Scaling Autologous CAR T Manufacturing for Autoimmune Patients

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("we," "us," "our," "Cabaletta" or the "Company") and may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial condition, and include, but are not limited to, express or implied statements regarding our current beliefs, expectations and assumptions regarding: our business, future plans and strategies for our technology; our ability to grow our autoimmune-focused pipeline; the ability to capitalize on and potential benefits resulting from our research and translational insights; our expectations around the potential success, therapeutic benefits, safety, durability and activity profile of rese-cel, including our belief that rese-cel has the potential to provide drug-free, durable, transformative clinical responses through an immune reset; our ability to successfully research, develop, obtain regulatory approval for and commercialize rese-cel and our other product candidates in current and future indications; the timing, progress, results and clinical significance of our clinical trials, including the Phase 1/2 RESET-Myositis, RESET-SLE, RESET-SSc, RESET-MG and RESET-PV trials, our ability to enroll patients, dose each cohort as intended, and advance our trials as planned, and the potential applicability of our preliminary, interim and longer-term clinical data to larger patient populations, registrational studies and future clinical trials; our expectations that ongoing clinical results will continue to support rese-cel's safety and activity profile; our plans to leverage growing clinical data to support the continued development of rese-cel; the timing and outcome of planned regulatory filings, including IND applications, initiation of registrational cohorts, our plans to submit a BLA for rese-cel in myositis (including adult and juvenile dermatomyositis) and the timing of topline data expected to support such submission; our expectations regarding interactions with regulatory authorities, including such authorities' review of safety information from our ongoing clinical trials and discussions with regulatory agencies on potential registrational pathways for rese-cel in various indications, and the timing of trial design related thereto; our plans to include juvenile dermatomyositis data in our planned BLA submission and the potential eligibility for a Priority Review Voucher, subject to supportive clinical data and applicable regulatory requirements; our plans to initiate a registrational cohort for systemic sclerosis-associated interstitial lung disease, including the anticipated study design, endpoints and timing of data; the advancement of the RESET-PV and RESET-SLE trials with and without preconditioning, including anticipated timing of longer-term clinical data; our manufacturing strategy, including automated scalable manufacturing, elimination of preconditioning, replacement of apheresis with whole blood collection, other manufacturing innovations designed to improve scalability, patient experience and cost efficiency; our expectations regarding Cellares' automated manufacturing platform, including commercial implementation, scalability, supply chain logistics and post-approval expansion; our ability to establish and expand clinical and commercial supply through third-party manufacturers and suppliers; our expectations regarding market research, potential commercial opportunities, addressable patient populations, market penetration and commercialization of rese-cel across our target indications, including DM, SSc, SLE, LN, MG and PV, and the potential expansion into additional autoimmune indications; our anticipated commercial launch strategy, including launch sequencing through academic medical centers, community hospitals and outpatient treatment settings; the potential commercial and economic benefits of automated manufacturing and elimination of preconditioning, including reduced cost of goods, lower capital investment requirements and efficient global expansion of rese-cel; our expectations regarding outpatient administration, reimbursement, pricing, coverage decisions, Medicare Part B reimbursement, commercial payer dynamics, site-of-care utilization and market adoption; our financial position, capital resources, cash runway, operating expenses and expected future financial performance; our expectations regarding the potential for rese-cel to address larger autoimmune indications beyond our current clinical programs; and our expectations regarding the success of our clinical programs, commercialization strategy and business. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements.

Various risks, uncertainties and assumptions could cause actual results to differ materially from those anticipated or implied in our forward-looking statements. Such risks and uncertainties include, but are not limited to, risks related to the success, cost, and timing of our development activities and clinical trials, risks related to our ability to demonstrate sufficient evidence of safety, efficacy, durability and tolerability in our clinical trials, the risk that preliminary, interim or longer-term clinical data may not be predictive of future or final clinical results or the results of registrational studies; risks related to patient enrollment, site activation and trial execution, risks that modifications to trial design or development strategy may not achieve the intended benefits and that the trial design may need to be further modified; risks related to our manufacturing strategy, including automation, supply chain, comparability and commercial readiness; our ability to protect and maintain our intellectual property position, risks related to our relationships with third parties, uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates, our ability to retain and recognize the intended incentives conferred by any regulatory designations, risks related to regulatory filings, potential clearance and potential approval pathways, the risk that any of our product candidates may not be successfully developed, approved or commercialized, the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies, risks related to reimbursement, pricing and market acceptance, risks related to volatile market and economic conditions and our ability to fund operations and continue as a going concern. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ materially from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K and quarterly report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the Securities and Exchange Commission. Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. The Company is the owner of various trademarks, trade names and service marks. Certain other trademarks, trade names and service marks appearing in this Presentation are the property of third parties. Solely for convenience, the trademarks and trade names in this Presentation are referred to without the ® and TM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Global CAR T demand drives innovations to improve manufacturing capacity

- Autologous cell therapies have transformed treatment across multiple disease areas
- Manufacturing capacity has been one of the major bottlenecks to patient access
  - Only 20–30% of eligible oncology patients receive CAR T today[1]
  - Autoimmune diseases may represent a much larger patient population than oncology
- A wide range of innovations to improve manufacturing scalability are in development
  - Allogeneic and iPSC derived platforms engineer consistency into the starting material, and enabling manufacturing processes to be scaled up
- In autoimmunity, autologous cell therapies have the potential to achieve greater scalability and economy via robust process design and automation

1 It's Time for CAR T, CAR T Vision, June 2025

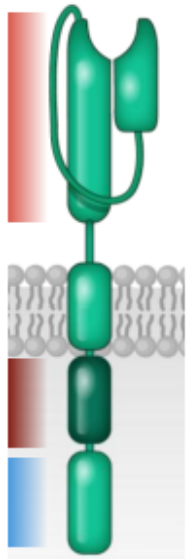
Rese-cel: CD19-CAR T specifically designed for autoimmunity

