



CARTESIAN THERAPEUTICS

Pioneering mRNA Cell Therapy for Autoimmunity

May 2024



Forward-Looking Statements

Disclosures

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Any statements in this presentation about the future expectations, plans and prospects of the Company, including without limitation, statements regarding the Company’s expected cash resources and cash runway, the Company’s estimated cash on hand, conversion of the Company’s remaining Series A Non-Voting Convertible Preferred Stock, the Company’s in-house manufacturing capabilities, the potential of RNA Armory® to enable precision control and optimization of engineered cells for diverse cell therapies leveraging multiple modalities, the potential of Descartes-08, Descartes-15, Descartes-33 and the Company’s other product candidates to treat myasthenia gravis, systemic lupus erythematosus, or any other disease, the anticipated timing or the outcome of ongoing and planned clinical trials, studies and data readouts, the anticipated timing or the outcome of the FDA’s review of the Company’s regulatory filings, the Company’s ability to conduct its clinical trials and preclinical studies, the timing or making of any regulatory filings, the anticipated timing or outcome of selection of developmental product candidates, the ability of the Company to consummate any expected agreements and licenses and to realize the anticipated benefits thereof, the novelty of treatment paradigms that the Company is able to develop, the potential of any therapies developed by the Company to fulfill unmet medical needs, the Company’s ability to enter into and maintain its strategic partnerships, and enrollment in the Company’s clinical trials and other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “hypothesize,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including, but not limited to, the following: the uncertainties inherent in the initiation, completion and cost of clinical trials including proof of concept trials, including uncertain outcomes, the availability and timing of data from ongoing and future clinical trials and the results of such trials, whether preliminary results from a particular clinical trial will be predictive of the final results of that trial and whether results of early clinical trials will be indicative of the results of later clinical trials, the ability to predict results of studies performed on human beings based on results of studies performed on non-human subjects, the unproven approach of the Company’s RNA Armory® technology, potential delays in enrollment of patients, undesirable side effects of the Company’s product candidates, its reliance on third parties to conduct its clinical trials, the Company’s inability to maintain its existing or future collaborations, licenses or contractual relationships, its inability to protect its proprietary technology and intellectual property, potential delays in regulatory approvals, the availability of funding sufficient for its foreseeable and unforeseeable operating expenses and capital expenditure requirements, the Company’s recurring losses from operations and negative cash flows, substantial fluctuation in the price of the Company’s common stock, risks related to geopolitical conflicts and pandemics and other important factors discussed in the “Risk Factors” section of the Company’s most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and in other filings that the Company makes with the Securities and Exchange Commission. In addition, any forward-looking statements included in this presentation represent the Company’s views only as of the date of its publication and should not be relied upon as representing its views as of any subsequent date. The Company specifically disclaims any intention to update any forward-looking statements included in this presentation, except as required by law.

Clinical-stage company pioneering mRNA cell therapies designed to expand the reach of cell therapy to autoimmunity

- Pipeline of mRNA cell therapies designed to be dosed more reliably and safely in an outpatient setting **without lymphodepletion**
- Descartes-08: Potential first-in-class mRNA CAR T-cell (CAR-T) demonstrated **deep and durable clinical responses** in Phase 2a study in patients with myasthenia gravis (MG)
- **Wholly-owned GMP manufacturing** designed to enable rapid optimization of processes in iterative manner

MULTIPLE ANTICIPATED NEAR-TERM CATALYSTS

DESCARTES-08

- Phase 2b topline data in MG expected mid-2024
- Initiation of Phase 2 study in SLE expected in 1H 2024
- Initiation of studies in additional autoimmune indications expected in 2H 2024

DESCARTES-15

- Next-generation mRNA CAR-T candidate
- IND cleared, with first-in-human Phase 1 planning activities underway

STRONG CASH RESOURCES

\$104.8M as of March 31, 2024; expected to fund currently planned operations into 2H26

Expected to provide for continued clinical development of Descartes-08 in MG through Phase 3 and multiple additional clinical programs

Experienced management team to lead the mRNA cell therapy company of the future

MANAGEMENT



Carsten Brunn, PhD
President and CEO



Blaine Davis
CFO



Metin Kurtoglu, MD, PhD
CTO



Emily English, PhD
SVP, Head of
Manufacturing Operations



Chris Jewell, PhD
CSO



Milos Miljkovic, MD
CMO



Jessica Keliher
CPO



Matthew Bartholomae
General Counsel

BOARD MEMBERS



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S. Cox**
Chairman



**Timothy
Barabe**
Director



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De Silva, MD**
Director



**Murat
Kalayoglu, MD, PhD**
Director



**Michael
Singer, MD, PhD**
Director



**Timothy
Springer, PhD**
Director



**Patrick
Zenner**
Director

Cartesian's mRNA approach is designed to expand the reach of potent cell therapy products to address potential autoimmune indications

Cartesian[®] mRNA Cell Therapy

No Lymphodepleting Chemotherapy Required

No requirement for cell proliferation → no expected need for pre-treatment chemotherapy → no Grade 3-4 cytopenias

Administered Outpatient

Reduced patient burden and lower indirect cost

Delivered at Therapeutic Levels

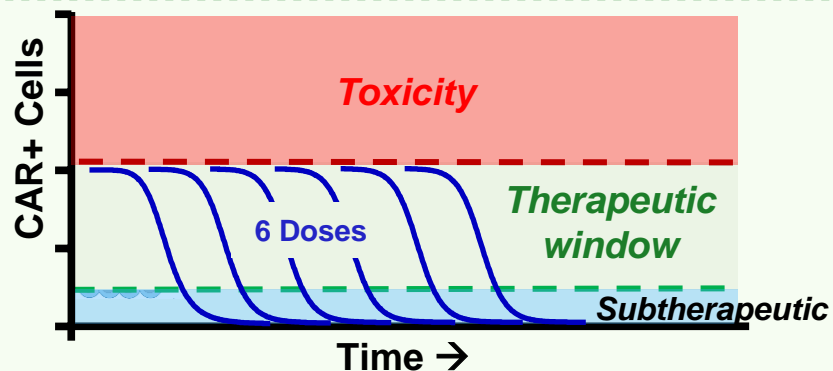
Expectation for cells to be administered at therapeutic, but sub-toxic doses

Controllable PK/PD

mRNA does not replicate → predictable half-life with more controllable PK/PD defined by the dose

Transient Cell Modification

Does not carry risk of genomic integration



Conventional DNA Cell Therapy



Requires Lymphodepleting Chemotherapy

Associated with high rates of toxicity, including cytokine release syndrome



Requires Inpatient Administration

High patient burden resulting in higher indirect costs



Administered at Subtherapeutic Levels



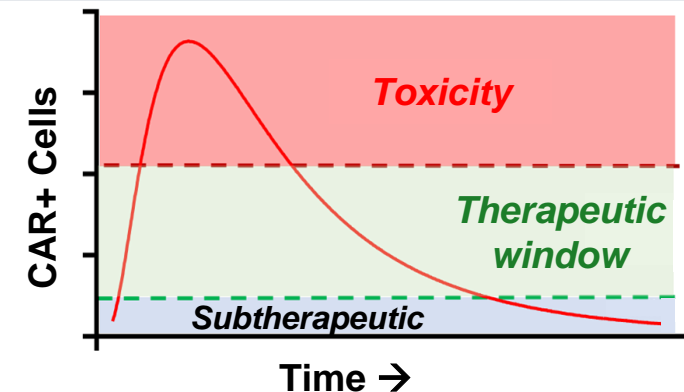
Uncontrollable PK/PD

Effector function of cell therapy engineered with DNA amplifies exponentially with cell replication



Permanent Cell Modification

Associated with insertional mutagenesis leading to potential secondary malignancies



Wholly-owned pipeline targets autoimmune disease

Asset	Indications	Discovery/Preclinical	Phase 1	Phase 2	Pivotal
Descartes-08 Autologous mRNA CAR-T	Myasthenia Gravis	[Progress bar: ~85%]			
	SLE, other Autoimmune Diseases	[Progress bar: ~65%]			
Descartes-15 Autologous mRNA CAR-T	Autoimmune Diseases*	[Progress bar: ~45%]			
Descartes-33 Allogeneic mRNA MSC	Autoimmune Diseases	[Progress bar: ~25%]			
<i>In situ</i> LN transfection	Undisclosed	[Progress bar: ~20%]			

SLE, Systemic Lupus Erythematosus
mRNA MSC, Mesenchymal Stem Cells transfected with mRNA

