



TEMPEST[®]
THERAPEUTICS

Building the Future of In Vivo CAR-T

July 15, 2026

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Tempest: A Clinical-Stage CAR-T Company Targeting the Future of In Vivo CAR-T

In vivo CAR-T program combines clinically supported dual-CAR architecture with advanced CD7-targeted mRNA LNPs

In Vivo CAR-T Pipeline (Wholly Owned, Multi-Indication-Potential Asset)					
Asset	Modality	Target	Indications	Stage	Strategic Role
TPST-4003	In Vivo Dual CAR-T	CD19/BCMA	MG / MS IIT validation; multiple autoimmune and oncology indications, including pediatric	2026 IIT-track	Dual-target in vivo CAR-T asset built on clinically supported dual-targeting CAR architecture, designed for broad B-cell lineage reset, with multiple autoimmune and oncology indications.

Clinical CAR-T Asset (China Development Sponsored by Partner; Tempest Has Exclusive Rights outside China, Russia, India & Turkey)					
Asset	Modality	Target	Indications	Stage	Strategic Role
TPST-2003	Dual CAR-T	CD19/BCMA	rrMM, POEMS	Phase 1/2	Clinical-stage asset with supporting clinical safety and efficacy results in rrMM and POEMS syndrome, planned China BLA in 2027, provides clinical support for the company's dual-target in vivo CAR-T strategy.

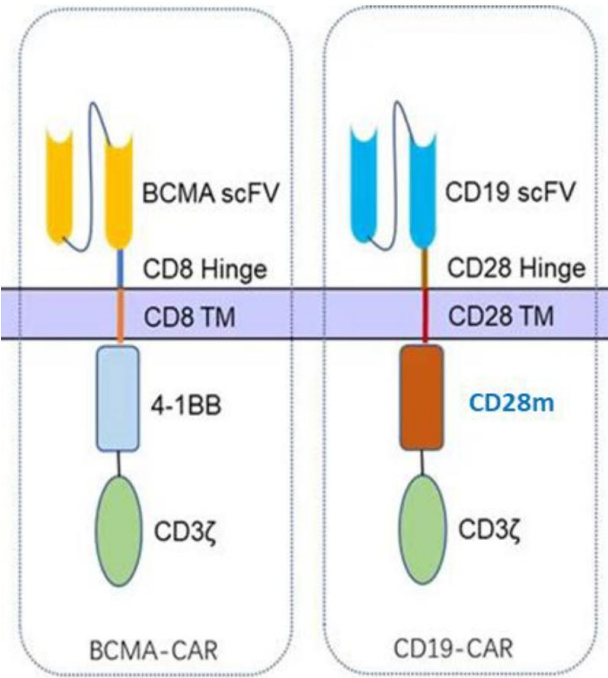
Other Portfolio Assets	Category	Indication	Stage
Amezalpat / TPST-1495	Small molecule	1L HCC / FAP	Phase 3-Ready / Ongoing NCI-Sponsored Phase 2
TPST-2206 / TPST-3003 / TPST-3206	CAR-T	RCC / rrMM / SLE	Preclinical

Pipeline Thesis: Tempest's TPST-4003 leading product candidate, next-generation CD7-tLNP in vivo CAR-T platform, utilizes a clinically supported dual-targeting CAR architecture pioneered in TPST-2003. Initial IITs in MG and MS are designed to validate Tempest's in vivo CAR-T platform in autoimmune disease, with expansion potential into oncology indications including LBCL, pediatric B-ALL, multiple myeloma, and selected T-cell malignancies including pediatric T-ALL, as well as rare diseases including POEMS syndrome.

Dual-CAR Architecture Clinical Results Support Lead In Vivo CAR-T Program

TPST-2003^{1,2} is the world's first parallel dual CAR-T for rrMM with EMD & POEMS syndrome – China BLA planned 2027

Dual-Target CAR-T Structure



REDEEM-1 Phase 1/2a (rrMM) and POEMS-1 Phase 1 (POEMS Syndrome)

44 patient target – 32 in REDEEM-1 and 12 in POEMS-1

20 patients dosed as of May 6, 2026 – 13 in REDEEM-1 and 7 in POEMS-1

100% CR rate among CAR-T-naïve patients (15/15) – REDEEM-1 (10/10 CR) and POEMS-1 (5/5 CR_{VEGF}) efficacy-evaluable as of March 31, 2026 and January 31, 2026, respectively