Risk-benefit profile reinforced by compelling clinical responses with safety data supporting outpatient use[5,8]

Fully human anti-CD19 binder

4-1BB costimulatory domain

CD3-ζ signaling domain



Rese-cel[2]

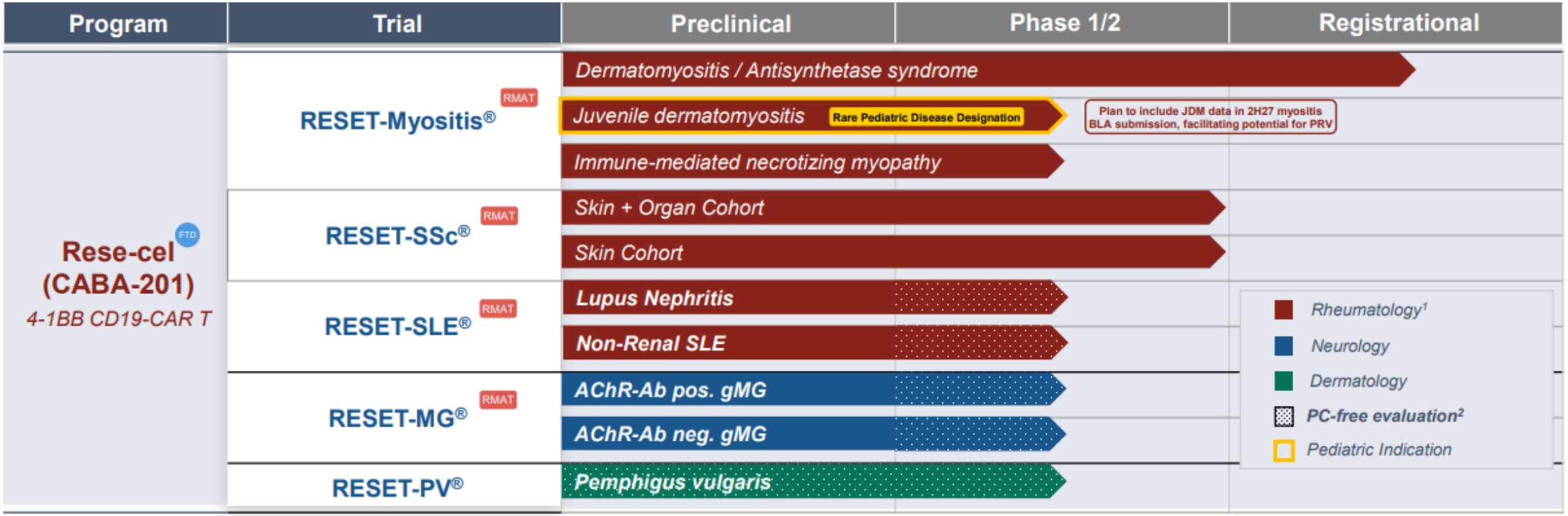
Rese-cel designed to optimize risk-benefit for autoimmune patients

1) Manufacturing uses standard, well-characterized 9-day expansion protocol
   - Leveraged academic CD19-CAR T clinical data[1]
   - Shorter processes yield more pro-inflammatory T cells[3]
2) Same weight-based dose employed as in academic studies
   - Safety data supports potential outpatient use for autoimmune patients[4,5]
   - Facilitates pediatric evaluation where weight-based dosing is common
3) Fully human anti-CD19 binder
   - Reduces anti-CAR immune rejection to enable re-dosing, if required[6,7]
4) 4-1BB costimulatory domain
   - Associated with lower CRS/ICANS risk in large oncology analyses[7]

1. Müller, F., Hagen, M., Wirsching, A. et al. “CD19 CAR-T cells for treatment-refractory autoimmune diseases: the phase 1/2 CASTLE basket trial.” Nature Medicine 32, 1142-1151 (2026).
2. Maschan, Michael, et al. “Multiple site place-of-care manufactured anti-CD19 CAR-T cells induce high remission rates in B-cell malignancy patients.” Nature Communications 12, 7200 (2021) Transmembrane domain in rese-cel is CD8α vs. TNFRSF19 (Troy) utilized in the academic construct. The two transmembrane domains have not been shown to have a significant difference in function or IFN-γ production in preclinical studies. The CD8α transmembrane domain is employed in tisagenlecleucel.
3. Dias J, et al. “CAR-T cell manufacturing landscape-Lessons from the past decade and considerations for early clinical development.” Molecular Therapy. Methods and Clinical Development. 32.2 (2024):101250
4. Volkov, Jenell, et al. “Case study of CD19 CAR T therapy in a subject with immune-mediate necrotizing myopathy treated in the RESET-Myositis phase I/II trial.” Molecular Therapy 32.11 (2024): 3821-3828.
5. Abstract 1733: Safety and Efficacy of CABA-201, a Fully Human, Autologous 4-1BB Anti-CD19 CAR T Cell Therapy in Patients with Immune-Mediated Necrotizing Myopathy and Systemic Lupus Erythematosus from the RESET-MyositisTM and RESET-SLETM Clinical Trials. ACR 2024.
6. Peng BJ, et al. Mol Ther Methods Clin Dev. 2024;32(2):101267.
7. Dai, Zhenyu, et al. "Development and functional characterization of novel fully human anti-CD19 chimeric antigen receptors for T-cell therapy." Journal of Cellular Physiology 236.8 (2021): 5832-5847.
8. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.

