RESET-PV: Initial clinical and translational data evaluating rese-cel (resecabtagene autoleucel), an autologous 4-1BB CD19-CAR T cell therapy, without preconditioning, in pemphigus vulgaris

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Pemphigus vulgaris (PV) is a painful blistering autoimmune disease mediated by anti-desmoglein (anti-DSG) autoantibodies that are derived from autoreactive B cells. The current standard of care with immunomodulatory therapies for PV rarely provides durable clinical responses without chronic use. Rese-cel (formerly CABA-201) is a fully human, autologous 4-1BB CD19-targeting chimeric antigen receptor (CAR) T cell therapy, designed to deeply and transiently deplete $CD19^+$cells following a weight-based, single infusion upon discontinuation of all other immunomodulatory medications. RESET-PV™ (NCT04422912) is an ongoing Phase 1/2 trial evaluating rese-cel in adults with active PV in the absence of any preconditioning. We report on the first month of clinical and translational data from the first PV patient dosed with rese-cel at the lowest dose being evaluated in the trial, $1x10^6$ CAR T cells/kg.

As of June 6th, 2025, one patient was dosed and had at least 29 days of follow-up. The patient was a 48-year-old male with severe mucosal pemphigus vulgaris (PDAI =24) with elevated levels of anti-DSG3 antibodies at baseline, who had inadequate responses to rituximab, methotrexate, mycophenolate and glucocorticoids since disease diagnosis 7 years earlier. Rese-cel was well-tolerated with no dose-limiting toxicity or immune effector cell-associated neurotoxicity syndrome (ICANS). The patient experienced grade 1 cytokine release syndrome (CRS), manifesting as fever without other associated symptoms, which resolved following antipyretics and tocilizumab. At Day 29, the patient demonstrated a meaningful clinical improvement on the PDAI to 14 without the use of any other immunomodulatory agents.

The infusion product (IP) was $CD4^+$ dominant product (86.65% of CAR T cells) comprised of 58.2% CAR positive T cells. Transduced cells in the IP were predominantly a central memory phenotype ($CCR7^+CD45RA^-$) and exhibited *in vitro* cytolytic activity against $CD19^+$NALM6 target cells. Both CAR^+CD8^+ and CAR^+CD4^+ fractions demonstrated similar *in vitro* cytolytic activity. Following rese-cel infusion, CAR T cells peaked in circulation at 14 days post-infusion (C_{max} was 4.0 cells/µL blood) and were undetectable at all other assessed time points throughout the first month. Serum IFN-γ increased in parallel with rese-cel C_{max} with no impact on serum IL-6 and IL-8. Circulating B cells were substantially reduced within the first month post rese-cel infusion with B cell counts dropping from 377 cells/µL to a nadir of 57.4 cells/µL at 22 days post-infusion. Serum levels of anti-DSG3 antibodies remained unchanged during the first month after rese-cel infusion.

In the first PV patient dosed with rese-cel without preconditioning in the ongoing Phase1/2 study, the therapy was well-tolerated, disease activity improved, and CAR T cells expanded to detectable

levels within the first 2 weeks, corresponding to increased serum IFN-γ, similar to other AD patients dosed with rese-cel to date. Peripheral B cells were substantially, but not fully, depleted post-infusion at this dose. Together, these data support further investigation and dosing of rese-cel without preconditioning in PV patients.