* Phase 1 dose escalation study in myeloma underway
LN, Lymph node

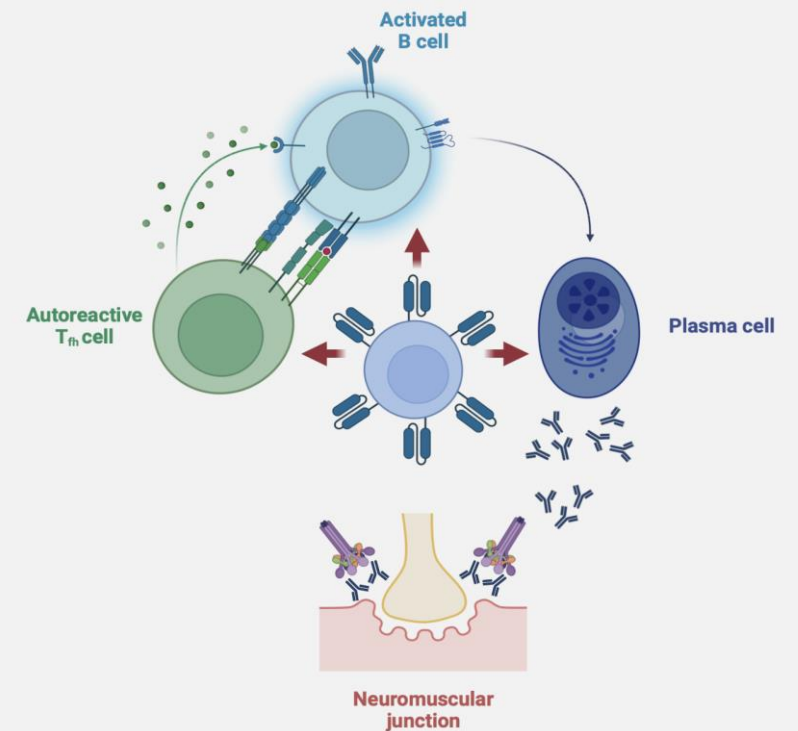
Descartes-08 is believed to be the first mRNA CAR-T in clinical development for autoimmune disease

Engineered by transfection of autologous CD8+ T cells with mRNA encoding anti-BCMA CAR

Typical lot processed for infusion within ~3 weeks

Positive Phase 2a data in myasthenia gravis underscores potential for deep and durable responses

Granted U.S. FDA orphan and RMAT designations for generalized myasthenia gravis



Descartes-08 is designed for dual action, precisely targeting two key BCMA+ cell populations involved in a spectrum of autoimmune diseases

Descartes-08 is designed to target BCMA, a surface antigen expressed on **plasma cells/plasmablasts** and **plasmacytoid dendritic cells**

PLASMA CELLS (PCs) AND PLASMABLASTS

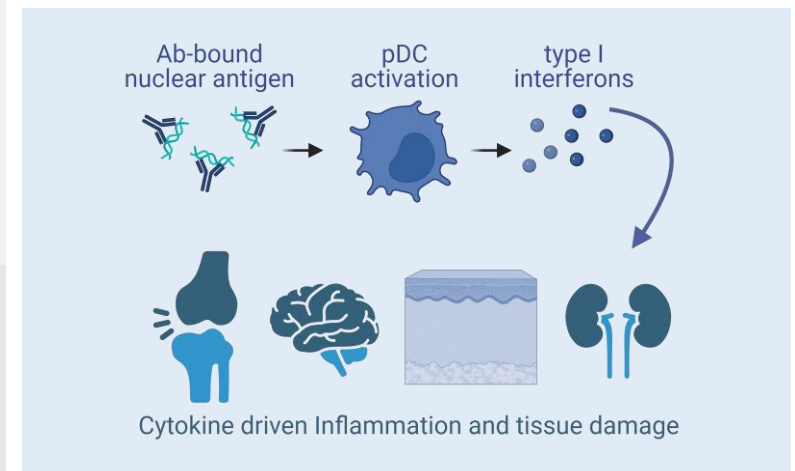
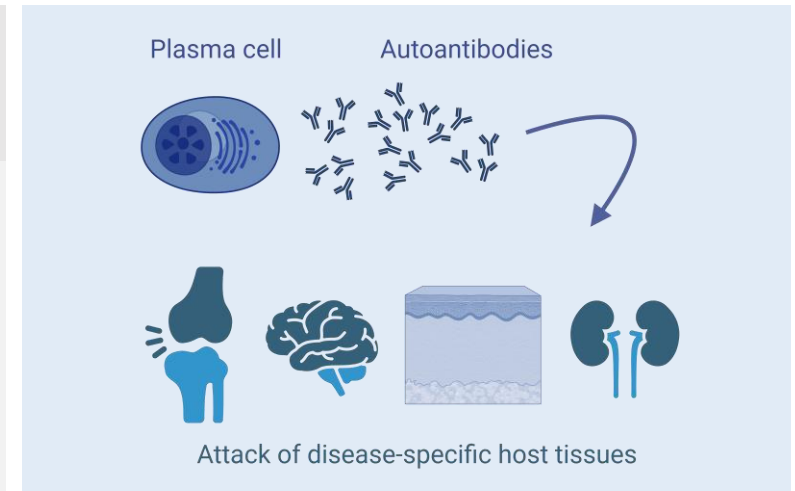
- PCs, plasmablasts and proliferating B cells targeted by Descartes-08 represent a tiny fraction of B cells
- These cells are entirely responsible for secreting pathogenic autoantibodies
- During autoimmunity, autoantibodies attack host tissue and drive inflammation

PLASMACYTOID DENDRITIC CELLS (pDCs)

- pDCs, which Descartes-08 is designed to target, are a rare subset of antigen-presenting cells
- These cells secrete high levels of cytokines (i.e., type I interferons) that cause inflammation and tissue damage during many human autoimmune diseases
- pDCs are increased in patients with autoimmunity (e.g., SLE) and interfere with optimal treatment

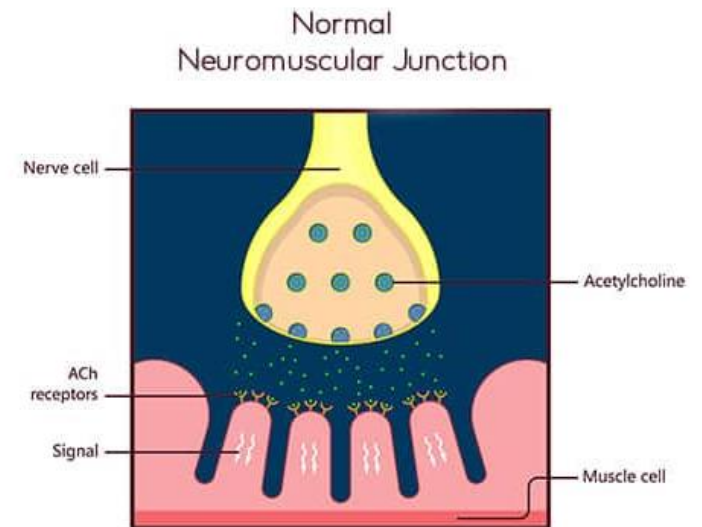
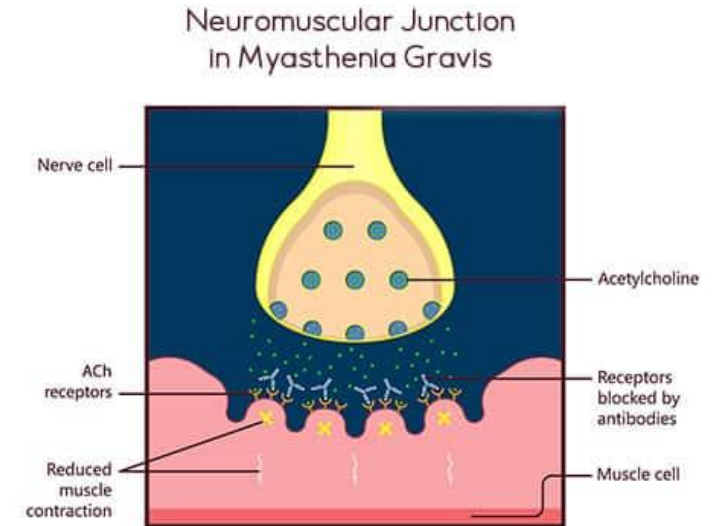
Several autoimmune disease segments involve pathogenic contributions from **both PCs/plasmablasts** and **pDCs**, including rheumatology, nephrology, neurology, and others

Selectively deleting PCs/plasmablasts and pDCs, if successful, may create a differentiated cell therapy platform

