



# Driving Next-Generation CAR-T Therapies: The *EndureCART™* Technology Platform

Integrated / Professional / Experienced / Efficient

## Contact Us

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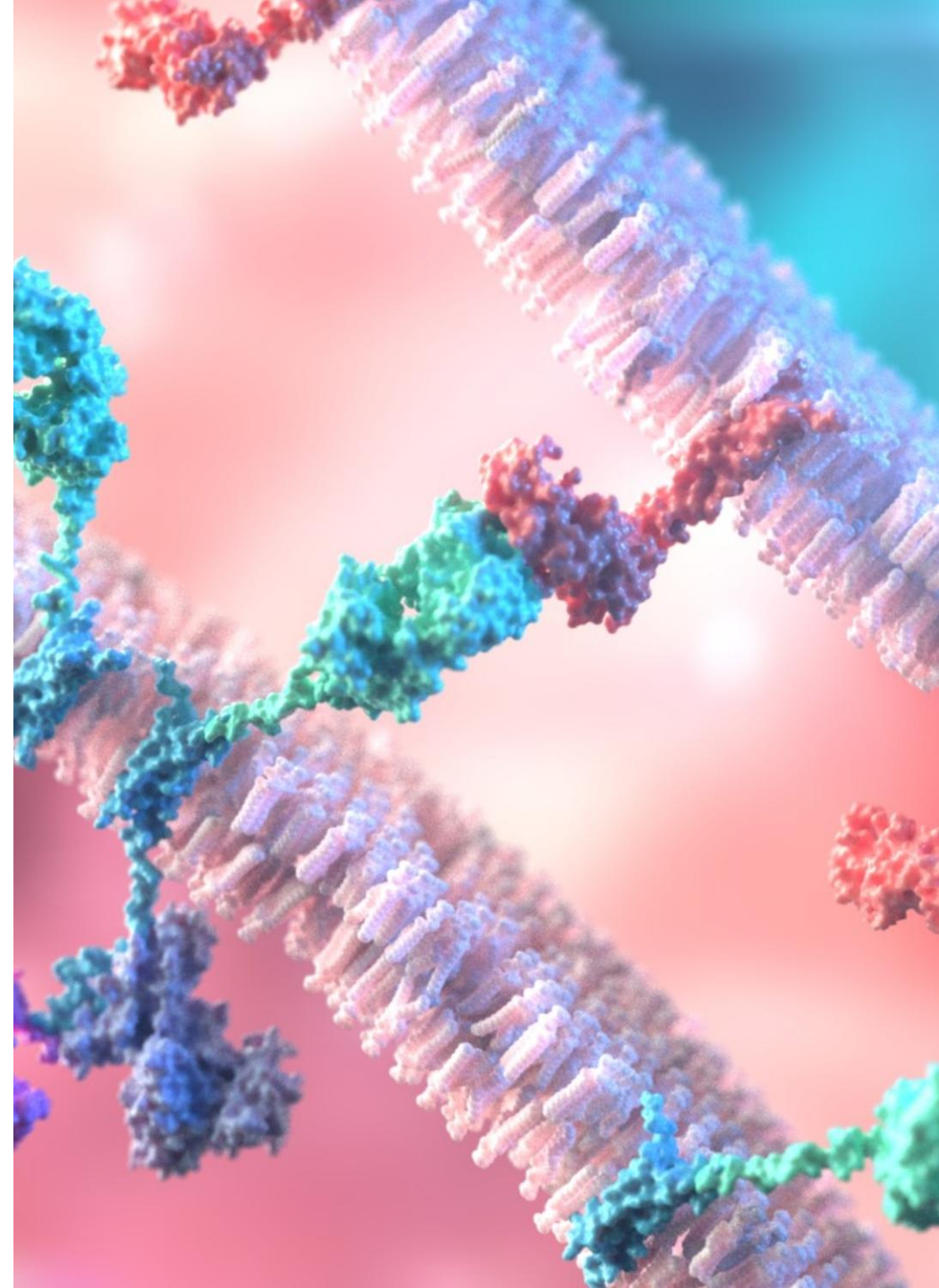
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# Overview