Innovative clinical strategy to support accelerated regulatory path

Myositis and SSc programs advancing to registrational trials with preconditioning



RESET™ – **RE**storing **SE**lf-**T**olerance; Ab – Antibody; AChR – Acetylcholine receptor; gMG – Generalized myasthenia gravis; JDM – Juvenile dermatomyositis; PC – Preconditioning; PRV – Priority review voucher; PV – Pemphigus vulgaris; SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis

1. Myositis patients can also be treated by neurologists or dermatologists; lupus nephritis patients can also be treated by nephrologists.
2. Includes planned and ongoing evaluation of the PC-free approach.

FDA Fast Track Designation received in dermatomyositis, SLE and lupus nephritis, systemic sclerosis, generalized myasthenia gravis and multiple sclerosis.

FDA Regenerative Medicine Advanced Therapy (RMAT) received in myositis, SLE, LN, systemic sclerosis, and generalized myasthenia gravis.

For more information, please visit our corporate web site here: https://www.cabalettabio.com/news-media/presentations

Cabaletta's lifecycle management approach to process evolution

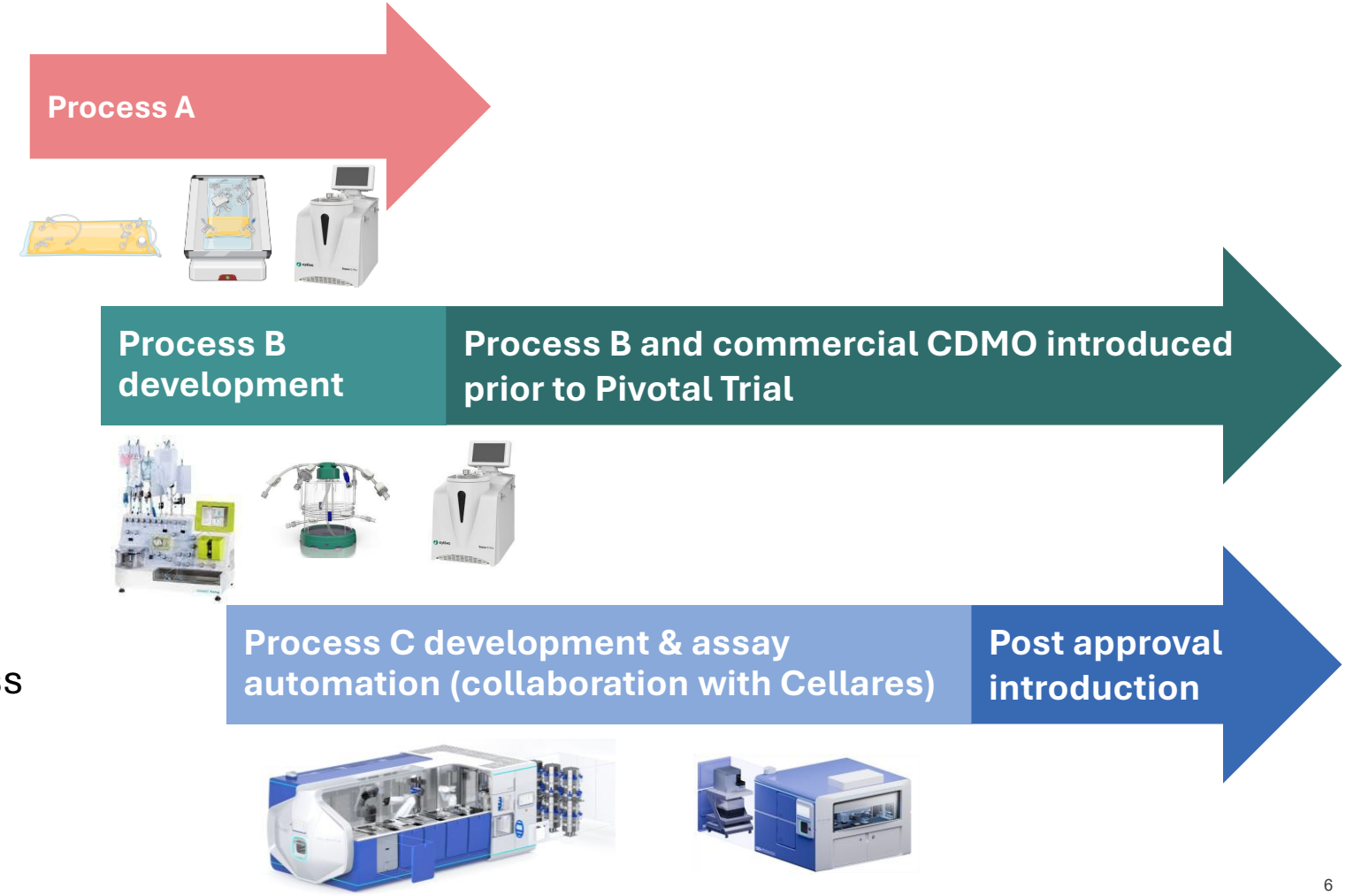
Balanced fast-to-clinic and invest early in long-term commercial success

Phase 1/2 Trial | Pivotal Trial | Commercial

Process A:
- Academic process enabled **fast to clinic**

Process B:
- Semi-automated process for **commercial launch** with 3x capacity increase

Process C:
- End-to-end automated process and release testing to meet **future commercial demand**



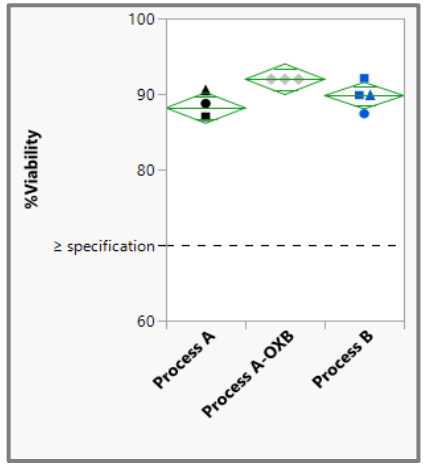
Rese-cel commercial process development strategy

- Risk assessment to determine the scope of manufacturing changes
  - No change to standard, well-tested 9-day manufacturing duration to ensure product safety profile
  - Adopted well-tested automated systems to minimize operational risks at commercial scale
  - Selected highly experienced commercial manufacturing partners
- Stage-gate process development with phase-appropriate comparability studies to maintain product quality consistency
- Leveraged FDA interactions to obtain clear guidance on comparability requirements
  - Preliminary data enabled use of previously dosed patients in safety database
  - Comprehensive comparability studies using statistically powered, split-donor materials in GMP facilities performed later to demonstrate full product comparability.