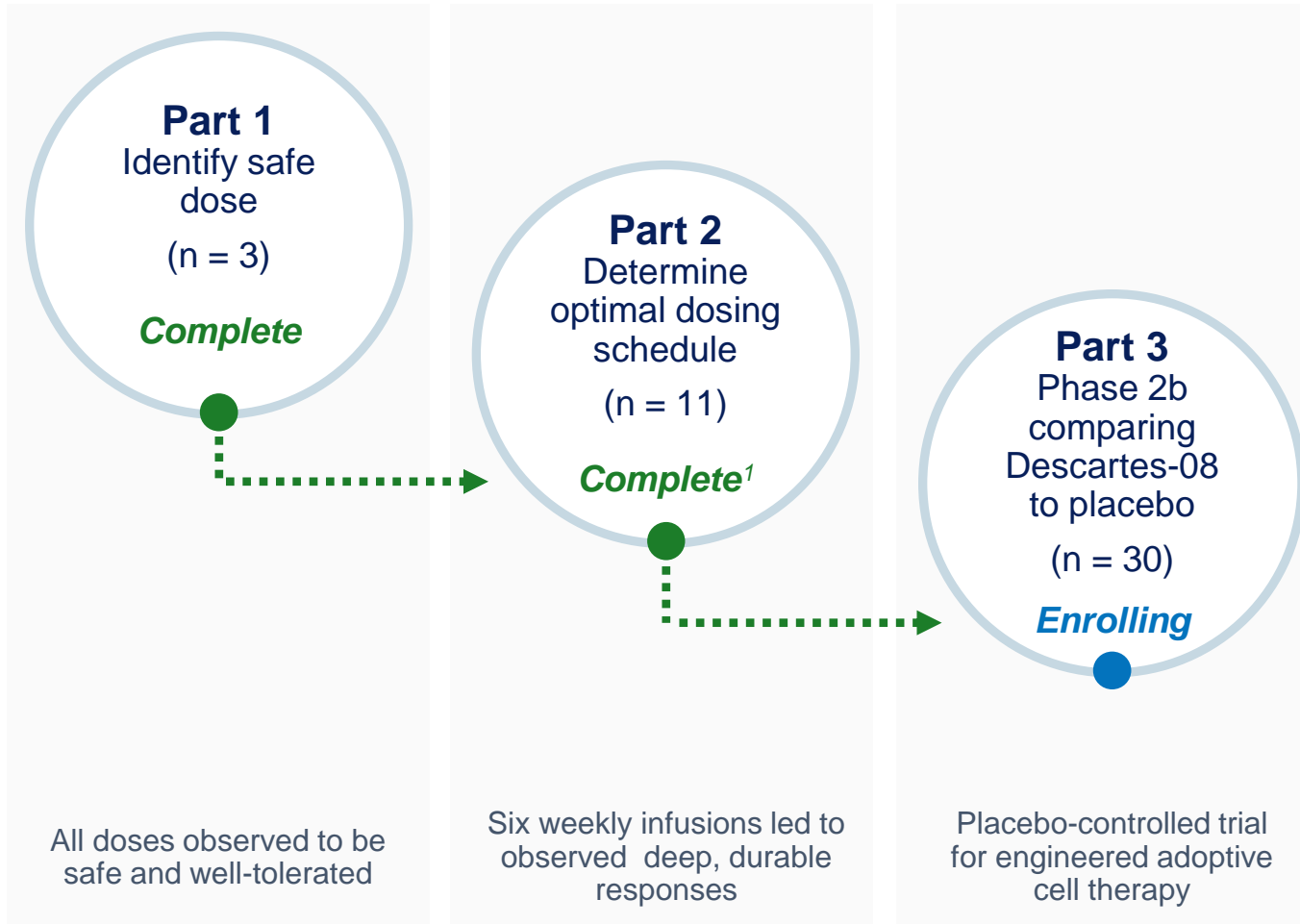


Initial indication for Descartes-08: Myasthenia gravis

- Affects **over 120,000 patients** in US and EU
- Characterized by debilitating weakness: limbs, respiratory, ocular, facial muscles
- **Standard of care** includes **chronic use of immunosuppressants**, which are **often toxic**:
 - Progressive disease that is fatal in 1/3 of patients without immunosuppressants
- Newer agents include **complement inhibitors and anti-FcRn mAbs**, which must be **administered chronically** to maintain responses
- **Pathogenesis is similar across many autoimmune diseases**; involves attack on self by both T cells and B/plasma cells



Phase 2 study of Descartes-08 in MG (NCT04146051)



Patient eligibility

- MG-ADL ≥ 6
- MGFA Class II-IV
- Stable medication dosing ≥ 8 wks prior to infusion
- 4-week washout for biologics
- IVIg and plasma exchange not allowed after starting Descartes-08

Patients on immunosuppression or complement inhibitors expected to be able to continue their treatment while receiving Descartes-08

Cell manufacturing platform tolerates most standard immunosuppressive therapies

Phase 1/2a study population comprises patients with significant disease

THE LANCET
Neurology

Volume 22, Issue 7, July 2023, Pages 578-590

- Baseline MG-ADL mean score of 10
- 79% were MGFA Class III-IV at screening
- All patients presented with disease that was not controlled with standard of care therapies

Mean age, years (SD)	52 (18)
Female	10 (71%)
Male	4 (29%)
Mean weight, kg (SD)	84 (21)
Mean BMI, kg/m² (SD)	31.6 (8.1)
Race and ethnicity	
White, non-Hispanic	11 (79%)
White, Hispanic	1 (7%)
Asian	2 (14%)
MGFA class at screening	
II	3 (21%)
III	10 (71%)
IV	1 (7%)
Median age of disease onset, years (range)	40 (14-79)
Median duration of disease, years (range)	14 (3-27)
Myasthenia gravis antibody status	
Anti-AChR antibody	11 (79%)
Anti-MuSK antibody	2 (14%)
Seronegative (for AChR, MuSK, and LRP4 antibodies)	1 (7%)
Mean baseline scores (SD)	
QMG	15.3 (4.1)
MG-ADL	10.0 (3.2)
MGC	21.9 (5.7)
MG-QoL-15r	19.9 (5.8)

Previous myasthenia gravis therapies (standard of care)	
Pyridostigmine	14 (100%)
Prednisone	14 (100%)
Other immunosuppressants	14 (100%)
Eculizumab	2 (14%)
Rituximab	2 (14%)
Previous intravenous immunoglobulin	12 (86%)
Previous plasma exchange	8 (57%)
Diagnosis of thymoma	0
Previous thymectomy	6 (43%)
Previous myasthenia gravis crisis requiring intubation	4 (29%)
Myasthenia gravis ongoing therapy	
Pyridostigmine	11 (79%)
Prednisone	10 (71%)
Azathioprine	1 (7%)
Mycophenolate mofetil	1 (7%)

Descartes-08 was observed to be safe and well-tolerated in MG

THE LANCET Neurology

Volume 22, Issue 7, July 2023, Pages 578-590

KEY OBSERVATIONS:

- No dose-limiting toxicities
- No cytokine release syndrome
- No neurotoxicity
- No pre-treatment chemotherapy and related cytopenias
- Outpatient treatment