No grade ≥3 CRS, no grade ≥3 ICANS in REDEEM-1, Phase 1 enrollment complete (12/12), Phase 2a currently enrolling, first patient dosed May 2, 2026

Phase 1/2 Investigator-Initiated Trial (rrMM) – Enrollment Complete (24 patients)

100% ORR among all 19 patients with measurable disease at baseline, 89.5% CR rate (17/19), 100% CR rate at highest dose level (5/5)

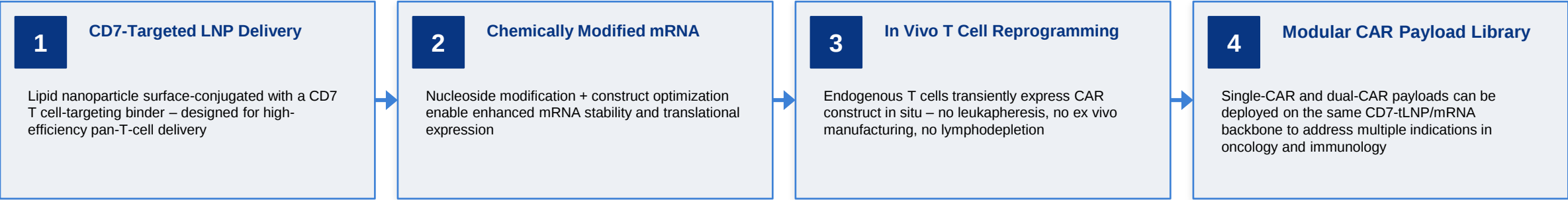
Median PFS of 23.1 months across all patients (24/24)

Median PFS of 23.1 months in EMD patients (15/15)

All evaluable patients at month 12 were MRD-negative (5/5)

Building Next-Generation In Vivo CAR-T for Oncology and Immunology

CD7-Targeted LNP In Vivo CAR-T Platform Architecture:



Product Matrix: Near-Term Clinical Asset + CD7-tLNP Platform Build-Out:

TPST-4003	TPST-001	TPST-002
CD7-tLNP · Next-Gen	CD7-tLNP · Platform Module	CD7-tLNP · Platform Module
Target: CD19/BCMA Lead product candidate dual-target CD7-tLNP asset designed for broad B-cell lineage reset. Targeting initial IIT validation in MG / MS, with multiple potential indications in oncology and immunology.	Target: Undisclosed Single-target module utilizing CD7-tLNP targeting and in vivo delivery with advanced payload for non-B-cell hematologic malignancies.	Target: Undisclosed Dual-target module utilizing CD7-tLNP targeting and in vivo delivery with advanced payload for solid tumors.
2026 IIT-TRACK	2027 IIT-TRACK	2027 IIT-TRACK

Sequencing Logic: TPST-4003 is the lead CD7-tLNP dual-target product candidate for initial IIT validation in MG and MS with treatment opportunities across multiple immunology and oncology indications. TPST-001 and TPST-002 add modules to the platform by leveraging advanced payloads, creating a modular in vivo CAR-T portfolio targeting bridging autoimmune disease and selected oncology indications beyond B-cell malignancies.

CD7-tLNP: Targeting Broader T-Cell Reach, Better Delivery Logic, Scalable In Vivo CAR-T

CD7-tLNP: Delivery Strategy Potential Advantages

Dimension	CD8-tLNP (Industry Standard)	CD7-tLNP (TPST Platform)
T Cell Coverage	CD8+ cytotoxic T cells only	Broader pan-T cell expression (CD4+ and CD8+ lineages)
Internalization / delivery efficiency	Standard kinetics	Rapid internalization reported – supports efficient mRNA delivery
Platform differentiation	Capstan/AbbVie CPTX2309 (Ph1, autoimmune)	Differentiated delivery ligand within same mRNA/LNP platform class

Literature Signal: Rapid receptor internalization potentiates CD7-targeted LNPs for efficient mRNA delivery to T cells and in vivo CAR-T engineering – a mechanistic rationale distinct from the CD8-targeting approach used by the leading clinical-stage competitor. (Zeng et al. J. Control. Release, 2026)

Chemically Modified mRNA: Payload Advantages

- ▶ Nucleoside chemical modification reduces innate immune recognition (TLR/RIG-I pathway activation) and extends functional mRNA half-life inside the target cell
- ▶ Construct-level optimization (UTR design, codon usage, tail design) designed to increase peak CAR protein expression per dose – supporting transient but robust in vivo CAR-T generation
- ▶ Potential combined effect: higher, more durable CAR expression per LNP particle – translating to lower required dose and improved manufacturing economics

In Vivo CAR-T: Structural Potential Advantages

◆ No Leukapheresis / No Ex Vivo Manufacturing

Endogenous T cells are reprogrammed in situ – designed to eliminate cell collection, viral transduction, and GMP expansion steps that drive ex vivo CAR-T cost and turnaround time (weeks → potentially days).