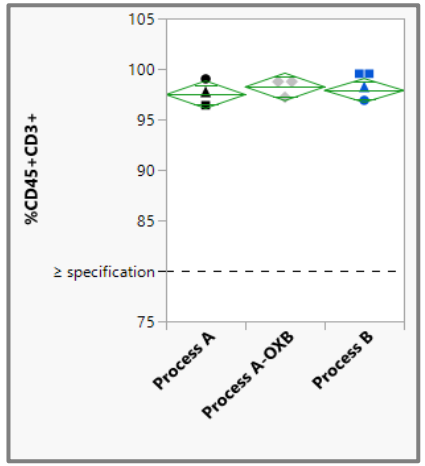
Full-scale split apheresis runs in process development

Comparable critical quality attributes between Process A and Process B

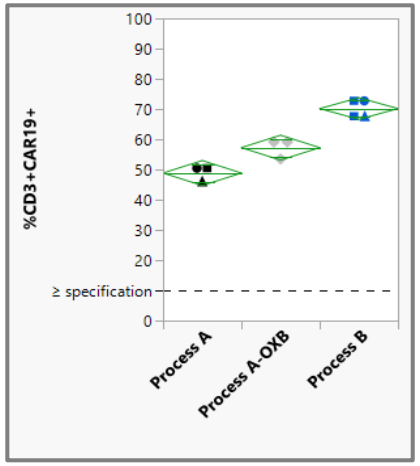
% Viability



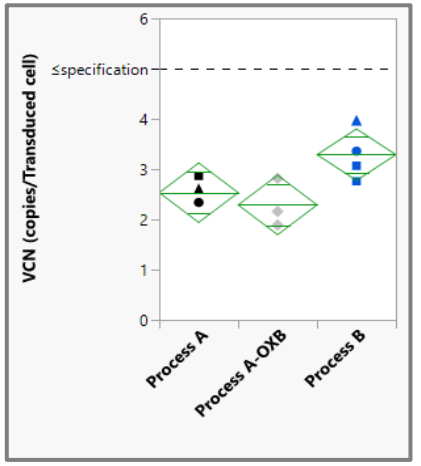
Purity: % CD45+CD3+



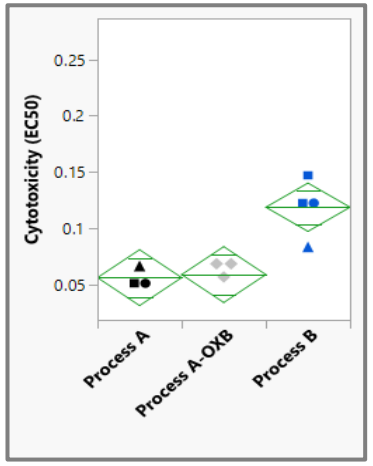
Transduction Efficiency: %CD3+CAR+



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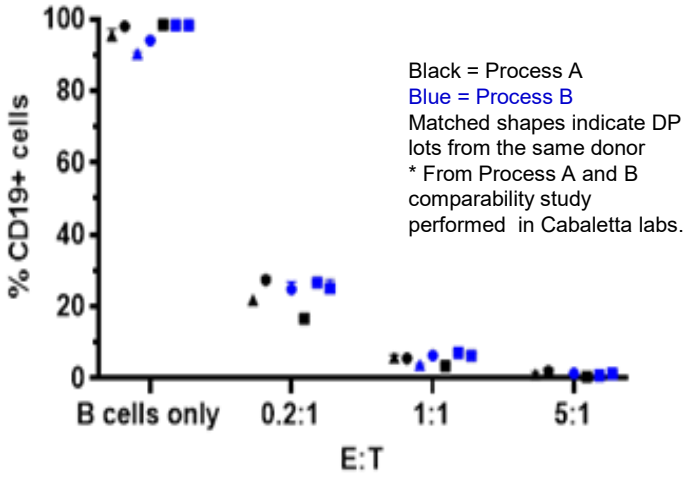


Potency Cytotoxicity: EC50



- Comparable viability and purity
- Higher transduction efficiency with Process B with acceptable VCN
- Cytotoxicity assay shows lower potency from Process B than Process A though donor matched Primary B cell killing show highly consistent results, indicating no meaningful difference between the biological activities of products from Process A and B.

Primary B Cell Killing*

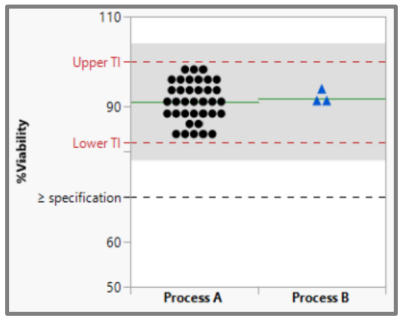


CAR=chimeric antigen receptor; CAROT= Center for Advanced retinal and Ocular Therapies; LVV=lentiviral vector; OxB=Oxford Biomedica; Plots represent 95% confidence interval.