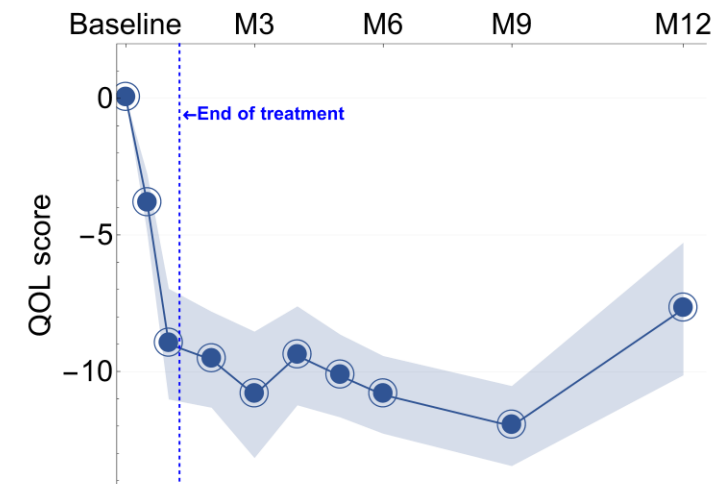
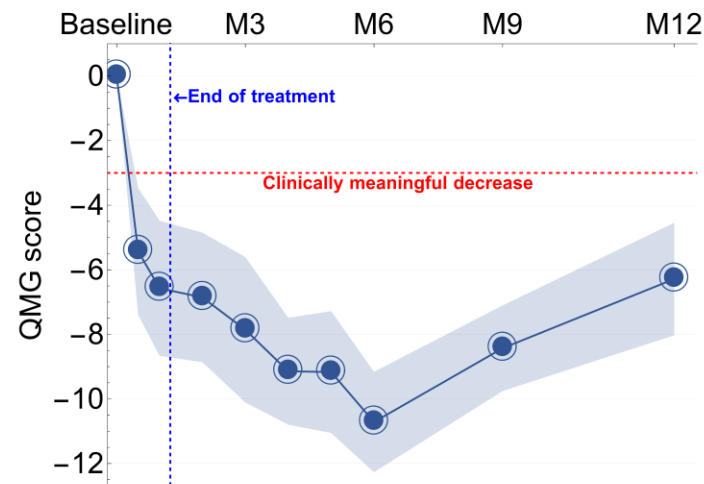
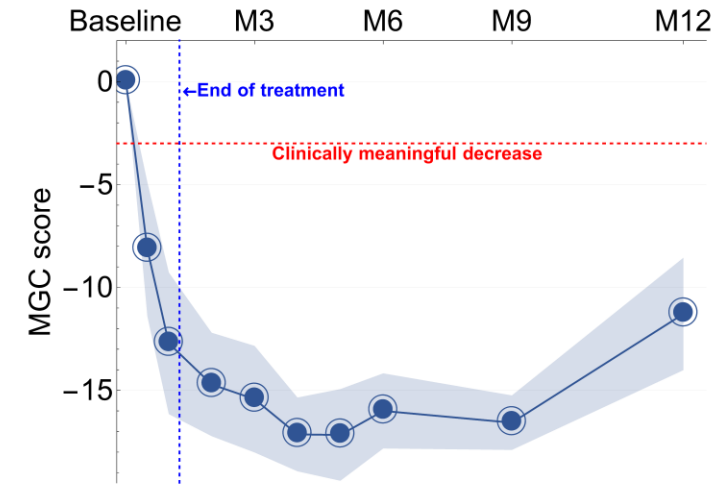
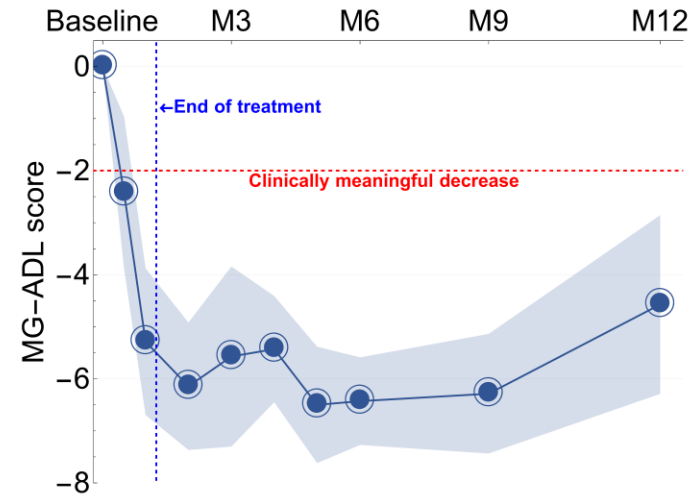
	Grade*	Part 1 (n=3)	Part 2: all groups (n=11)	Part 2: group 1 (n=3)	Part 2: group 2 (n=7)	Part 2: group 3 (n=1)
Hand numbness	2	1 (33%)	0	0	0	0
Headache	1	1 (33%)	5 (45%)	1 (33%)	3 (43%)	1 (100%)
Muscle soreness	1	1 (33%)	1 (9%)	0	1 (14%)	0
Nausea	1	1 (33%)	4 (36%)	2 (67%)	2 (29%)	0
Rash	3	0	1 (9%)	1 (33%)	0	0
Itchy throat	1	0	2 (18%)	0	1 (14%)	1 (100%)
Vomiting	1	0	3 (27%)	2 (67%)	1 (14%)	0
Weakness	1	0	2 (18%)	2 (67%)	0	0
Line infiltration	1	0	1 (9%)	1 (33%)	0	0
Fever	1	0	4 (36%)	1 (33%)	3 (43%)	0
Shortness of breath ¹	1	0	2 (18%)	1 (33%)	1 (14%)	0
Chills	1	0	2 (18%)	1 (33%)	1 (14%)	0
Diarrhoea	1	0	1 (9%)	1 (33%)	1 (14%)	0
Gum inflammation	1	0	1 (9%)	0	1 (14%)	0
Teeth sensitivity	1	0	1 (9%)	0	1 (14%)	0
Night sweats	1	0	1 (9%)	0	1 (14%)	0
Restless leg	1	0	1 (9%)	0	1 (14%)	0
Light-headedness	1	0	1 (9%)	0	1 (14%)	0

*There were no adverse events of grade 3 or higher reported in part 1, and no grade 2 or grade 4 events reported in part 2, where grade 1 is mild, grade 2 is moderate, grade 3 is severe, and grade 4 is life-threatening.

¹Not associated with hypoxia

Descartes-08 observed to induce deep and durable clinical improvement in MG

- Notable magnitude and duration of response across all 4 standard MG severity scales
- Responses appear to *deepen after completing treatment at Week 6*
- **Positive** twelve-month follow-up data from Phase 2a study reinforce prior findings published in *Lancet Neurology*

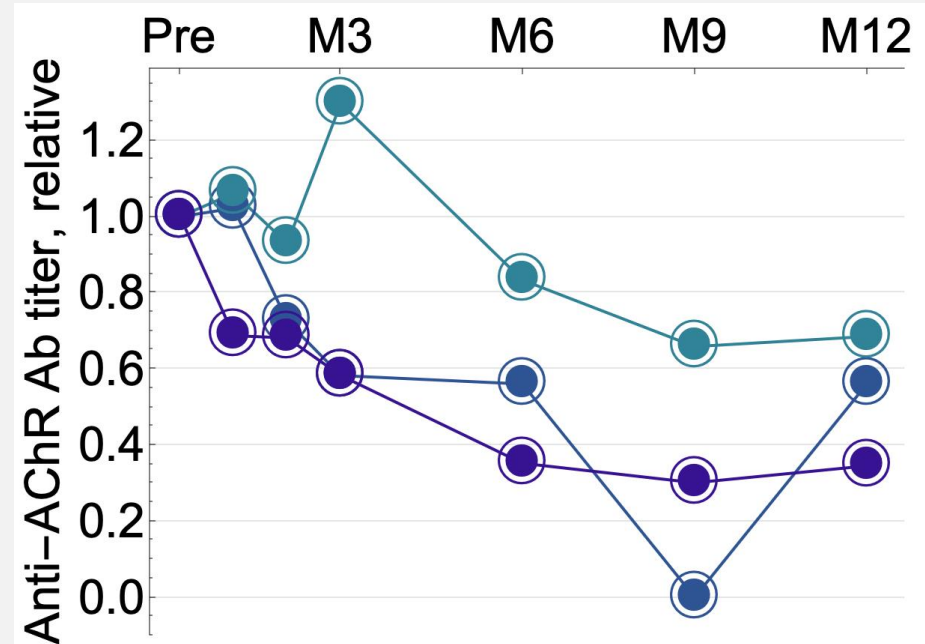


Manuscript submitted for peer review; pre-print available at medRxiv.org

Efficacy dataset includes all MG patients completing the 6-dose once-weekly regimen (n=7). Data are mean score improvement (point) and standard error (light blue shading). Note that QOL scale does not have an agreed-upon threshold for clinically meaningful disease improvement; MG-ADL, MGC and QMG scales are validated, quantitated, standardized instruments of disease severity and have been acceptable endpoints for registration studies.

Descartes-08: Durable depletion of autoantibodies consistent with observed clinical responses and MoA

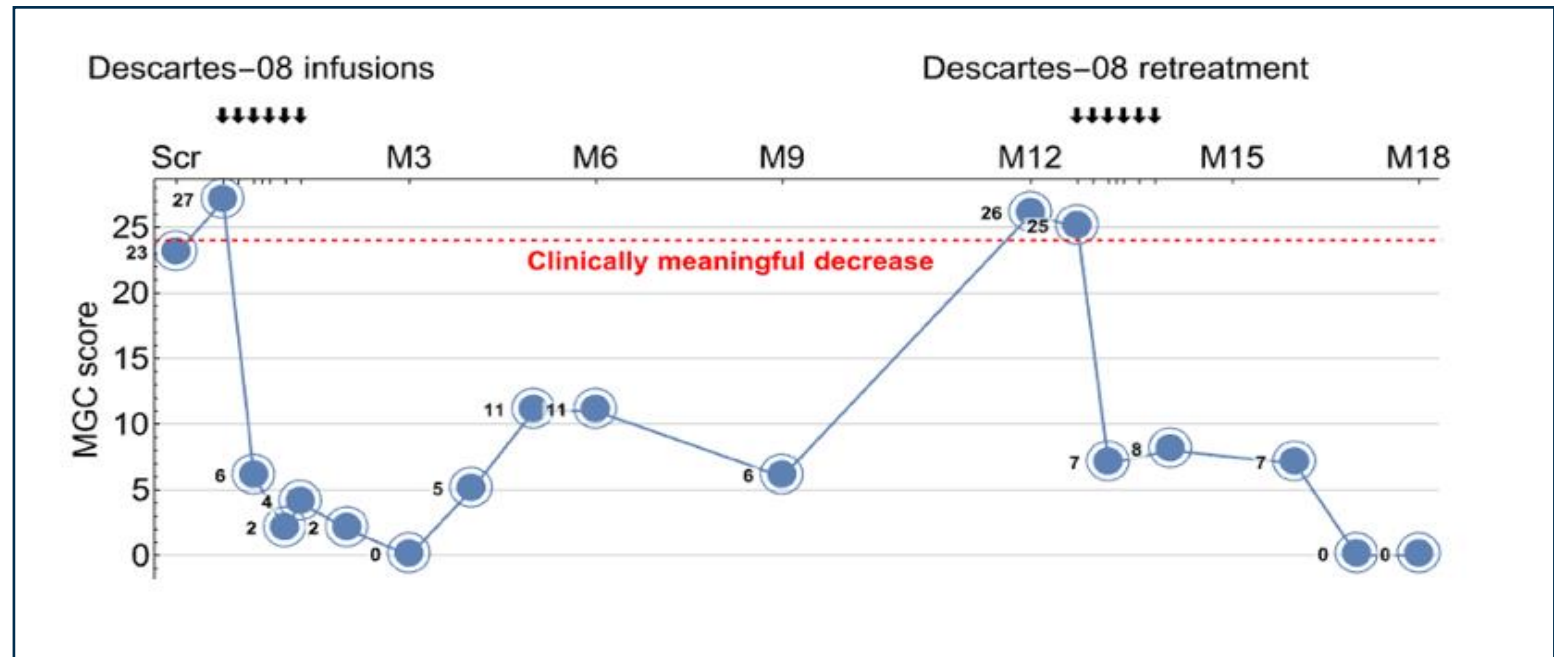
- All three participants with detectable AChR antibody levels at baseline experienced autoantibody reductions by Month 6
- Reductions deepened further by Month 9, and were maintained at Month 12