◆ No Lymphodepletion Conditioning

Designed to avoid chemotherapy-based conditioning required by ex vivo CAR-T, reducing toxicity burden – particularly relevant for chronic autoimmune populations not tolerant of repeated cytotoxic conditioning.

◆ Transient Expression, Repeat-Dosing Capable

mRNA-driven CAR expression is self-limiting (no genomic integration), which may enable redosing as a flexible treatment approach rather than a single irreversible cell-therapy event.

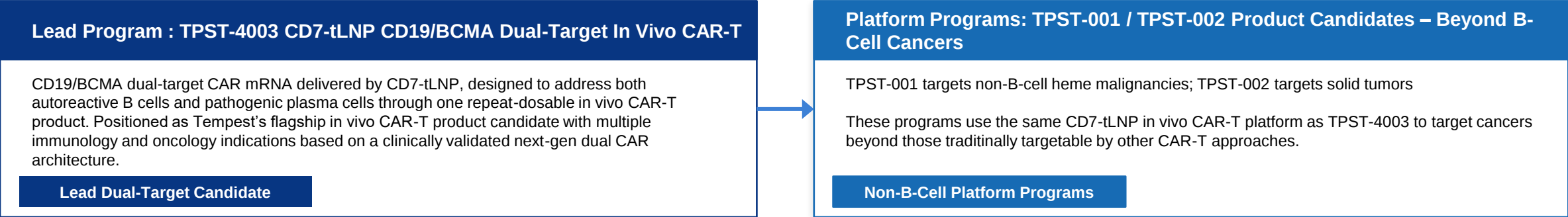
◆ Manufacturing & Access Economics

LNP-mRNA production is a standardized chemical/biologic process (vs. patient-specific cell manufacturing) – can support broader geographic access and lower per-dose cost structure at scale.

Product Implications: A differentiated CD7 delivery ligand may translate into broader addressable T-cell coverage, scalable repeat-dosing potential, and a more commercially attractive in vivo CAR-T format. This supports an autoimmune-first development strategy while preserving expansion optionality into oncology indications where rapid, accessible CAR-T generation could be clinically meaningful.

TPST-4003: CD19/BCMA Dual-Target In Vivo CAR-T

TPST-4003 targets broad B-cell lineage reset for durable responses across autoimmune and oncology indications



Strategic Rationale: TPST-4003 product candidate anchors the CD7-tLNP platform as a high-potential-value dual-target lead asset, combining CD19 and BCMA targeting to enable deep B-cell lineage reset. Initial IITs in MG and MS are intended to validate in vivo delivery, safety, and biologic activity, while TPST-001 and TPST-002 support modular expansion across autoimmune and oncology indications.

TPST-4003 Dual-Target Construct Overview

CD19/BCMA dual-target design is intended to clear both CD19+ B cells and BCMA+ plasmablasts / plasma cells, supporting deeper B-cell lineage reset through a single in vivo construct. This creates a differentiated positioning in autoimmune disease, with potential across B-cell-lineage indications, including multiple myeloma and POEMS syndrome.



Competitive Landscape – In Vivo Dual-Target CAR-T		
Program	Target	Status / Notes
TPST-4003 (Tempest)	CD19/BCMA	CD7-tLNP lead; in vivo repeat-dosing; dual B/plasma-cell coverage
CARTESS / academic dual-CAR (SLE)	CD19/BCMA (ex vivo)	Early case series only – ex vivo, single/sequential infusion
KYV-101 / Descartes-08	CD19 or BCMA (ex vivo)	Ph2/Ph3 – single-target only; no dual B/plasma cell coverage
Strategic Position: TPST-4003 product candidate combines three differentiators not currently represented by leading competitors: CD7-tLNP delivery, repeat-dosing mRNA format, and clinically validated dual CD19/BCMA targeting. This positions the asset as a differentiated lead program for large autoimmune markets, with validated biology supporting oncology expansion.		

