



CARTESIAN THERAPEUTICS

# Pioneering mRNA Cell Therapy for Autoimmunity

April 2024



# Forward-Looking Statements

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# 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

## PRO FORMA CASH RESOURCES\*

**\$118.3M as of end of 2023; 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

\*Reflects the receipt of \$40M through two delayed settlement payments previously announced as part of the November 2023 financing, which occurred in January 2024 and February 2024  
CAR, Chimeric antigen receptor  
SLE, Systemic Lupus Erythematosus

# 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



**Nishan  
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<sup>®</sup> 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

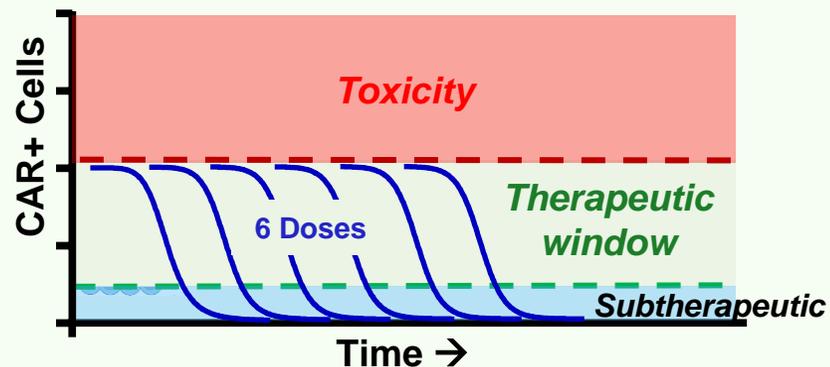
Expectation for cells to be administered at therapeutic, but sub-toxic doses

### 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

Cells proliferate rapidly beyond therapeutic window



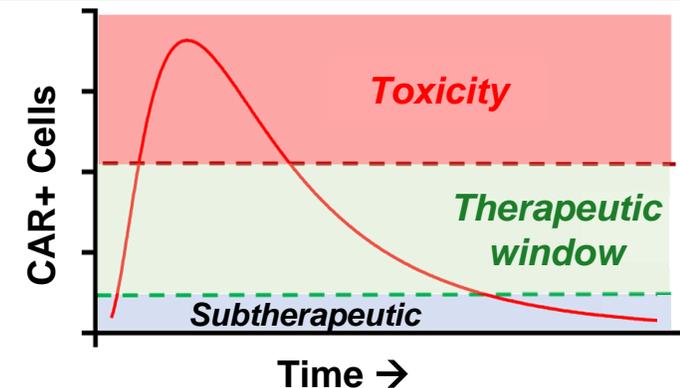
### Uncontrollable PK/PD

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: ~80%]			
	SLE, other Autoimmune Diseases	[Progress bar: ~60%]			
Descartes-15 Autologous mRNA CAR-T	Autoimmune Diseases*	[Progress bar: ~40%]			
Descartes-33 Allogeneic mRNA MSC	Autoimmune Diseases	[Progress bar: ~20%]			
<i>In situ</i> LN transfection	Undisclosed	[Progress bar: ~15%]			

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

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

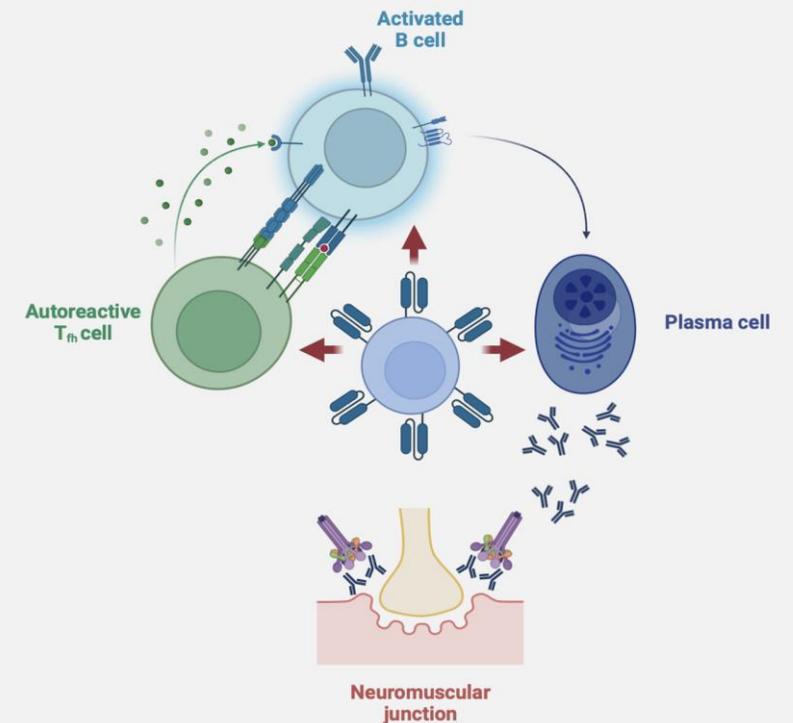
# Descartes-08 is believed to be the first mRNA CAR-T in clinical development for autoimmune disease

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 designation 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