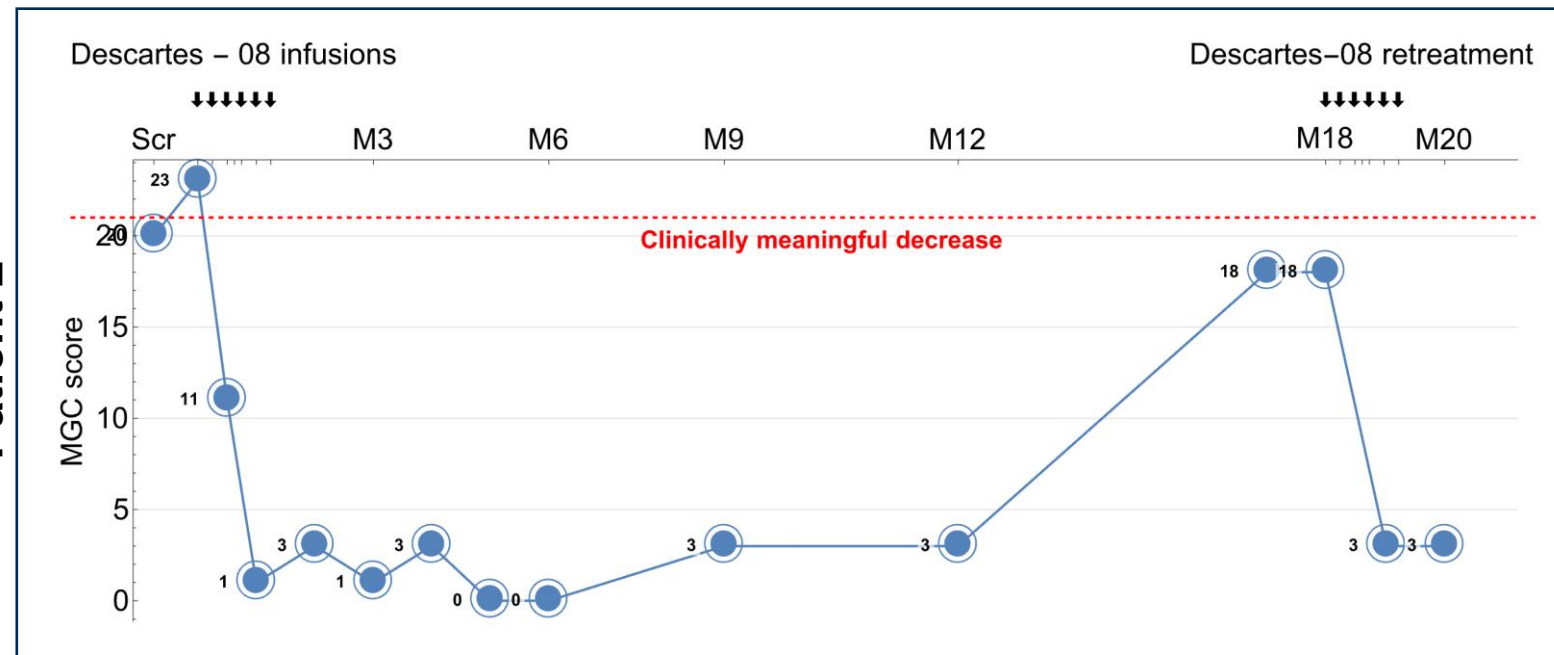
Descartes-08 retreatment led to a rapid decrease in MG-specific clinical scores

- Retreated patients experienced rapid improvement in clinical scores and minimal symptom expression

Patient 1



Patient 2



Phase 2b randomized, placebo-controlled, double-masked study of Descartes-08 in MG

Plan to treat ~30 patients

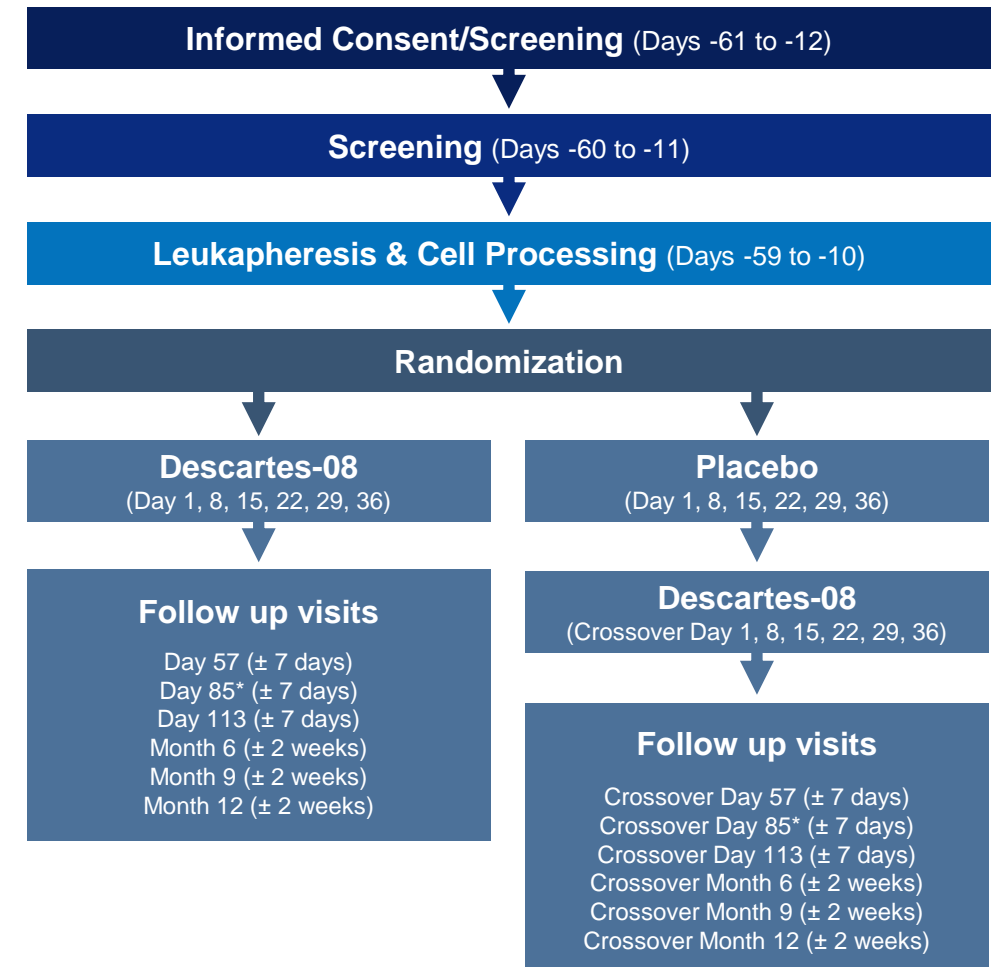
PRIMARY ENDPOINT

- Proportion of **MG Composite** responders (≥ 5 -point reduction) at Day 85

SECONDARY OBJECTIVES

- Safety and tolerability
- Quantify clinical effect of Descartes-08 over 1 year
- QMG, MG QoL 15R, MG ADL, and MG PIS (change from baseline to Day 85)
- Compare effect of Descartes-08 versus placebo on MG scales (change from baseline to Day 85) in patients who cross over from placebo to Descartes-08

Top-line results expected in mid-2024



Exploring potential of Descartes-08 in Systemic Lupus Erythematosus (SLE)

IND CLEARED

PHASE 2 STUDY ON TRACK FOR 1H 2024

- Open-label study in up to 30 adults with moderate to severe multi-refractory SLE and no CNS involvement
- Designed to assess safety, tolerability, and manufacturing feasibility of Descartes-08 in patients with SLE
- Secondary objectives include standard measures of clinical activity in SLE:
 - Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)
 - Physician Global Assessment (PGA)
 - Systemic Lupus Erythematosus Responder Index (SRI)
 - British Isles Lupus Assessment Group (BILAG)–based Composite Lupus Assessment (BICLA)

Screening (Days -60 to -15)

Leukapheresis & Cell Processing (Days -59 to -14)

2 - 3 Weeks

Descartes-08
(Day 1, 8, 15, 22, 29, 36)