TPST-4003 Market Opportunity Across Autoimmune Disease and Oncology

Market supports a focused CD7-tLNP in vivo CAR-T strategy spanning high-value autoimmune and oncology indications

Autoimmune Disease Opportunity			
Indication	U.S. Epidemiology	Market Size Framing	Strategic Implications
MG	~82.7k U.S. adults [1]	Global MG treatment market: \$1.75B (2026) → \$3.21B (2034) [2]	Premium biologic market with validated B-cell / plasma-cell biology; severe refractory populations support high-value positioning.
MS	~1.0M people living with MS in the U.S. [3]	Global MS drugs market: \$22.3B (2025) → \$39.7B (2036) [4]	Large chronic neurology market; B-cell biology already validated; repeat-dosing format could support chronic disease management.
SLE	~204k people with SLE in the U.S. [5]	Global SLE market: \$2.60B (2023) → \$4.26B (2030) [6]	High unmet need and relapse burden; dual CD19/BCMA could support deeper immune reset.

Autoimmune thesis: Premium chronic autoimmune markets support a redosable, non-lymphodepleting in vivo CAR-T format.

Oncology Opportunity			
Indication	U.S. Epidemiology	Market Size Framing	Strategic Implications
LBCL	~25k–30k U.S. cases / year; DLBCL incidence 5.6 per 100k [7,8]	7MM DLBCL market: \$5.3B (2025) → \$16.6B (2034) [9]	Large commercial CD19 hematology setting and attractive opportunity once in vivo delivery is validated.
B-ALL / Pediatric	~3,100 children and adolescents diagnosed with ALL / year; majority are B-ALL [10]	U.S. ALL therapeutics market: \$1.33B (2025) → \$3.57B (2035) [11]	Pediatric B-cell malignancy with meaningful unmet need; scalable format could broaden access beyond specialized centers.
rrMM / EMD	EMD incidence 3–14% in rrMM; up to 37% in late-line pts [12]	CAR-T MM market: \$3.1B (2024) → \$15.4B (2034); Carvykti FY2025 \$1.9B [12]	Large BCMA CAR-T market with high unmet EMD subgroup; CD19/BCMA dual-targeting supports differentiation.
POEMS	~3,200 U.S. patients; 0.5–5 cases / 1M / year [13]	Global POEMS market: \$2.5B (2024) → \$4.5B (2033) [13]	Rare plasma-cell disease with no approved cell/gene therapy; orphan potential and defined clinical catalyst.

Oncology thesis: LBCL, pediatric B-ALL, rrMM/EMD and POEMS provide high-value opportunities once in vivo delivery, safety and biologic activity are validated.

TPST-4003 Competitive Landscape and Strategic Differentiation

TPST-4003 Key Product Characteristics

Asset	Delivery	CAR Target	Cell Compartment Cleared	Candidate Indications	Timeline
TPST-4003	CD7-tLNP/mRNA	CD19/BCMA	B cells + plasma cells (dual)	MG / MS IIT validation; autoimmune, oncology & rare disease expansion	2026 IIT-track

Competitive Landscape and TPST-4003 Strategic Differentiation

Program / Company	Delivery	Target	Modality	vs. TPST Portfolio
CPTX2309 / AbbVie (Capstan)	CD8-tLNP	CD19	In vivo, Ph1 autoimmune	Closest tLNP benchmark; single-target CD19 and CD8-restricted delivery vs. TPST CD7 pan-T + dual CD19/BCMA.
ORN-252 / Lilly (Orna)	LNP / circular RNA	CD19	In vivo, clinical-ready autoimmune	Validates RNA/LNP-enabled in vivo CAR-T in B-cell-driven autoimmunity; single-target CD19.
KLN-1010 / Lilly (Kelonia)	Targeted lentiviral	BCMA	In vivo, Ph1 rrMM	Validates oncology value of in vivo CAR-T after early clinical proof; viral/integrating approach vs. transient mRNA/tLNP.
EsoBiotec ENaBL / AstraZeneca	Targeted lentiviral	Immune-cell programs	In vivo cell therapy platform	Validates in vivo cell therapy platform value; viral/integrating approach vs. transient mRNA/tLNP.
UB-VV111 / Umoja–AbbVie	VivoVec lentiviral	CD19	In vivo CAR-T, IND-enabling	Supports pharma appetite for in vivo CAR-T; oncology-focused CD19 program and viral delivery.
KYV-101 / Kyverna	Ex vivo	CD19	Ex vivo, Ph2 autoimmune	Validates CD19 immune-reset biology; specialist-center manufacturing and one-time dosing constraints.
Descartes-08 / Cartesian	Ex vivo mRNA	BCMA	Ex vivo mRNA, Ph3 gMG	Validates BCMA biology in autoimmune disease; requires ex vivo manufacturing.
BMS-986353 (BMS)	Ex vivo	CD19	Ex vivo, one-time	Validates CD19-in-SSc biology; durability window is finite, non-redosable
TPST-4003 (Tempest)	CD7-tLNP	CD19 + BCMA	In vivo, repeat-dosing	CD7 pan-T-cell delivery + dual CD19/BCMA + repeat dosing