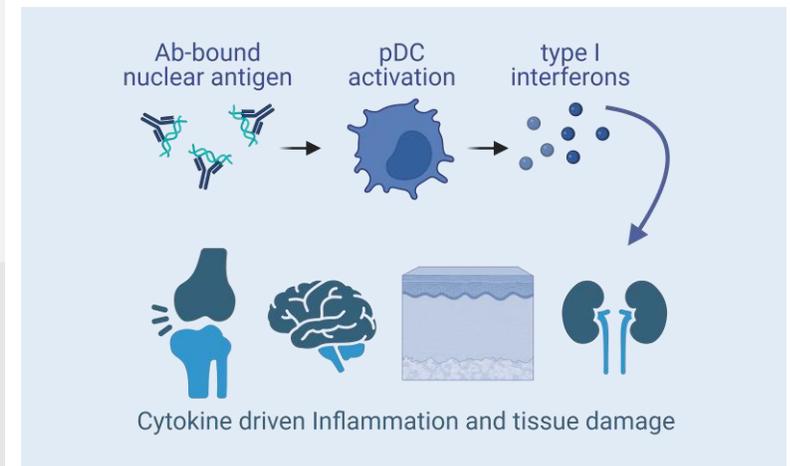
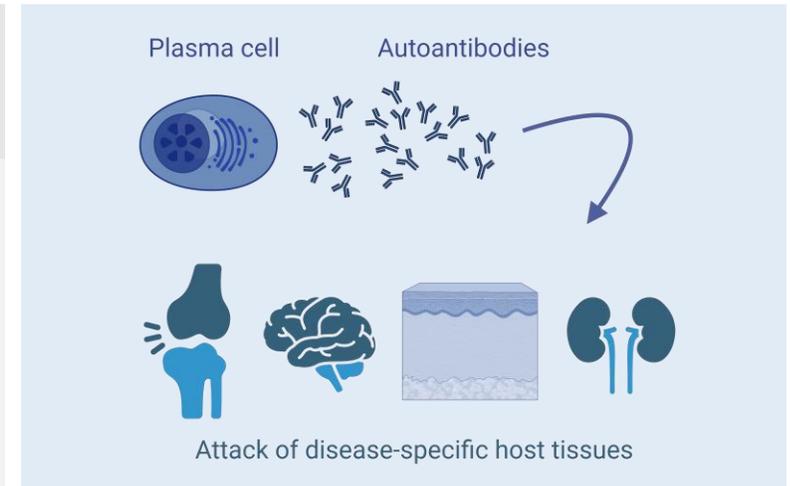
- PCs, plasmablasts and proliferating B cells targeted by Descartes-08 represent a tiny fraction of B cells
- These cells are entirely responsible for secreting pathogenic autoantibodies
- During autoimmunity, autoantibodies attack host tissue and drive inflammation

## 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

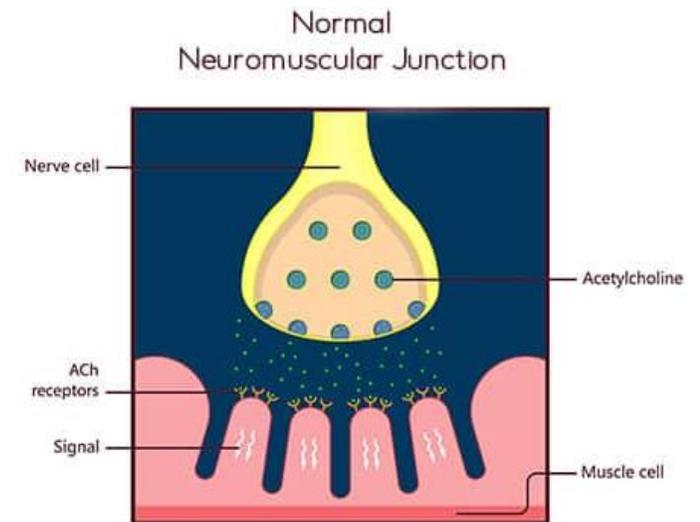
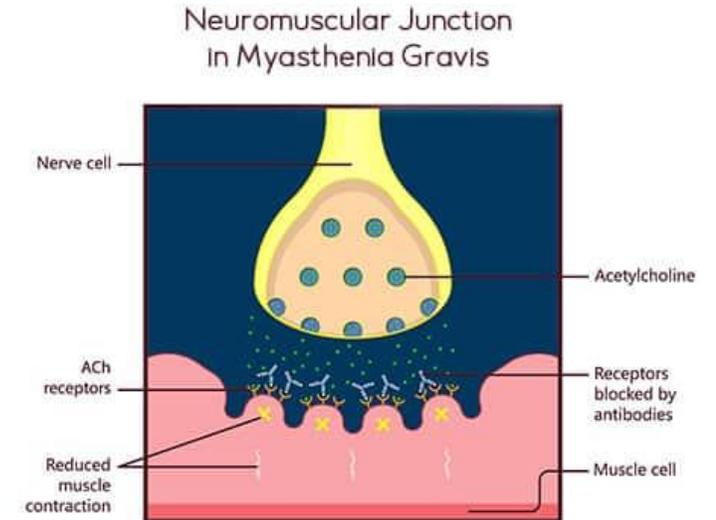
Several autoimmune disease segments involve pathogenic contributions from **both PCs/plasmablasts** and **pDCs**, including rheumatology, nephrology, neurology, and others

