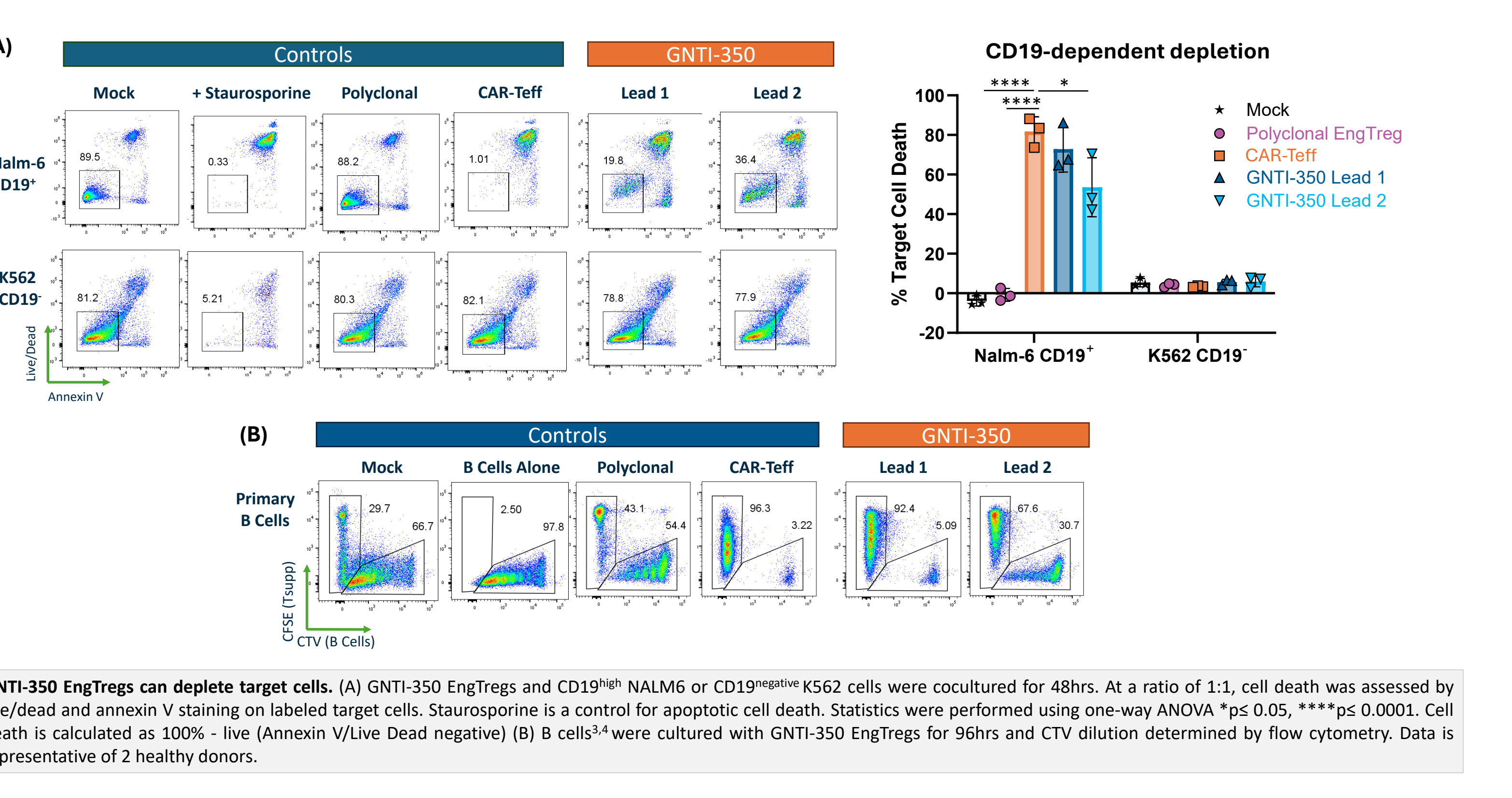
## Figure 3: Autologous GNTI-350 decreases B cell proliferation, plasmablast formation, and plasma cell differentiation after early intervention of B cell culture differentiation