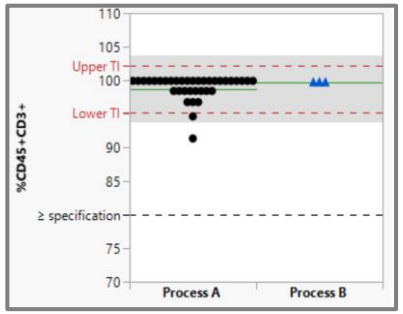
Process B engineering runs at new manufacturing site supported INDa clearance

Agreement with FDA on pooling of safety data from patients dosed with Process A and Process B drug products

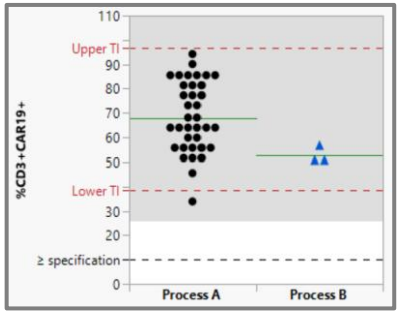
% Viability



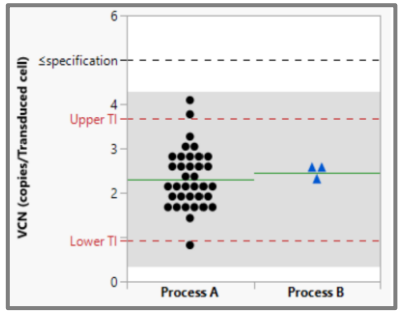
% CD45+CD3+



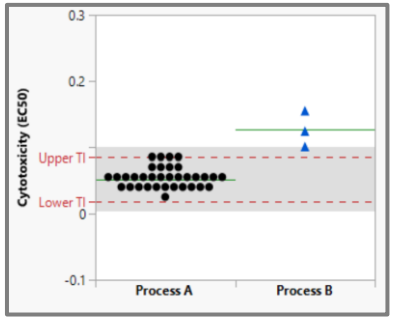
% CD3+CAR+



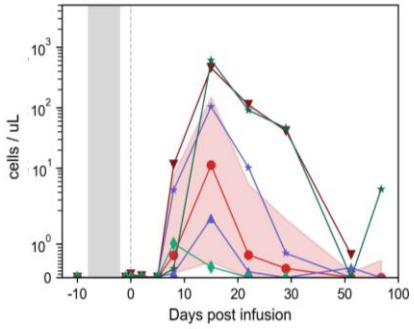
VCN



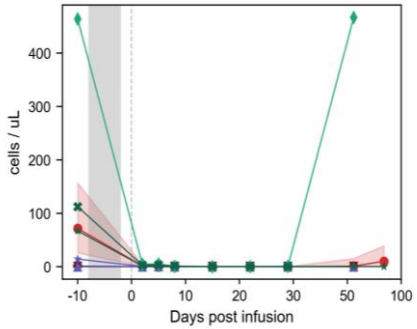
EC50

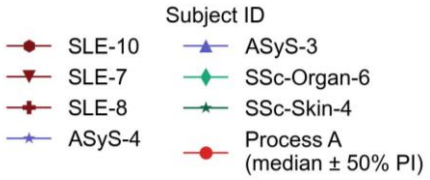


CAR T Cell Expansion[1,2,3]



B Cell Depletion[2,3]





Rese cel manufactured by Process B exhibited comparable in vivo behavior to rese cel products manufactured by Process A; comprehensive comparability studies using statistically meaningful split apheresis runs recently completed.

VCN=vector copy number; ASyS=antisynthetase syndrome; SSc=systemic sclerosis; SLE=systemic lupus erythematosus

1 Median and 50th percentile intervals of values from subjects manufactured with Process A shown in gray
2 Less follow up with Process B patients as compared to Process A at this time
3 Source: Cabaletta bio data as of 28 Jan 2026

Cellares Cell Shuttle™ automated manufacturing platform

Implementing automation in cell manufacturing can improve scalability, consistency, and cost-efficiency

- Fully closed, automated manufacturing system
  - Improves manufacturing consistency and reduces contamination
- Shuttles can be installed in controlled, non-classified space
  - No special cleanrooms to maintain
- Up to 16 concurrent processes in one shuttle
  - Allows great flexibility in shuttle use
- >500 rese-cel batches per year per Cell Shuttle[1]
- Rapid global technology transfer
  - Rapid access to capacity



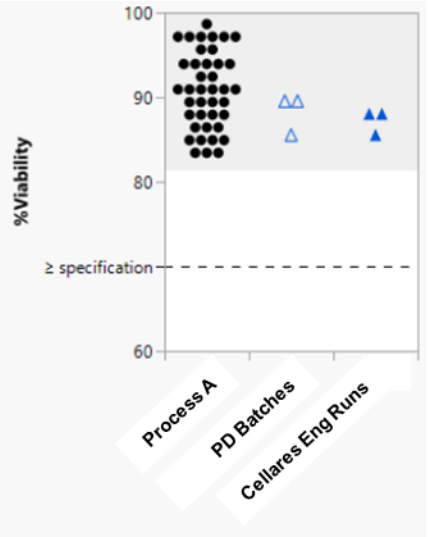


1 Based on a 9-day manufacturing process
2 Automated feasibility runs completed under TAP program, see PR on cellares.com (https://www.cellares.com/news/cellares-and-cabaletta-bio-successfully-complete-manufacturing-technology-adoption-program-for-rese-cel-using-the-cell-shuttletm-platform/)