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

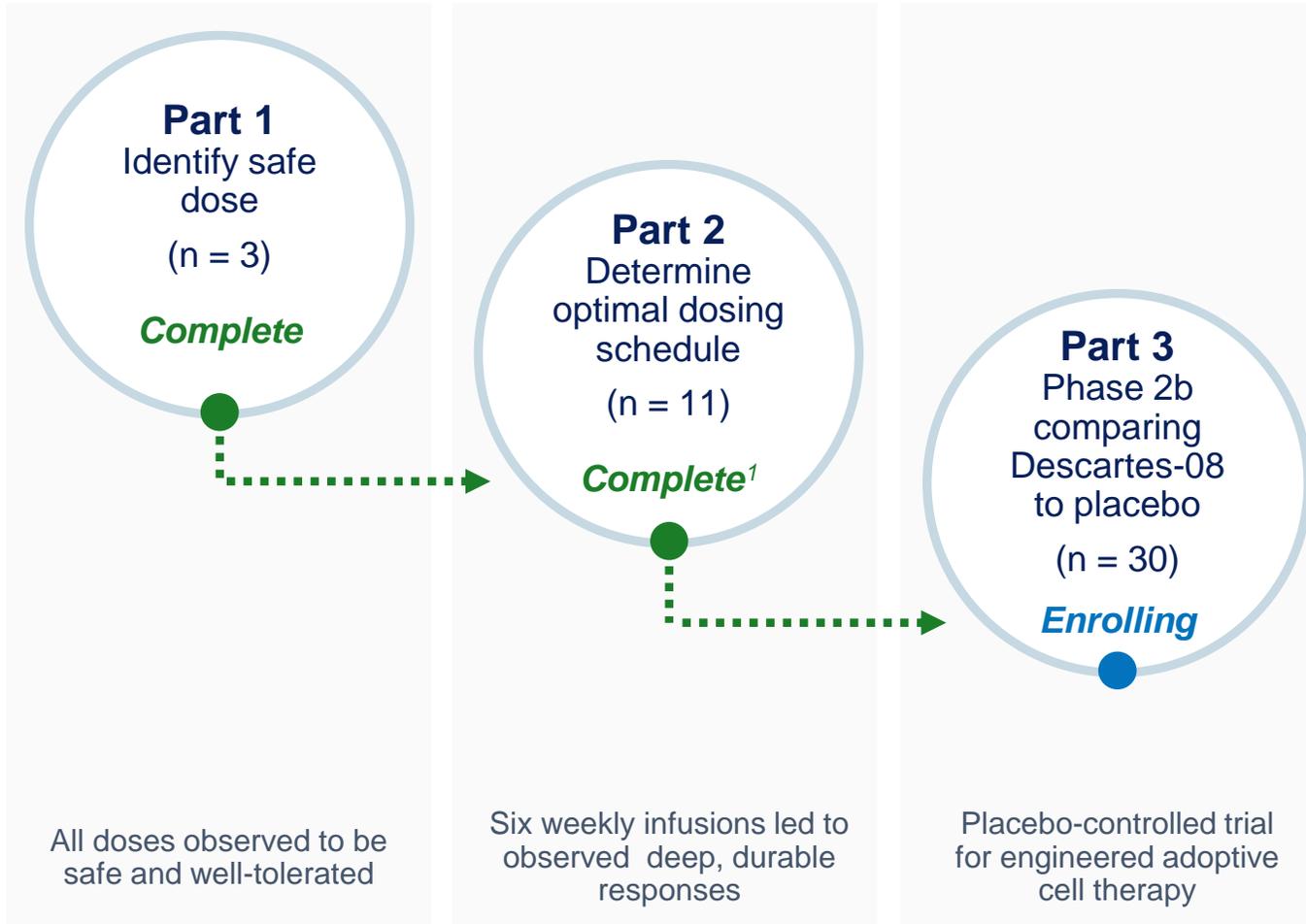


# Initial indication for Descartes-08: Myasthenia gravis

- 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  $\geq 6$
- MGFA Class II-IV
- Stable medication dosing  $\geq 8$  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

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

<b>Previous myasthenia gravis therapies (standard of care)</b>	
Pyridostigmine	14 (100%)
Prednisone	14 (100%)
Other immunosuppressants	14 (100%)
Eculizumab	2 (14%)
Rituximab	2 (14%)
<b>Previous intravenous immunoglobulin</b>	12 (86%)
<b>Previous plasma exchange</b>	8 (57%)
<b>Diagnosis of thymoma</b>	0
<b>Previous thymectomy</b>	6 (43%)
<b>Previous myasthenia gravis crisis requiring intubation</b>	4 (29%)
<b>Myasthenia gravis ongoing therapy</b>	
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