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# About Protheragen

## Accelerating CAR-T Innovation with *EndureCART™* Platform

Pioneering advancements in cellular therapeutics, **Protheragen** provides premier CAR-T technology platforms and comprehensive therapy development services. Our proprietary *EndureCART™* technology platform features enhanced intracellular signaling domains that augment CAR receptor functionality, facilitating the generation of sustained responses in CAR-T cell therapeutics.

Furthermore, as a specialized CAR-T research solutions provider, we deliver tailored services for your individualized CAR-T therapy development, leveraging our state-of-the-art technology platform and integrated research capabilities.

*Empowering Next-Generation CAR-T Therapies:  
Your End-to-End Development Partner*

### About Us

Accelerating Innovation in Cell Therapy



#### Our Vision

To be the leading provider of innovative and comprehensive CAR-T therapy development services, transforming the landscape of cancer and other disease therapy.



#### Our Mission

To empower our clients with the advanced tools, expertise, and integrated services necessary to efficiently and effectively develop and deliver next-generation CAR-T therapies to individuals in need.

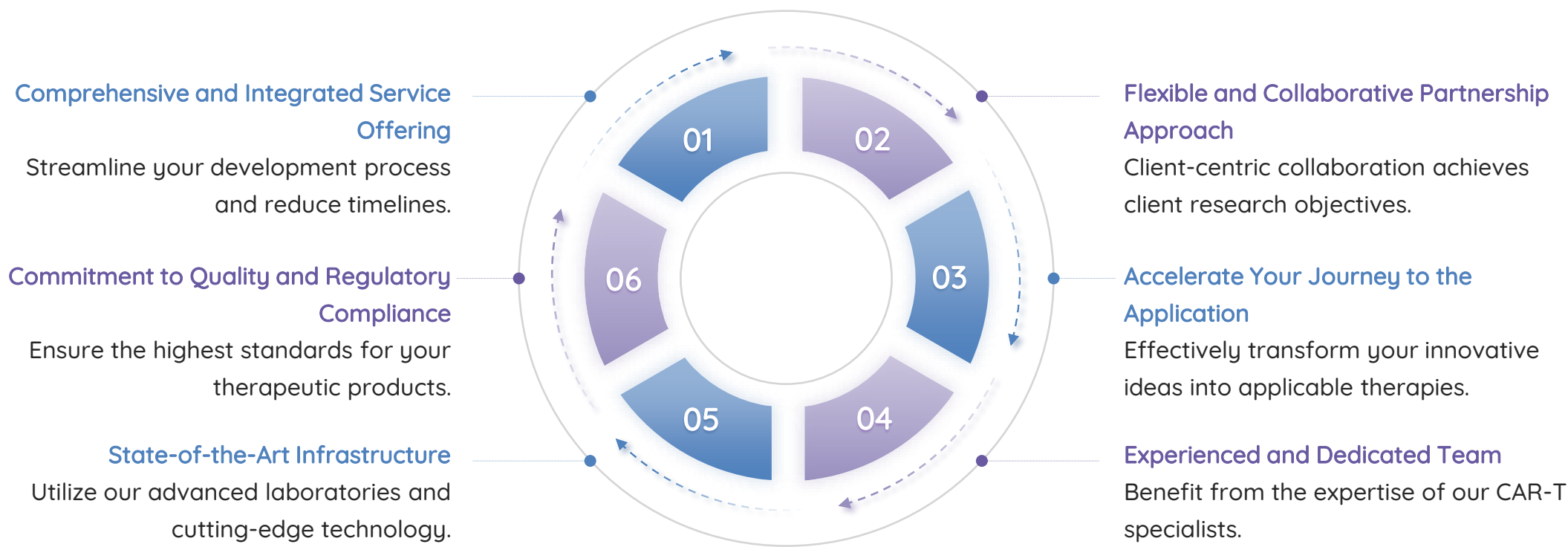




# About Protheragen

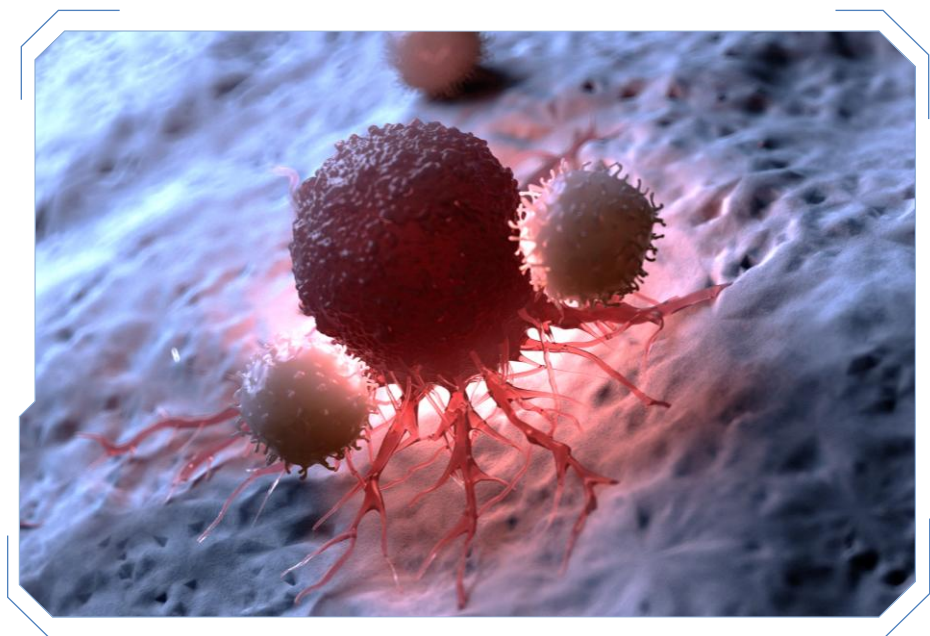
## Why Partner with Protheragen?

Choose us as your CAR-T therapy development partner and gain a strategic advantage through our pioneering *EndureCART™* technology platform and comprehensive, client-centric approach. We are dedicated to accelerating your journey from concept to commercialization, offering unparalleled expertise and integrated solutions that ensure efficiency, quality, and ultimately, the successful development of transformative cell therapies.