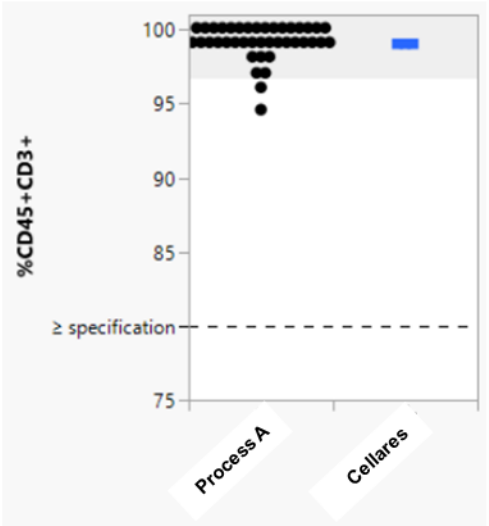
Rese-cel engineering runs with Cellares supported INDa clearance

Three successful engineering runs completed in 2025 led to IND amendment (INDa) clearance

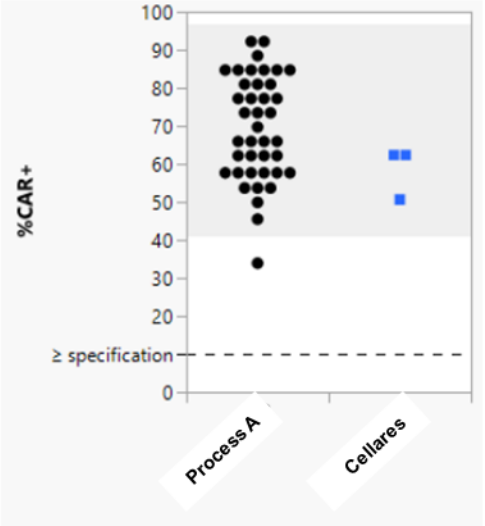
Viability[1]
(assesses T cell health)



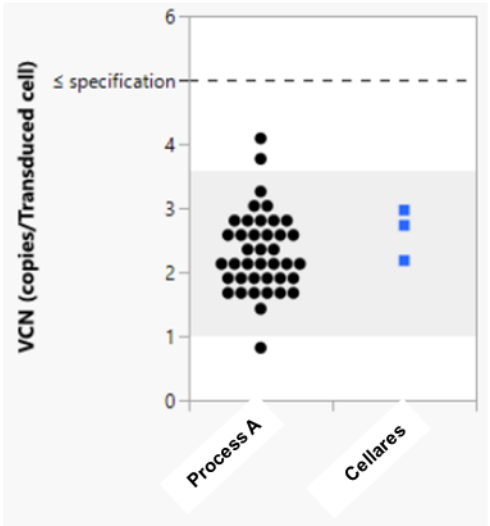
%CD45+ CD3+
(Total T cells produced)



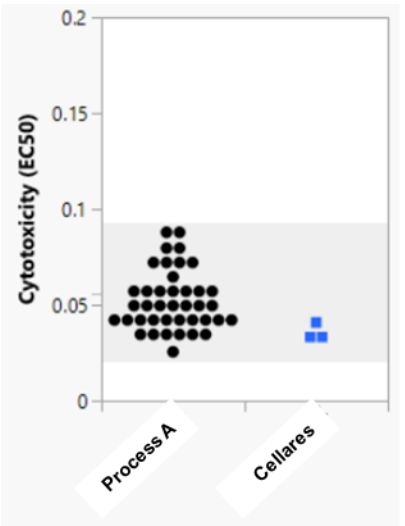
%CD3+ CAR+
(Total CAR-T cells produced)



Vector copy number
(Amount of vector per cell)



Potency
(Cytotoxicity)

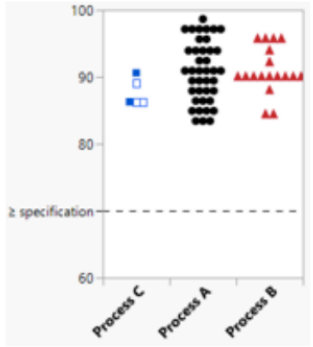


1 Cellares use Celleca for cell count to enable automated testing, while historical Process A data were collected using NC200. Data generated in Cabaletta Analytical Development lab using NC200 showed Engineering batches are within historical ranges.
Shaded areas represent historical ranges defined by tolerance intervals that covers 90% of the population with 95% confidence.

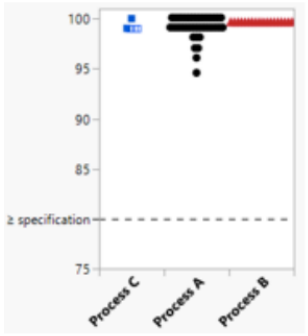
Initial automated manufacturing & translational data

Cellares automation: consistent manufacturing and translational rese-cel data in 1st 2 patients vs. traditional CDMOs

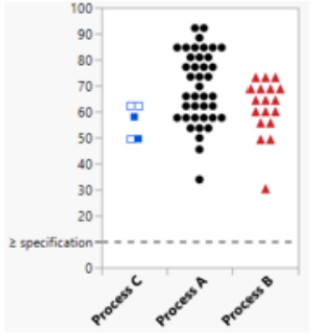
Viability [1]
(accesses T cell health)



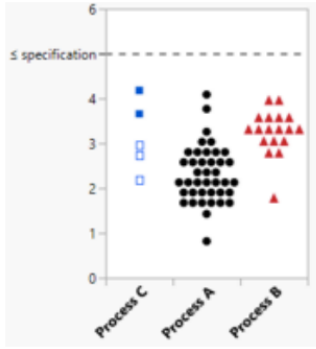
%CD45+ CD3+
(Total T cells produced)



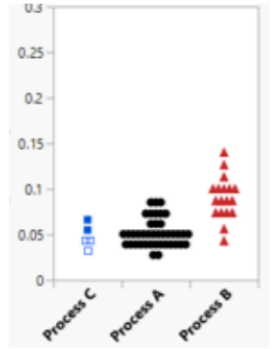
%CD3+ CAR+
(Total CAR-T cells produced)