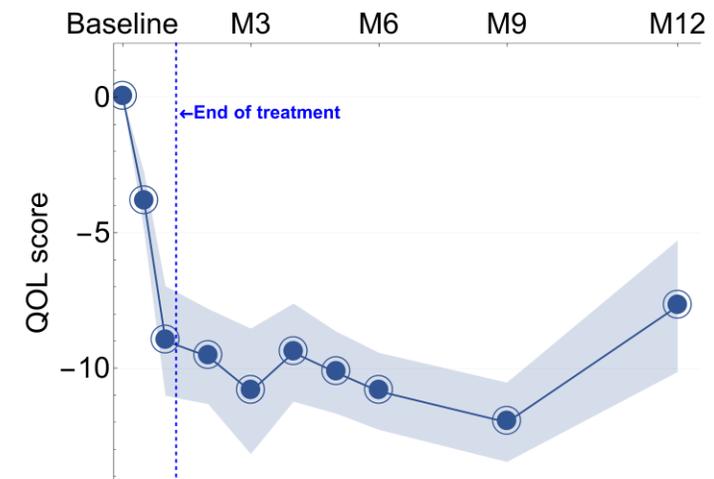
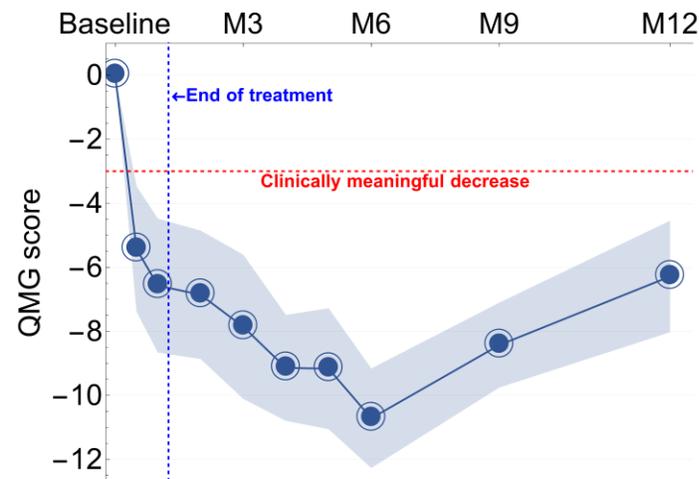
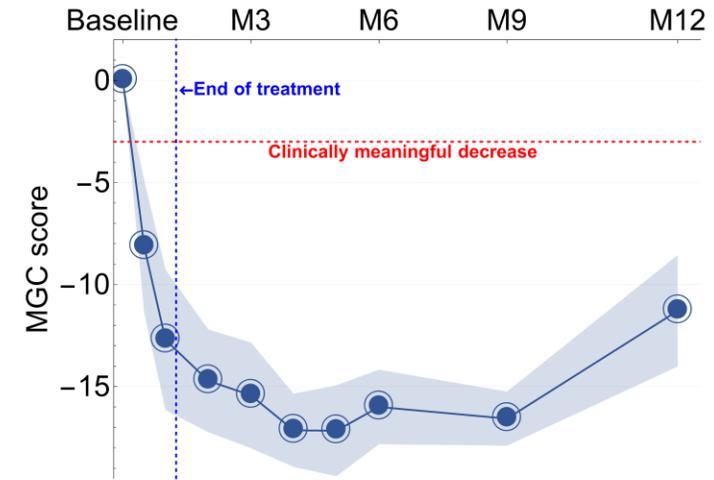
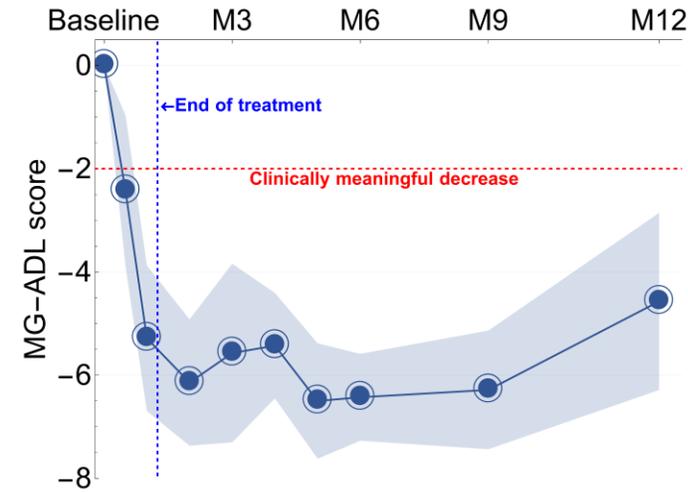
	Grade*	Part 1 (n=3)	Part 2: all groups (n=11)	Part 2: group 1 (n=3)	Part 2: group 2 (n=7)	Part 2: group 3 (n=1)
Hand numbness	2	1 (33%)	0	0	0	0
Headache	1	1 (33%)	5 (45%)	1 (33%)	3 (43%)	1 (100%)
Muscle soreness	1	1 (33%)	1 (9%)	0	1 (14%)	0
Nausea	1	1 (33%)	4 (36%)	2 (67%)	2 (29%)	0
Rash	3	0	1 (9%)	1 (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 <sup>1</sup>	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.