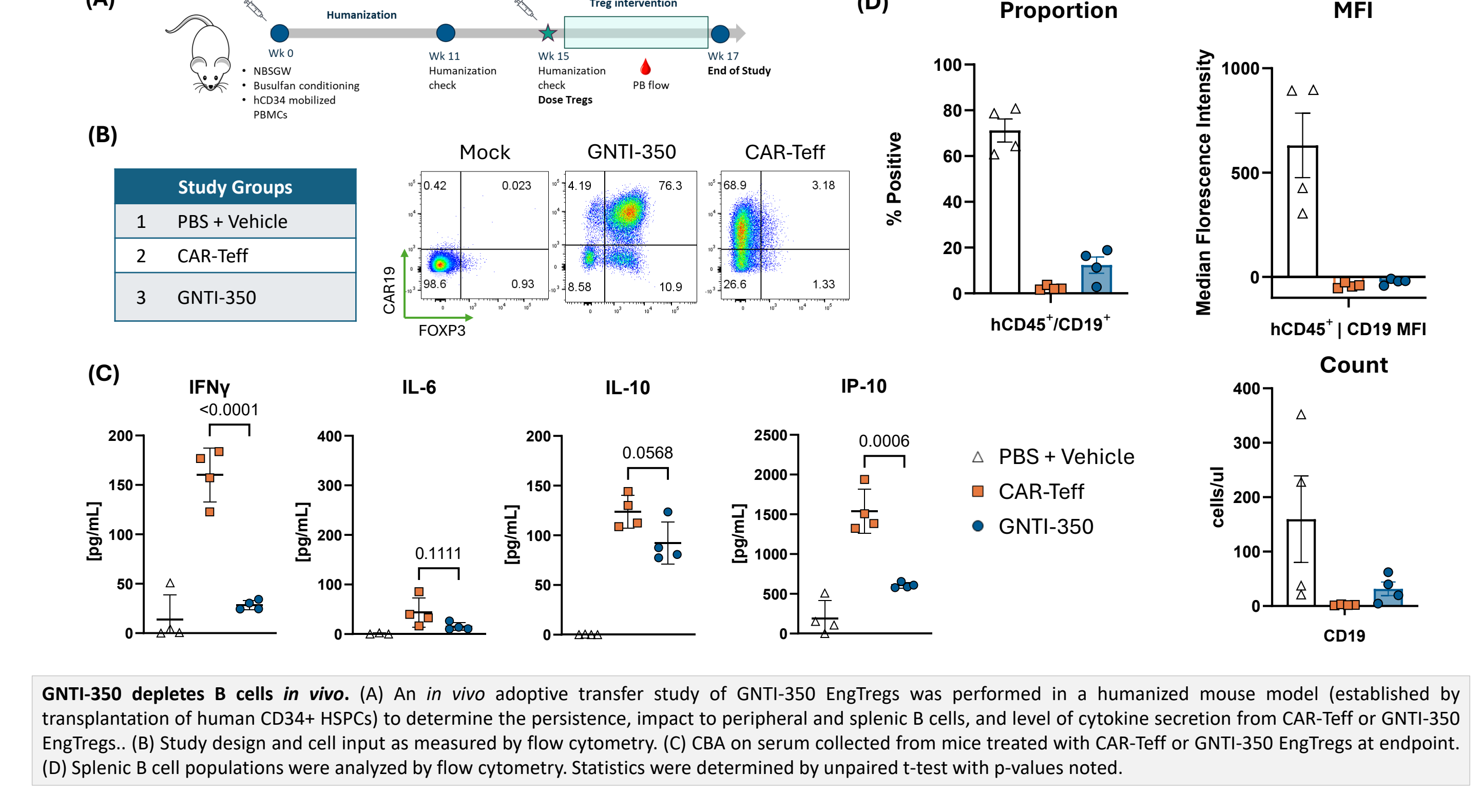
## Figure 4: GNTI-350 upregulate activation and Treg markers after B cell co-culture and actively suppress CD4+ T-effectors



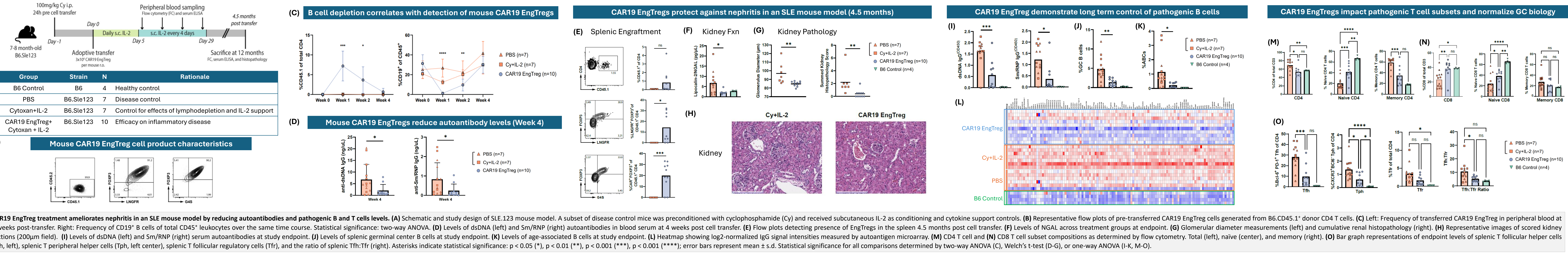
## Figure 5: GNTI-350 depletes CD19+ cells lines and primary B cells



## Figure 6: GNTI-350 results in similar B cell depletion but lower inflammatory cytokine response compared to CAR19 Teff in a humanized B cell inflammation model



## Figure 7: CAR19 EngTreg cells ameliorate disease in SLE.123 murine model



## CONCLUSIONS

- GNTI-350 can be engineered with stable FOXP3, IL-2 support through CISC, CD19 targeting, and demonstrates a Treg phenotype by surface markers and function.
- GNTI-350 demonstrates a targeted cytotoxic mechanism against CD19 expressing NALM6 and primary B cells, which suggests a CAR-Teff like B cell depletion without cytokine release syndrome side effects.
- GNTI-350 suppresses T cells and curtails plasmablast and plasma cell differentiation as a means of B-cell specific suppression.
- Lower proinflammatory cytokines compared to CAR-Teff comparators indicates a better safety profile.
- In an SLE animal model, mouse CAR19 EngTreg treatment protected against nephritis and was associated with a long-term reduction in autoantibodies and autoreactive GC and ABC B cells. Impacts were observed beyond B cells in multiple immune cell populations involved in disease pathogenesis, including reductions in levels of Tfh and Tph cells, lower activated CD8<sup>+</sup> T cells, and normalization of Tfh:Tfr ratio.

References:  
1. Cook et al. "A chemically inducible IL-2 receptor signaling complex allows for effective in vitro and in vivo selection of engineered CD4<sup>+</sup> T cells". Molecular Therapy, August 2023  
2. Uenishi et al. "GNTI-122: an autologous antigen-specific engineered Treg cell therapy for type 1 diabetes". JCI Insight, February 2024  
3. Cheng et al. "Ex vivo engineered human plasma cells exhibit robust protein secretion and long-term engraftment in vivo". Nature Communications, October 2021  
4. Hung et al. "Engineering protein-secreting plasma cells by homology directed repair in primary human B cells". Molecular Therapy, August 2017