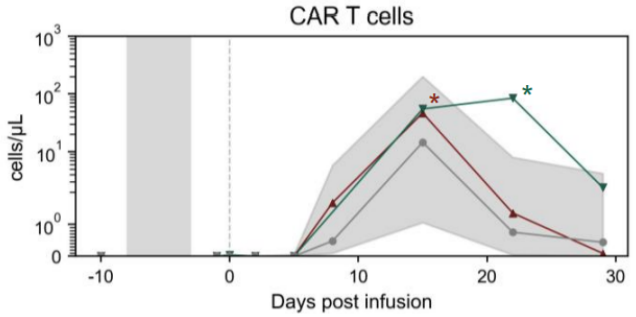
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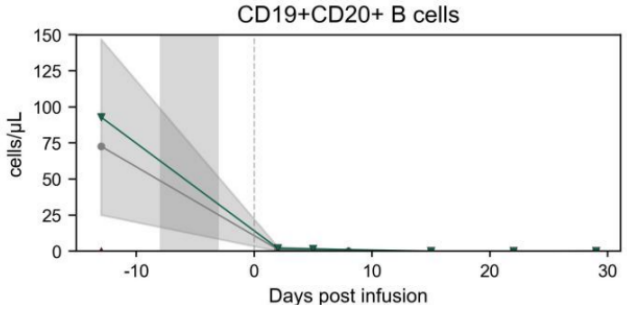
Potency
(Cytotoxicity)



CAR T Cell Expansion[2,3]



B Cell Depletion[3]



1st 2 rese-cel clinical manufacturing runs met release specifications including product quality attributes within historical ranges; initial data suggest rese-cel manufactured by Cellares exhibited comparable in vivo behavior to rese-cel products manufactured using conventional processes

1 Cellares uses Celleca for viability measurement to enable automated testing. Viability data for Process C shown in this figure were measured using NC200 to enable direct comparison with Process A and Process B, for which NC200 was also used
2 Data points with asterisks had low DNA input per assay recommendation.
3 Median and 50th percentile intervals of values from subjects manufactured with conventional manufacturing (conv) shown in gray

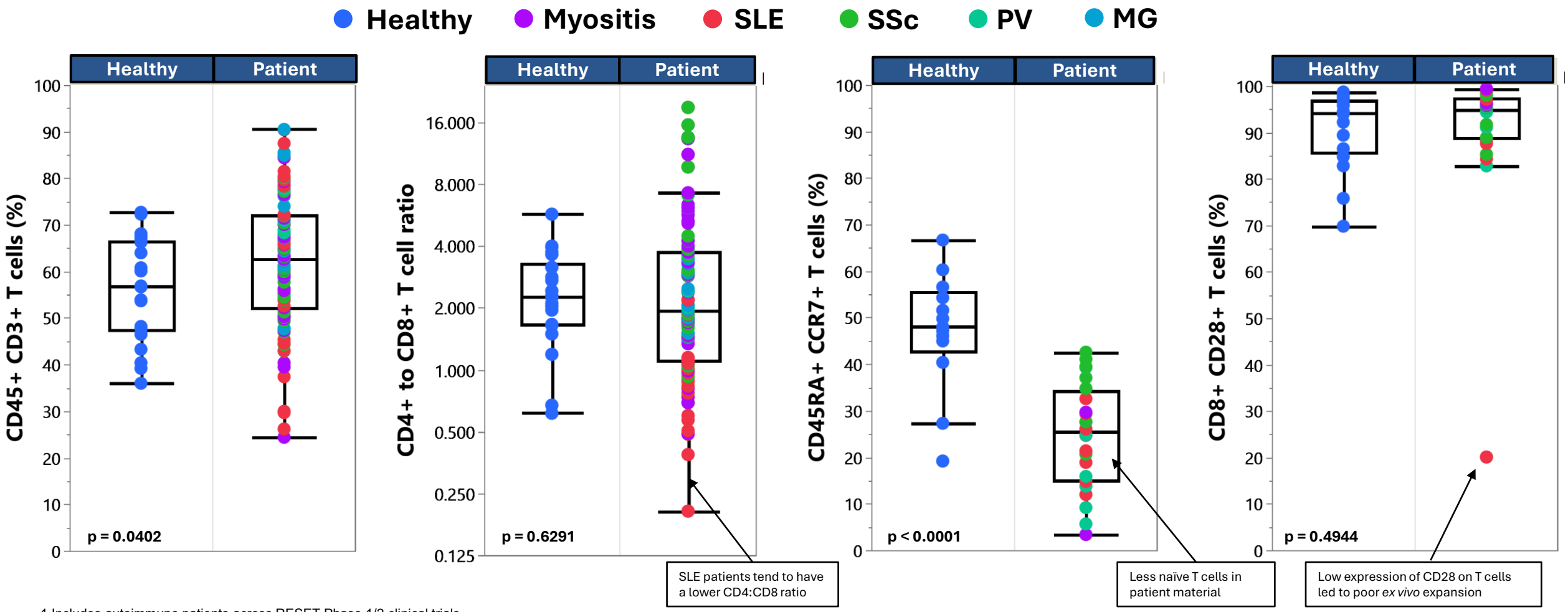
Apheresis quality from autoimmune patients provides wider opportunity for manufacturing changes

- Apheresis quality from oncology patients has historically impacted ability to meet dose requirements and relevant product quality criteria[1,2]
  - In oncology, up to 11% manufacturing failure rate across approved CD19-CAR T cell therapies[3]
- Cabaletta Bio has manufactured rese-cel for more than 106 autoimmune patients[4] across RESET phase 1/2 clinical trials and three manufacturing platforms[5]
  - Only 1 manufacturing failure attributed to patient starting material due to low expression of CD28 on T cells
- We observed autoimmune patient material behaves similarly to healthy donors[5]
  - Supports translation of early development and process characterization data from healthy donors to clinical and commercial manufacturing
  - Reduces risk of manufacturing failure and supports expanding to other autoimmune indications