<sup>1</sup>Not 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*

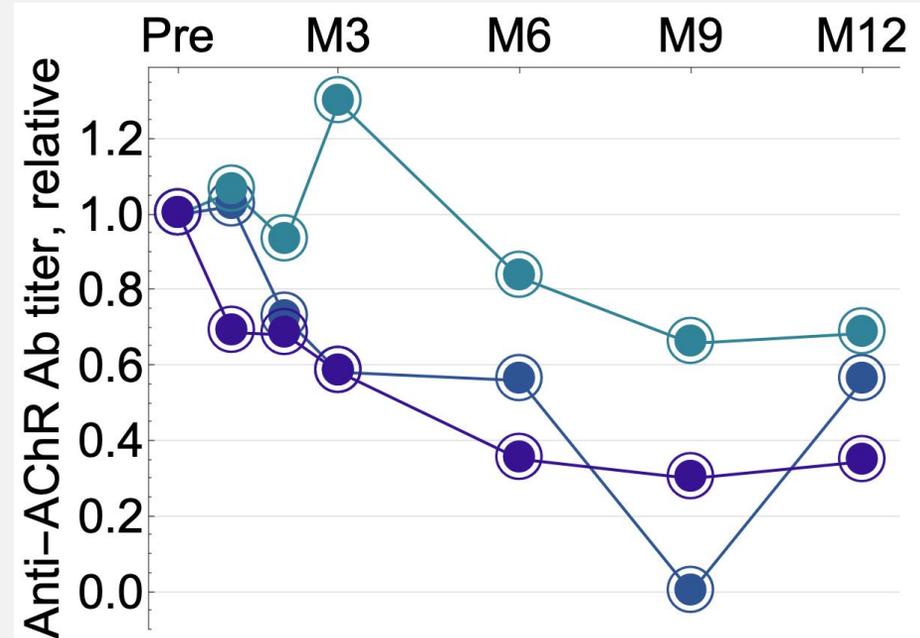


Manuscript submitted for peer review; pre-print available at medRxiv.org

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

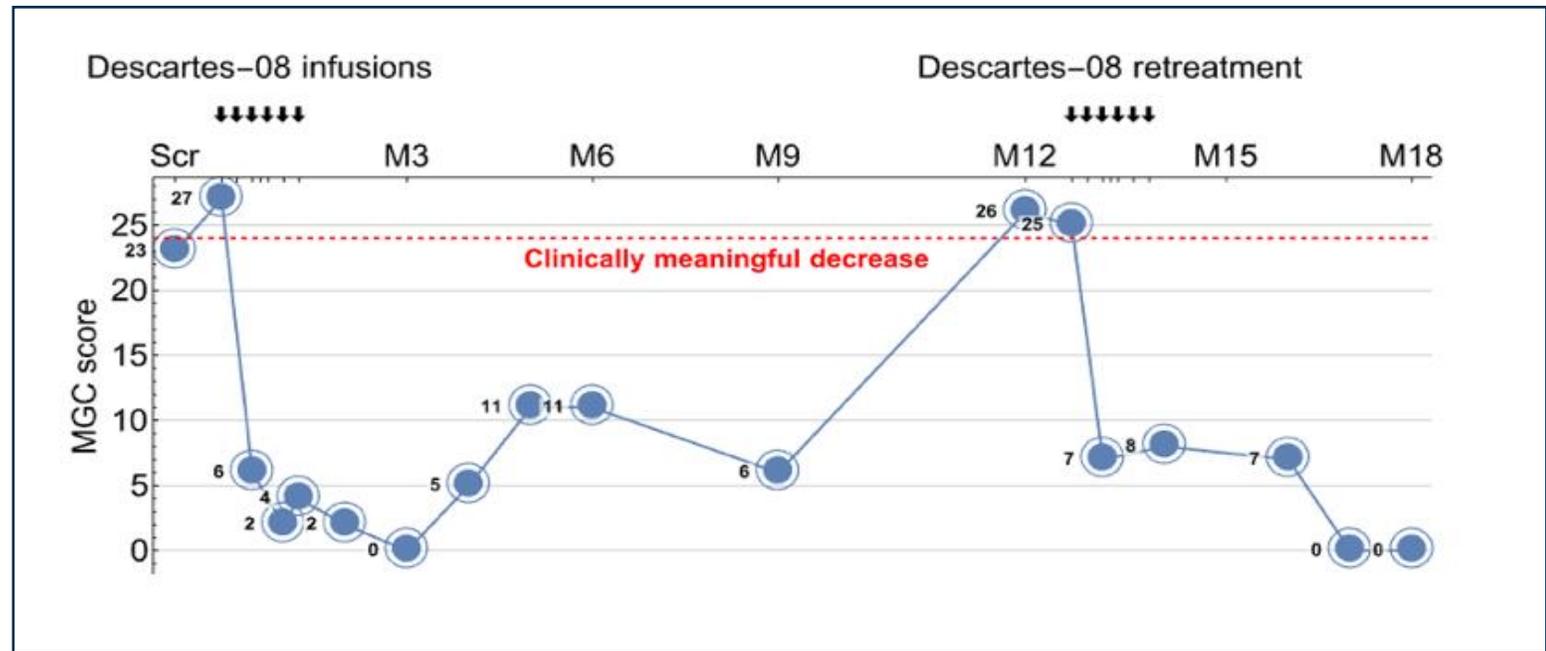
- All three participants with detectable AChR antibody levels at baseline experienced autoantibody reductions by Month 6
- Reductions deepened further by Month 9, and were maintained at Month 12



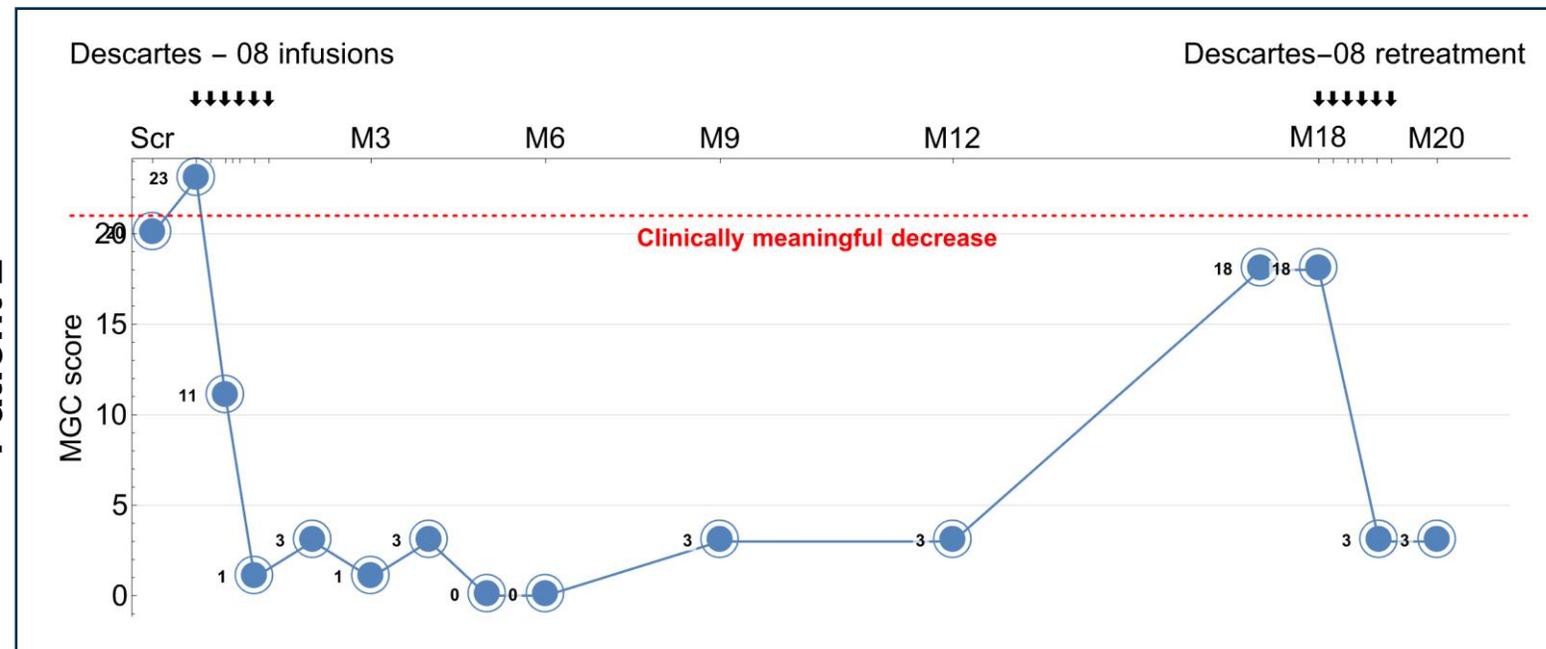
# Descartes-08 retreatment led to a rapid decrease in MG-specific clinical scores