Platform Thesis: TPST-4003 is the lead CD7-tLNP dual-target product candidate for initial IIT validation in MG and MS with treatment opportunities across multiple immunology and oncology indications. TPST-001 and TPST-002 leverage the same CD7-tLNP delivery platform with advanced payloads to expand the platform beyond B-cell malignancies.

In Vivo CAR-T Emerging as a Strategic M&A Category

Recent billion-dollar BD and M&A transactions show that scalable in vivo CAR-T platforms may command substantial value

Date	Transaction	Deal Value / Stage	Strategic Impact
Jan 2024	AbbVie × Umoja	Strategic collaboration; up to \$1.44B aggregate milestones	Signals early big-pharma appetite for multi-asset in-situ / in vivo CAR-T platforms before broad clinical proof
Mar 2025	AstraZeneca acquires EsoBiotec	Up to \$1.0B (\$425M upfront)	Supports in vivo cell therapy as a scalable platform category built around simple IV delivery and no immune-cell depletion
Jun 2025	AbbVie acquires Capstan	Up to \$2.1B; lead asset CPTX2309 in Phase 1	Highlights strategic interest in tLNP-based in vivo CAR-T for autoimmune disease
Feb 2026	Lilly acquires Orna	Up to \$2.4B; ORN-252 clinical trial-ready	Demonstrates investment in RNA/LNP-enabled in vivo CAR-T for B-cell-driven autoimmune disease
Apr 2026	Lilly acquires Kelonia	Up to \$7.0B (\$3.25B upfront); KLN-1010 Phase 1	Demonstrates significant value creation following early clinical data in hematologic malignancy

Tempest Impact

- Big pharma shown interest in vivo CAR-T platforms – not just for single assets, but for scalable delivery capabilities.
- The key value inflection includes early clinical data of delivery, safety, and biologic activity.
- TPST-4003 product candidate leads Tempest's in vivo CAR-T portfolio with planned early clinical data in MG and MS, and multiple potential indications of Tempest's in vivo CAR-T platform across oncology and immunology, including LBCL, multiple myeloma, pediatric B-ALL, selected T-cell malignancies such as pediatric T-ALL, and rare diseases such as POEMS syndrome.

Tempest Therapeutics: Building the Future of In Vivo CAR-T

Next-gen in vivo CAR-T platform leveraging clinical CAR-T positive results and targeting future CD7-tLNP clinical validation catalysts

Clinical positive results

TPST-2003

Ph1/2 dual CD19/BCMA CAR-T in rrMM + POEMS

Early efficacy signal

100% CR

CAR-T-naïve evaluable patients across REDEEM-1 + POEMS-1

Next catalyst

2026 IIT

TPST-4003 CD7-tLNP in vivo CAR-T validation in MG / MS

Category validation

\$1B–\$7B+

Recent strategic transactions in in vivo cell therapy

1 Clinical-stage foundation

TPST-2003 supports the biology

- Dual CD19/BCMA CAR-T in rrMM + POEMS
- Clinical data package supports dual-target biology
- Supported CAR for TPST-4003 in vivo strategy

2 Differentiated CD7-tLNP platform

CD7-tLNP takes CAR-T in vivo

- CD7-tLNP/mRNA delivery for broader T-cell reach
- No ex vivo manufacturing, no lymphodepletion
- Single-target and dual-target payload modularity

3 Multiple value inflection paths

Autoimmune & Oncology

- TPST-4003: MG / MS IIT validation path
- Potential to treat LBCL, B-ALL, MM, POEMS, etc.
- Large markets, M&As may create valuation asymmetry

Near-term strategy

Now Focus all internal development on next-gen in vivo CAR-T program

2026 IIT initiation / first dosing for TPST-4003

Next Safety, CAR expression and B-cell biology readouts

Later Develop for select oncology and immunology indications



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