Safety/Response Assessment
(Day 50)

Follow up visits
(Months 3, 6, 9, 12)

Exploring additional applications for Descartes-08 in autoantibody-associated autoimmune diseases (AAAD)

- Clinical data suggest that Descartes-08 could lead to clinical benefit along with disappearance of disease-associated autoantibodies, suggesting potential in additional autoimmune indications

Potential significant Descartes-08-associated improvement observed in a patient with autoimmune retinitis (AIR)

61-year-old man with DPPX antibody-positive AIR, colitis, encephalitis refractory to prednisone, rituximab, bortezomib, IVIg; positive for 5/5 disease-associated autoantibodies pre-treatment

Post-treatment: experienced a clinically-significant, 2-line improvement in visual acuity; 3 of 5 autoantibodies became undetectable

Test	Pre-treatment	Month 2	Month 4	Month 6
Visual acuity	20/60	20/40	20/40	20/40
Carbonic anhydrase II Ab	+	-	-	NP*
Tubulin Ab	+	-	-	NP*
PKM2 Ab	+	-	-	NP*
Aldolase Ab	+	+	+	NP*
Enolase Ab	+	+	+	NP*

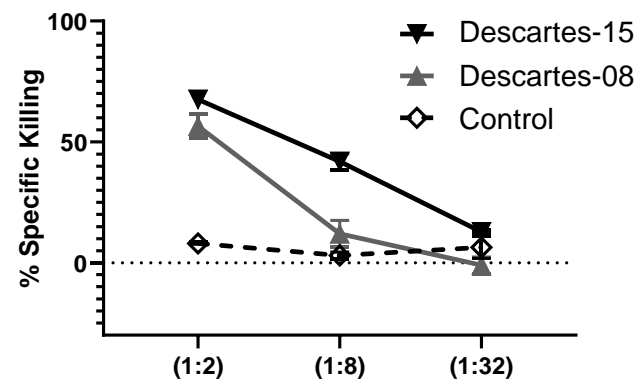
*NP – not performed

RNA Armory[®] example: Descartes-15, a next generation anti-BCMA mRNA CAR-T with >10x potency observed in preclinical studies

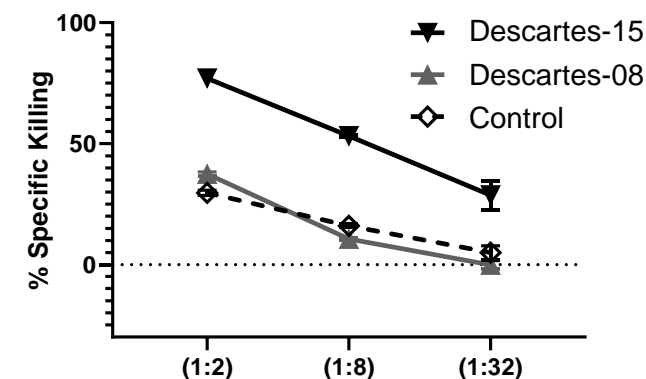
Descartes-15 is an anti-BCMA mRNA CAR-T with potential disruptive features:

- Engineered for maximum potency and CAR stability, even in the presence of target-driven suppression of CAR
- Clinical strategy expected to leverage safety and clinical activity data from Descartes-08

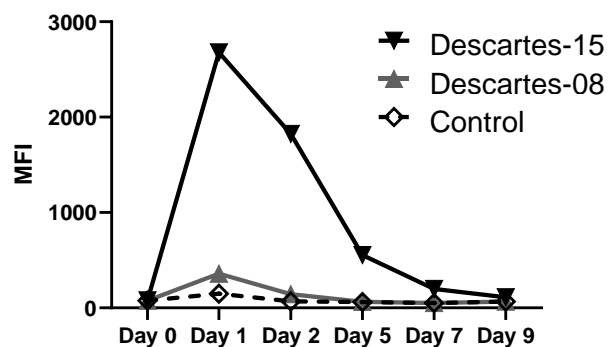
Potent killing (single target exposure)



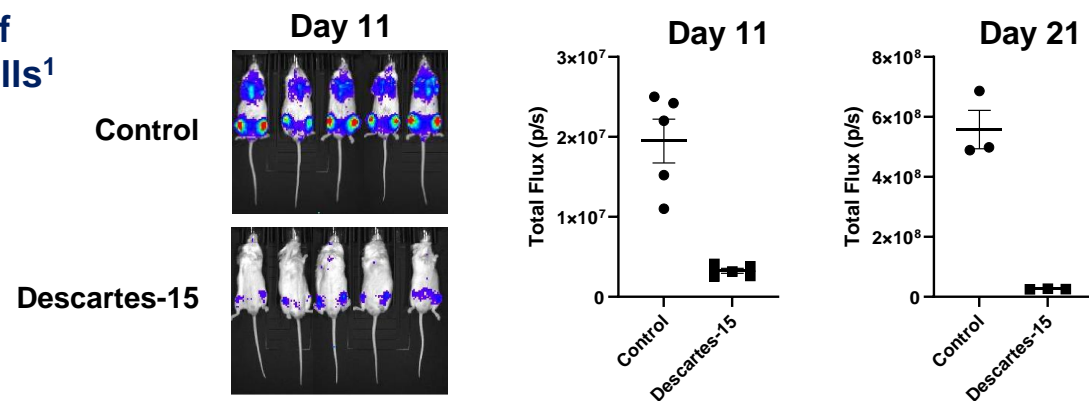
Persistent killing (multiple exposures)



Superior CAR expression

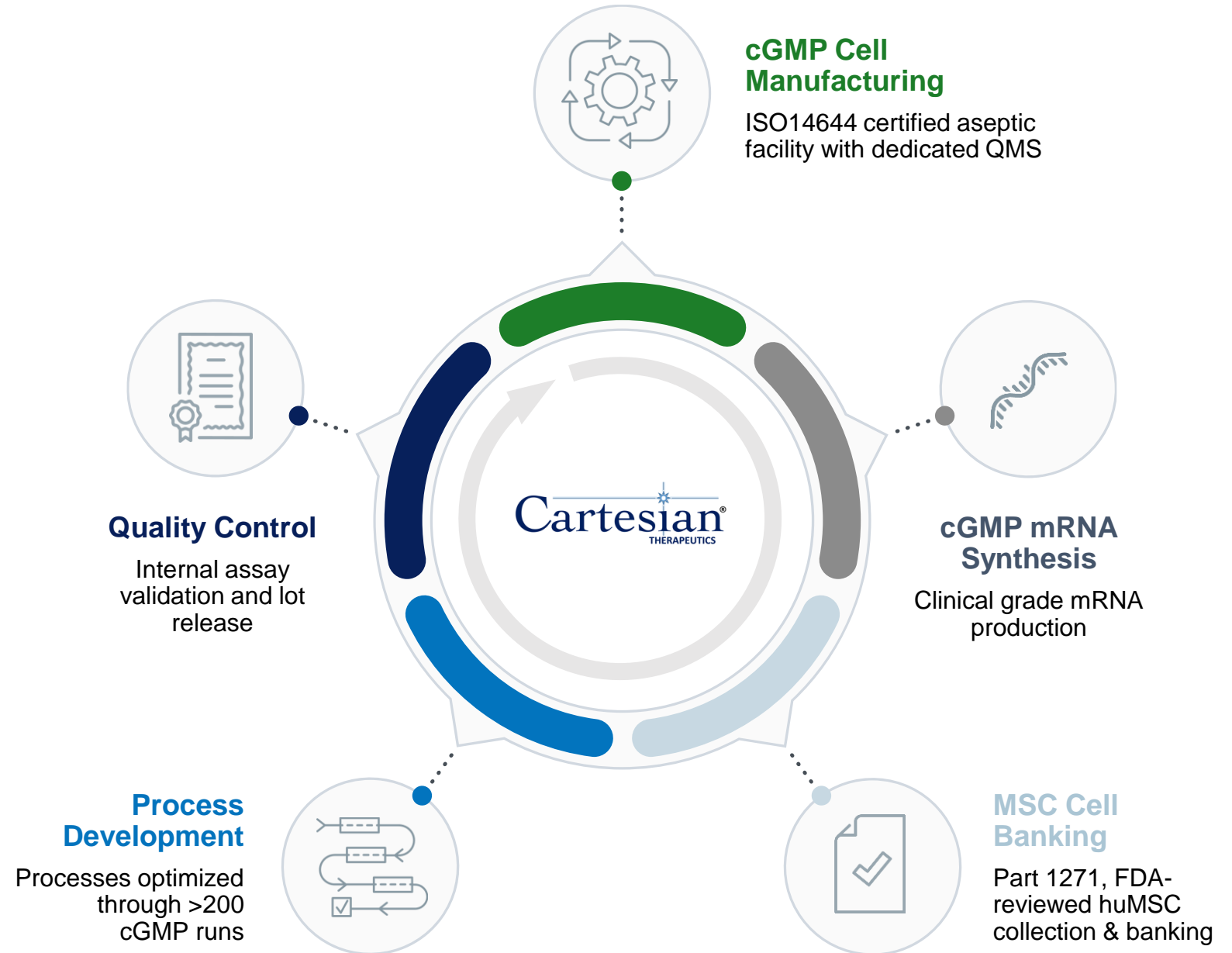


Efficient killing of BCMA+ target cells¹



¹ MM1-S disseminated myeloma model in NSG mice infused with either control T-cells or Descartes-15