- 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

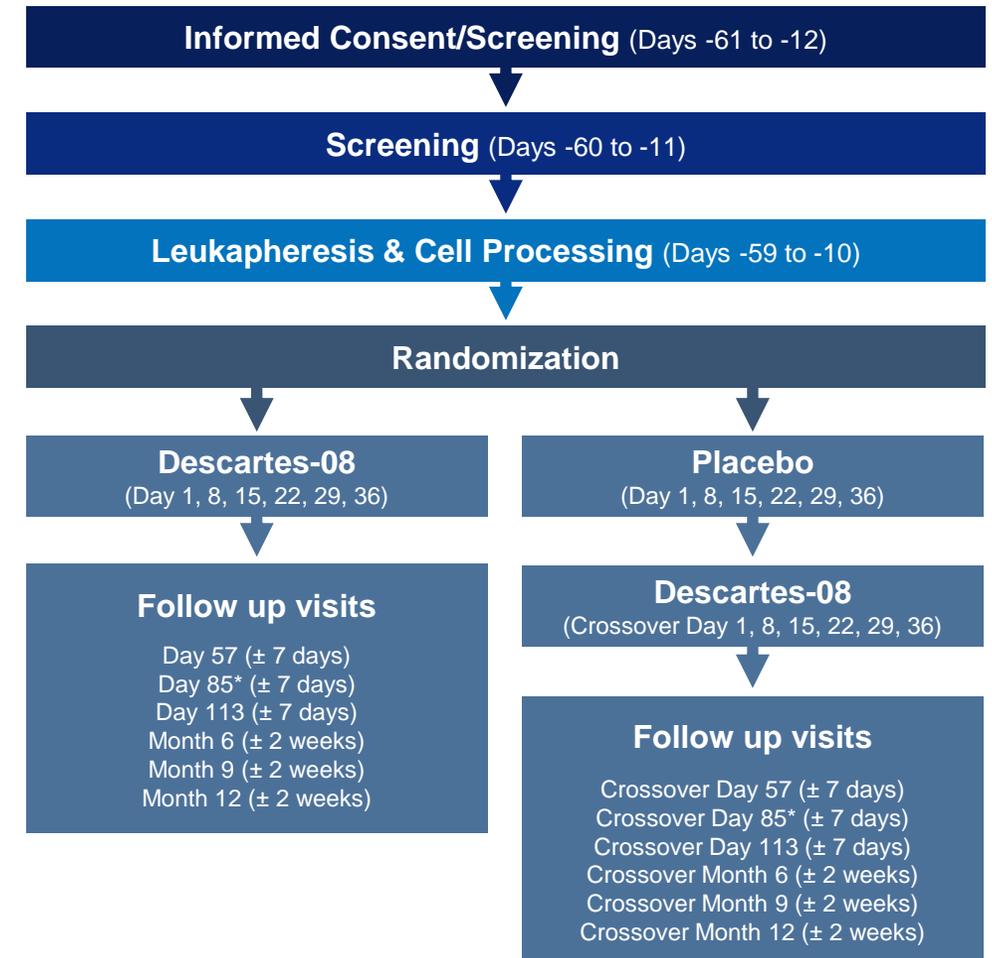
## PRIMARY ENDPOINT

- Proportion of **MG Composite** responders ( $\geq 5$ -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

Enrollment underway, with 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*

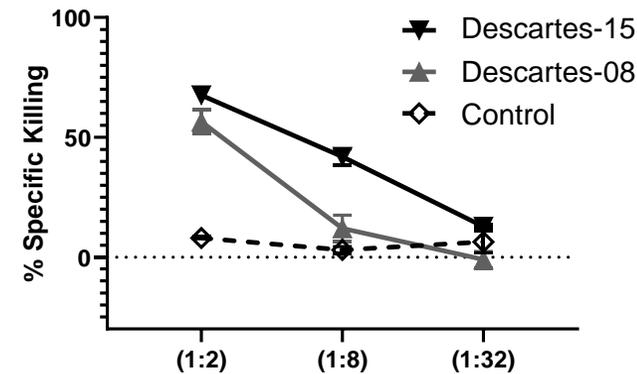
\*NP – not performed

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

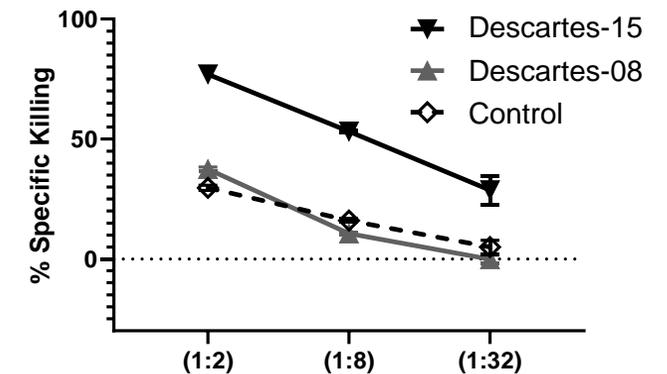
Descartes-15 is an anti-BCMA mRNA CAR-T with potential disruptive features:

- 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

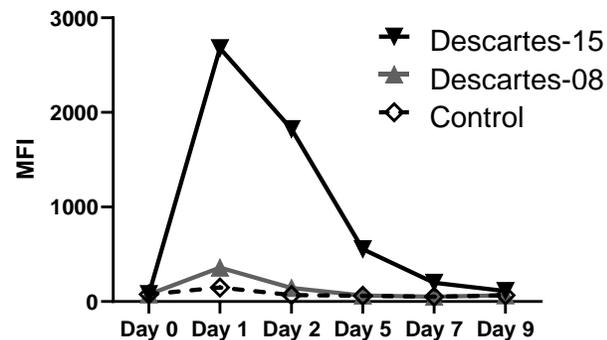
Potent killing (single target exposure)



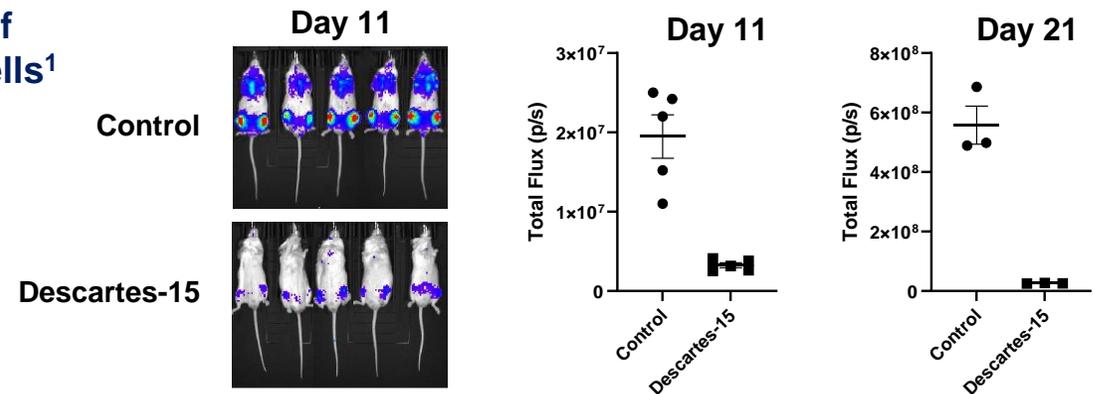
Persistent killing (multiple exposures)