1 Jo,et al. Risk factors for CAR-T cell manufacturing failure among DLBCL patients: A nationwide survey in Japan. BJHaem (2023).
2 Dulobdas, et al. Risk factors for CAR T-cell manufacturing failure and patient outcomes in large B-cell lymphoma: a report from the UK National CAR T Panel. Nature (2025).
3 U.S. Food and Drug Administration. Kymriah (tisagenlecleucel), Breyanzi (lisocabtagene maraleucel), Yescarta (axicabtagene ciloleucel). Prescribing Information.
4 Manufacturing data as of September 2026
5 Sharma et al. Consistency in resecabtagene autoleucel product quality across RESET phase 1/2 clinical trials and manufacturing platforms, ASGCT Oral Presentation, May 2026

Apheresis immunophenotype from healthy and autoimmune patients[1]

No meaningful differences in CD3+ T cells (%), CD4:CD8 ratio, or CD28 expression[2]
Less naïve T cells in apheresis from autoimmune patients[3]



1 Includes autoimmune patients across RESET Phase 1/2 clinical trials
2 Characterization data available for limited starting materials
p-values were calculated using the Wilcoxon signed-rank non-parametric test

Rese-cel commercial model – manufacturing and COGM

Health status of patient population and slower disease progression improve manufacturing cost efficiency

In oncology, disease progress & out of specification (OOS) rates increase costs and reduce margins

Late-stage oncology patients have high drop-off rate due to rapid disease progression and compromised T cell fitness, leading to higher manufacturing OOS rates[1,2,3]

- Increased OOS rates; ↑ COGM + ↓ revenue since out of spec products not reimbursed
- Disease progression reduces revenue capture because unused product not reimbursed
- Reduced eligible patients, resulting in economies of scale not being achieved
- Manufacturing capacity constraints → delayed commercial ramp-up

Rese-cel manufacturing can lead to reduced COGM via higher success rate and automation potential



Autoimmune patients are not heavily pretreated with chemotherapy → more fit immune cells that support reliable manufacture, reducing COGM



Autoimmune patients typically do not progress as rapidly as cancer patients → more reliable revenue realization for manufactured product



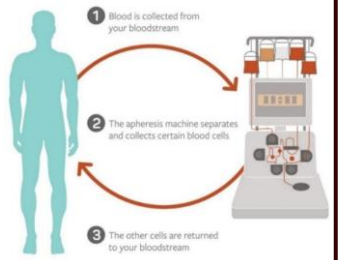
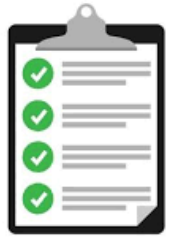
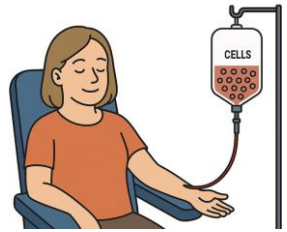
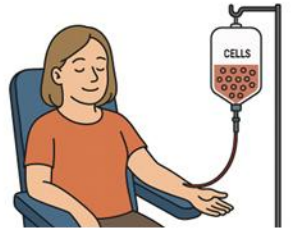
Building manufacturing capacity at CDMOs to enable successful launch; Cellares automation has the potential to facilitate post-approval expansion

COGM – Cost of goods manufactured

- U.S. Food and Drug Administration. Kymriah (tisagenlecleucel) Prescribing Information. Revised 2025, U.S. Food and Drug Administration, https://www.fda.gov/media/107296/download
- U.S. Food and Drug Administration. Breyanzi (lisocabtagene maraleucel) Prescribing Information. Revised 2025, U.S. Food and Drug Administration, https://www.fda.gov/media/145711/download
- U.S. Food and Drug Administration. Yescarta (axicabtagene ciloleucel) Prescribing Information. Revised 2025, U.S. Food and Drug Administration, https://www.fda.gov/media/108377/download

Advancing breakthrough innovations to improve scalability and costs

Automation and elimination of preconditioning and apheresis could enhance patient experience

	T cell collection	Rese-cel manufacture and harvest (9 day)			Product release	Rese-cel administration	
CURRENT	 apheresis	 cell selection and activation	 cell expansion	 cell harvest	 post-production testing and QA review	 preconditioning	 infusion
INNOVATIONS	***Blood draw to replace apheresis[1,2]***			***Cellares Cell Shuttle[3]*** • ***Fully closed, end-to-end automation*** • ***Rapid & global scalability*** • ***Shorter turn-around-time***			 ***One outpatient infusion without preconditioning[4]***

1. Stratton et al, ESGCT 2024. Poster available at https://www.cabalettabio.com/technology/posters-publications
2. (https://d1io3yog0oux5.cloudfront.net/_cdcc45a1b07d9c1e0fc529e815f21ec3/cabalettabio/db/947/8240/pdf/Whole+Blood+Mfg+Poster+ESGCT+2024.pdf)
3. Automation run feasibility completed under TAP program, see PR on cellares.com (https://www.cellares.com/news/cellares-and-cabaletta-bio-successfully-complete-manufacturing-technology-adoption-program-for-rese-cel-using-the-cell-shuttletm-platform/)
4. Under evaluation in an ongoing study in Pemphigus Vulgarus (NCT004422912); presented at ESGCT Conference 2025, presentation is available at https://www.cabalettabio.com/technology/posters-publications.

Key Takeaways

- Scalability challenges for autologous CAR T therapies can be mitigated by engineering robustness into the manufacturing process and leveraging automation
- Long-term manufacturing strategy should be developed early in the lifecycle of product to ensure commercial success
- Comprehensive data across CMC, Translational Science and Clinical Research should be considered to minimize risk to product profile due to manufacturing changes