In-house manufacturing enhances control of product quality, production schedules and costs



Wholly-owned, in-house manufacturing: 27,000 sq ft state-of-the-art cGMP facility



Clinical and commercial manufacturing scale capabilities support maturing pipeline and future growth



Flexibility to quickly adapt to changes in processes or needs



Ownership of quality control and production timelines



Cost efficiency

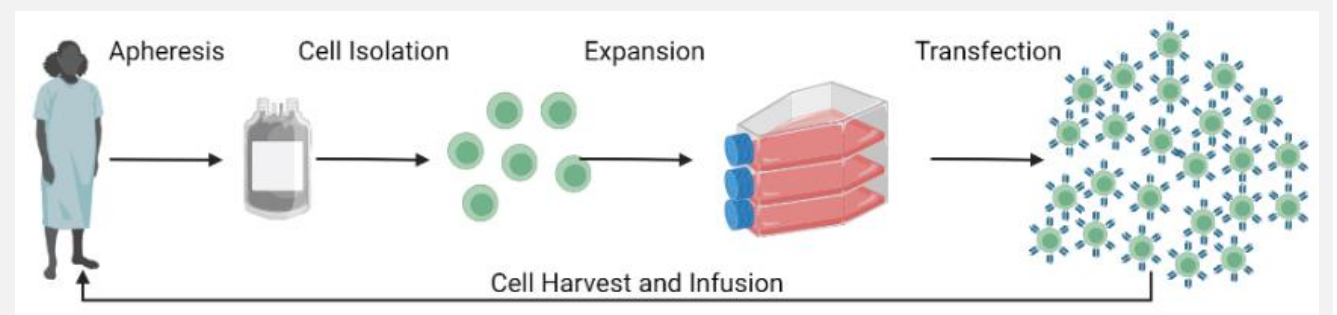
Facility located in Frederick, MD

cGMP, current good manufacturing practice

Platform offers potential development opportunities via three modalities: autologous, allogeneic and *in situ*

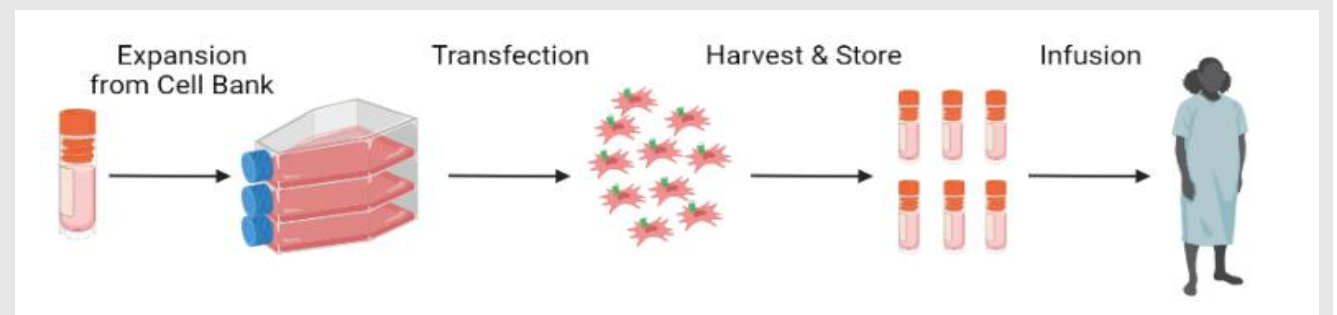
Autologous mRNA CAR-T

- Descartes-08
- Descartes-15: next generation anti-BCMA mRNA CAR-T with >10x potency observed in clinical studies



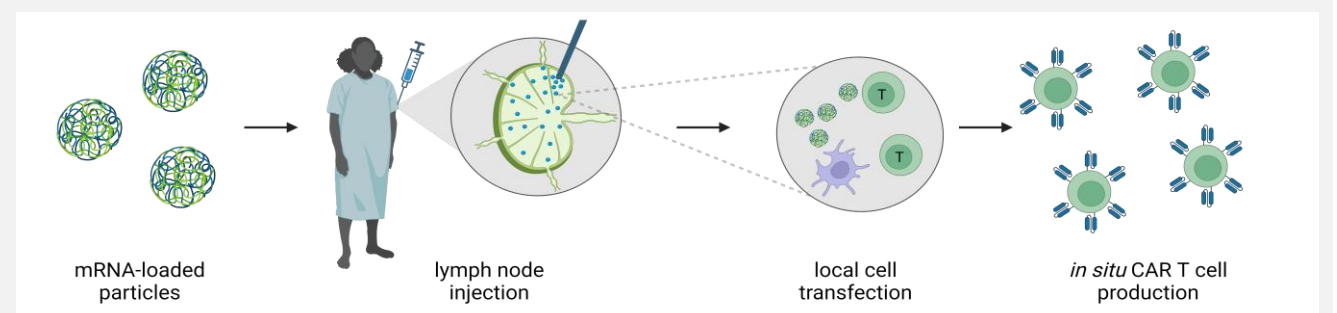
Allogeneic mRNA MSC

- Descartes-33



rLN: *In situ* lymph node transfection

- Undisclosed program



Maturing pipeline offers potential for multiple catalysts

Descartes-08 in MG

Expect to report Phase 2b data mid-2024

Mid 2024

Descartes-08 in SLE

Plan to initiate Phase 2 in 1H 2024

1H 2024

Descartes-08 Additional Indications

Plan to initiate basket studies in additional autoimmune indications in 2H 2024

2H 2024

Descartes-15

IND cleared, with first-in-human Phase 1 planning activities underway

2024

Funding expected to support development of Descartes-08 through Phase 3 and advance additional programs

**Strong
Financial
Position
Expected to
Support
Pipeline
Through Key
Milestones**

\$104.8M

Cash as of 3/31/24

2H 2026

Anticipated cash runway into

<60 EMPLOYEES

Based in Gaithersburg, MD

17.8M

Basic shares outstanding

23.3M

Basic shares outstanding upon full conversion
of outstanding Series A Preferred*

26.6M

Fully diluted shares outstanding**

*Shares include approximately 166.3 thousand shares of Series A Non-Voting Convertible Preferred Stock that remain subject to beneficial ownership limitations that are convertible into approximately 5.5 million shares of common stock.

**Fully diluted shares include diluted shares as described above, as well as outstanding options, RSUs and warrants.

PIONEERING mRNA CELL THERAPIES

Pipeline designed to expand the reach of cell therapy to autoimmunity

MATURING PIPELINE WITH EXPECTED NEAR-TERM CATALYSTS

Validated lead program, Descartes-08, with Phase 2b data expected mid-year

CASH RESOURCES EXPECTED TO FUND OPERATIONS INTO 2H 2026

Expected to support Descartes-08 through Phase 3 and advance additional programs

EXPERIENCED LEADERSHIP TEAM

Focused on disciplined investment and creating value for stockholders and patients