Superior CAR expression

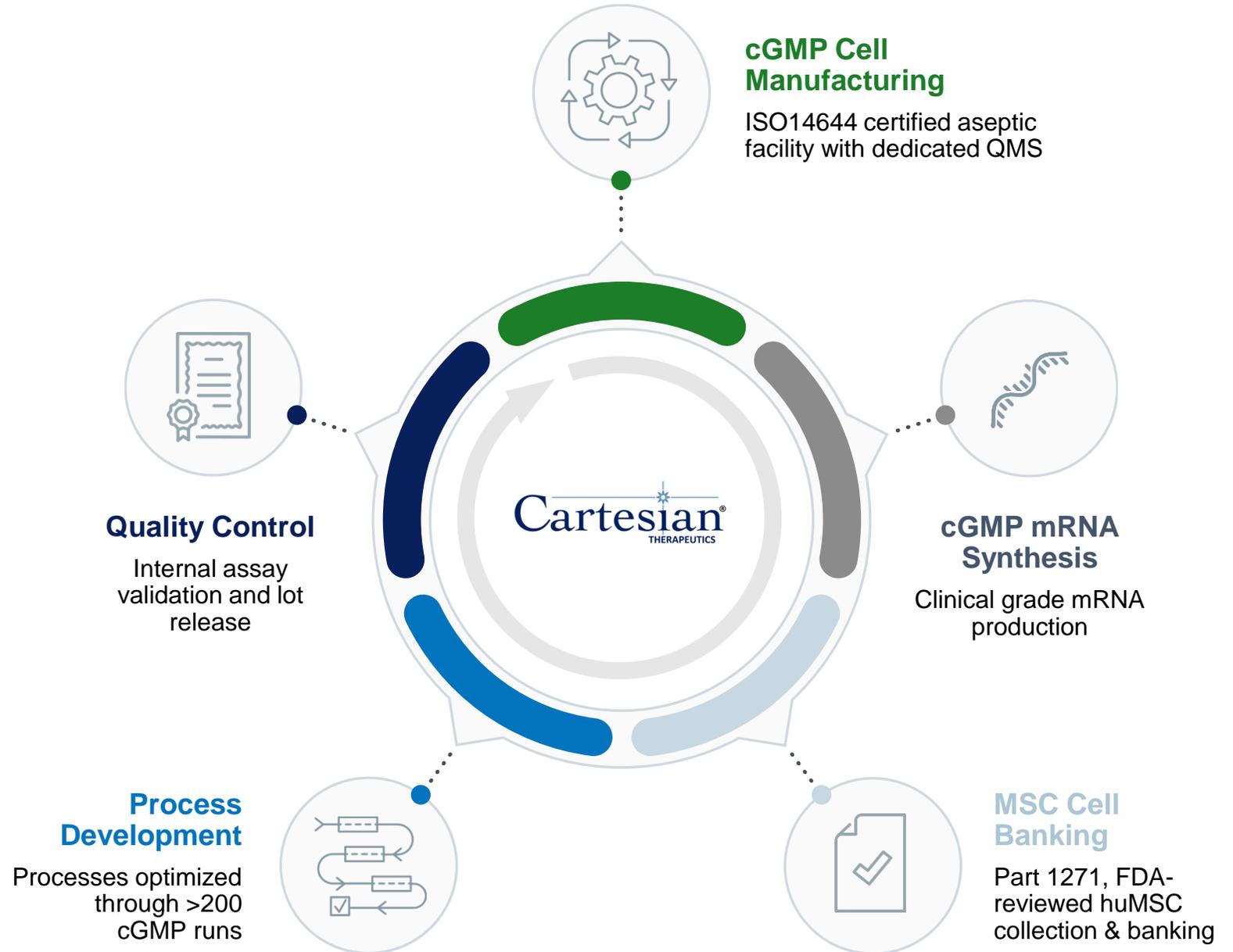


Efficient killing of BCMA+ target cells<sup>1</sup>



<sup>1</sup> 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: 20,000 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

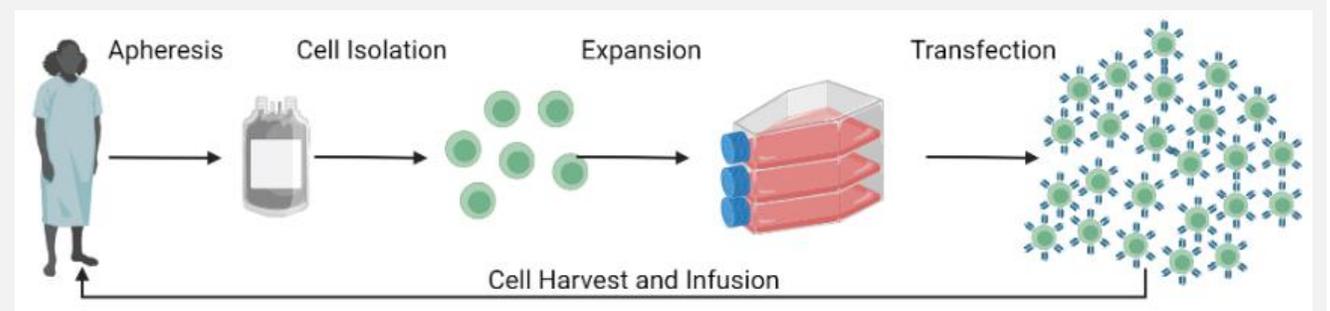
Facility located in Frederick, MD

cGMP, current good manufacturing practice

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

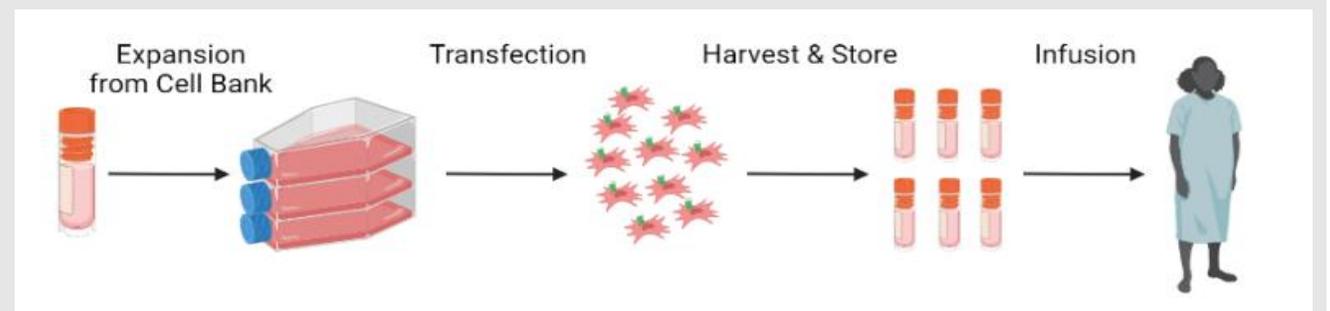
## Autologous mRNA CAR-T

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



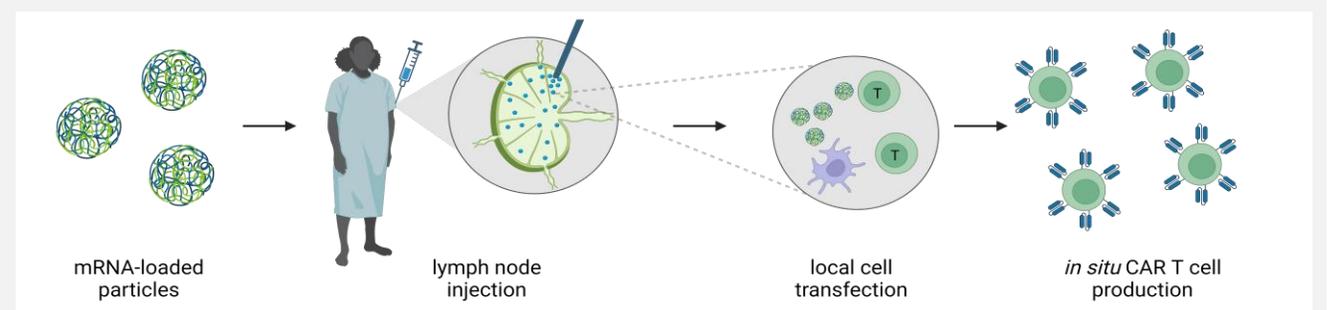
## Allogeneic mRNA MSC

- 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**

**\$118.3M**

**Pro forma cash as of 12/31/23\***

**2H 2026**

**Anticipated cash runway into**

**<50 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\*\*\***

\*Reflects the receipt of \$40M through two delayed settlement payments previously announced as part of the November 2023 financing, which occurred in January 2024 and February 2024.

\*\*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