CARTESIAN THERAPEUTICS

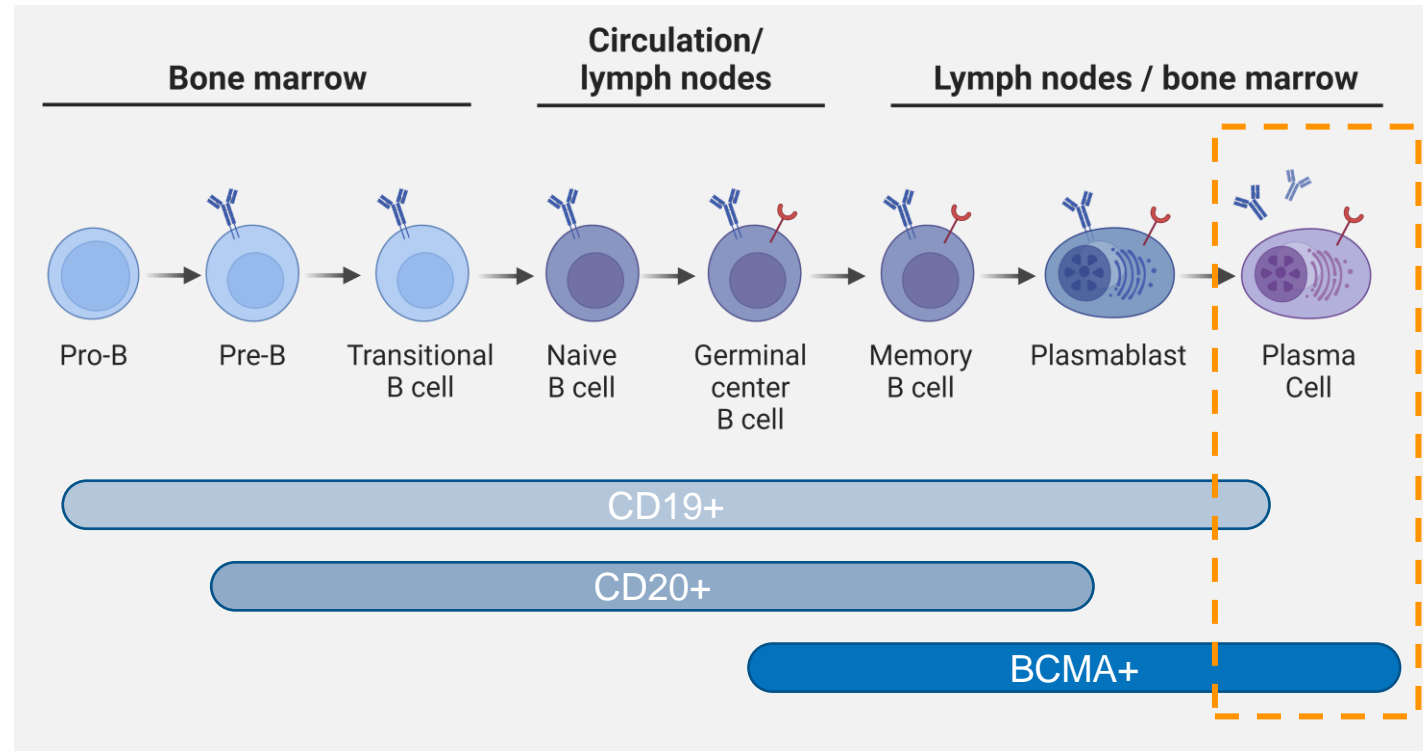
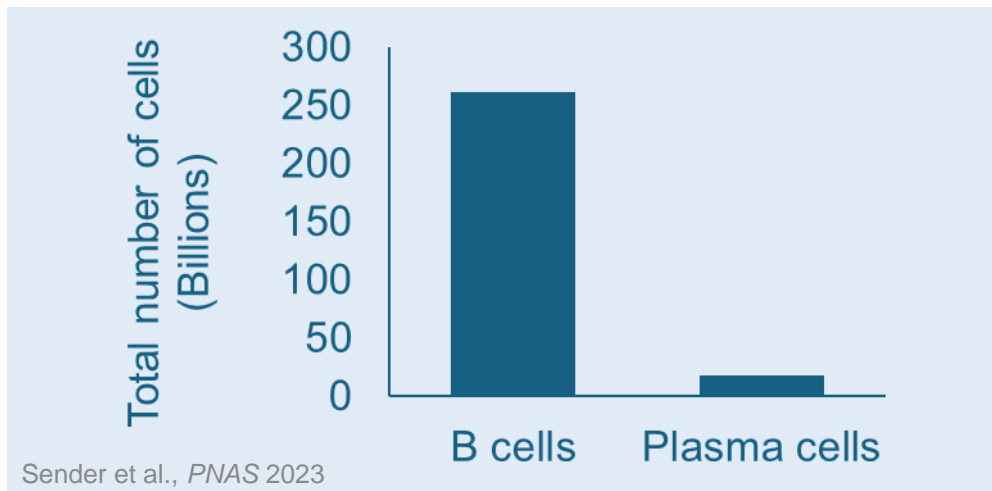
Pioneering mRNA Cell Therapy for Autoimmunity



Appendix

Differentially expressed B-cell antigens require distinct CAR-T strategies

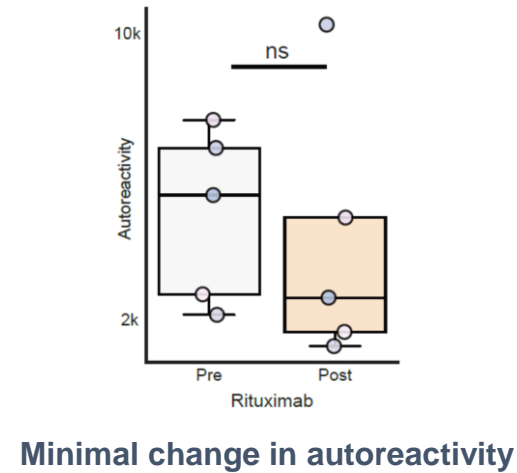
- CD19+ and CD20+ cells represent the vast majority of B cells and are ubiquitously distributed
- CD19+ and CD20+ are often expressed on the same B cells
- The exceptions are plasma cells, in which neither antigen is expressed, and plasmablasts, in which CD19+ is expressed, directly responsible for pathogenic autoantibodies
- Plasma cells are rare and tissue-restricted



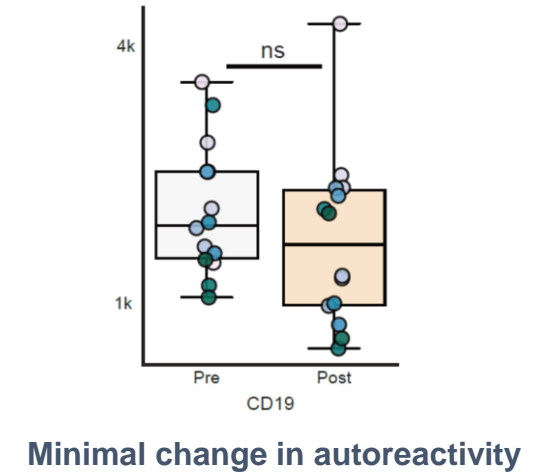
BCMA is a differentiated target with potential for precision CAR-T in patients with autoimmunity

Clinical analyses of antigen-depletion therapies show BCMA-targeting with CAR-T may enable precision reset of autoantibody-producing PCs

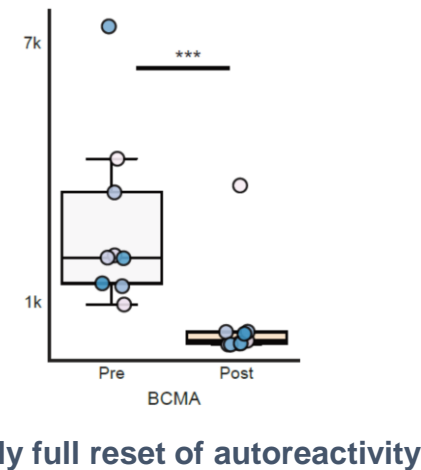
Rituximab (CD20+ cell depletion)



Anti-CD19 CAR-T (CD19+ cell depletion)



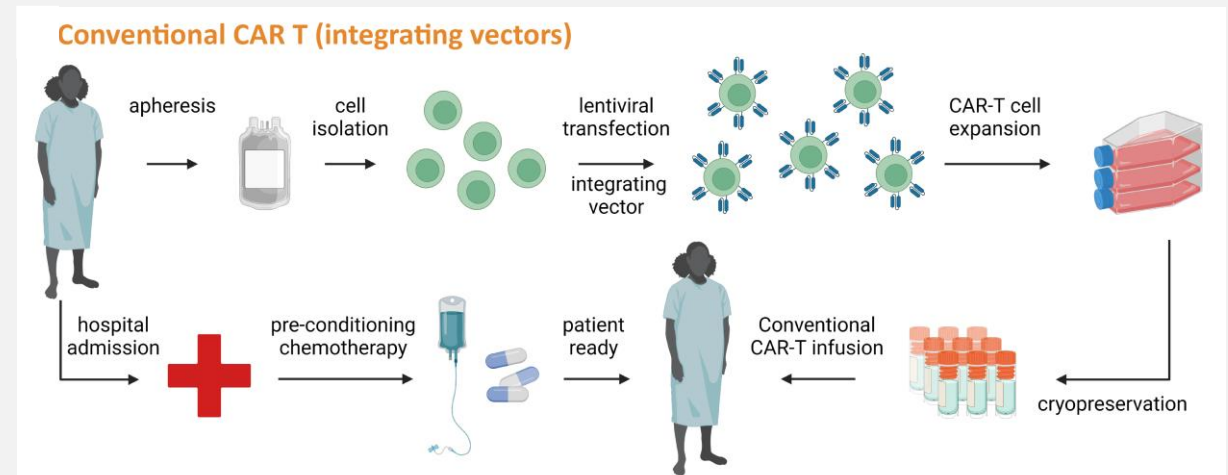
Anti-BCMA CAR-T (BCMA+ cell depletion)



Cartesian differentiation: All approved CAR T therapies and other trials in the autoimmune space face fundamental hurdles created by integrating vectors

Conventional CAR-T (integrating viral vectors) targeting CD19

- Creates significant burden for patients in three areas
 - hospital admission
 - lymphodepletion/chemotherapy
 - cytokine release syndrome (CRS) risk
- Patients with autoimmunity typically have much lower tolerance for these hurdles relative to cancer patients



mRNA CAR T (no integration) targeting BCMA

- mRNA enables transient expression → no need for significant T cell proliferation
- Eliminates lymphodepletion and enables outpatient administration without CRS