## EndureCART™: CAR-T Platform with Persistent Efficacy

Protheragen's *EndureCART™* technology platform signifies an advanced and groundbreaking methodology within CAR T-cell therapy research and development. This platform is meticulously engineered to overcome critical limitations and amplify the efficacy and durability of CAR T-cell therapies, ultimately striving to optimize therapeutic outcomes in oncology and potentially diverse disease areas.



The precise mechanism involves *EndureCART™* CAR-T cells with selective targeting that infiltrate tumor tissues, specifically engage antigens, and initiate intracellular signaling cascades, stimulating T-cell proliferation and cytokine secretion. This process modulates the tumor microenvironment, reverses immune suppression, and, with the collaboration of various immune cells, effectively eliminates tumor cells.

## The EndureCART™ Technology Platform: Driving Next-Generation CAR-T Therapies

### Core Innovation of EndureCART™

- Modification of the downstream signaling mechanism following CAR activation. The improved system enables activation of the STAT signaling pathway, a function conventional CARs typically lack regarding JAK-STAT pathway activation.
- Crucially, the high-intensity activation of the JAK-STAT signaling pathway is dependent on tumor antigens and independent of exogenous cytokines. This facilitates the sustained proliferation and activation of persistent CAR-T specifically within the tumor tissue.

## Conventional CAR-T Cell Therapy VS EndureCART™ CAR-T Cell Therapy

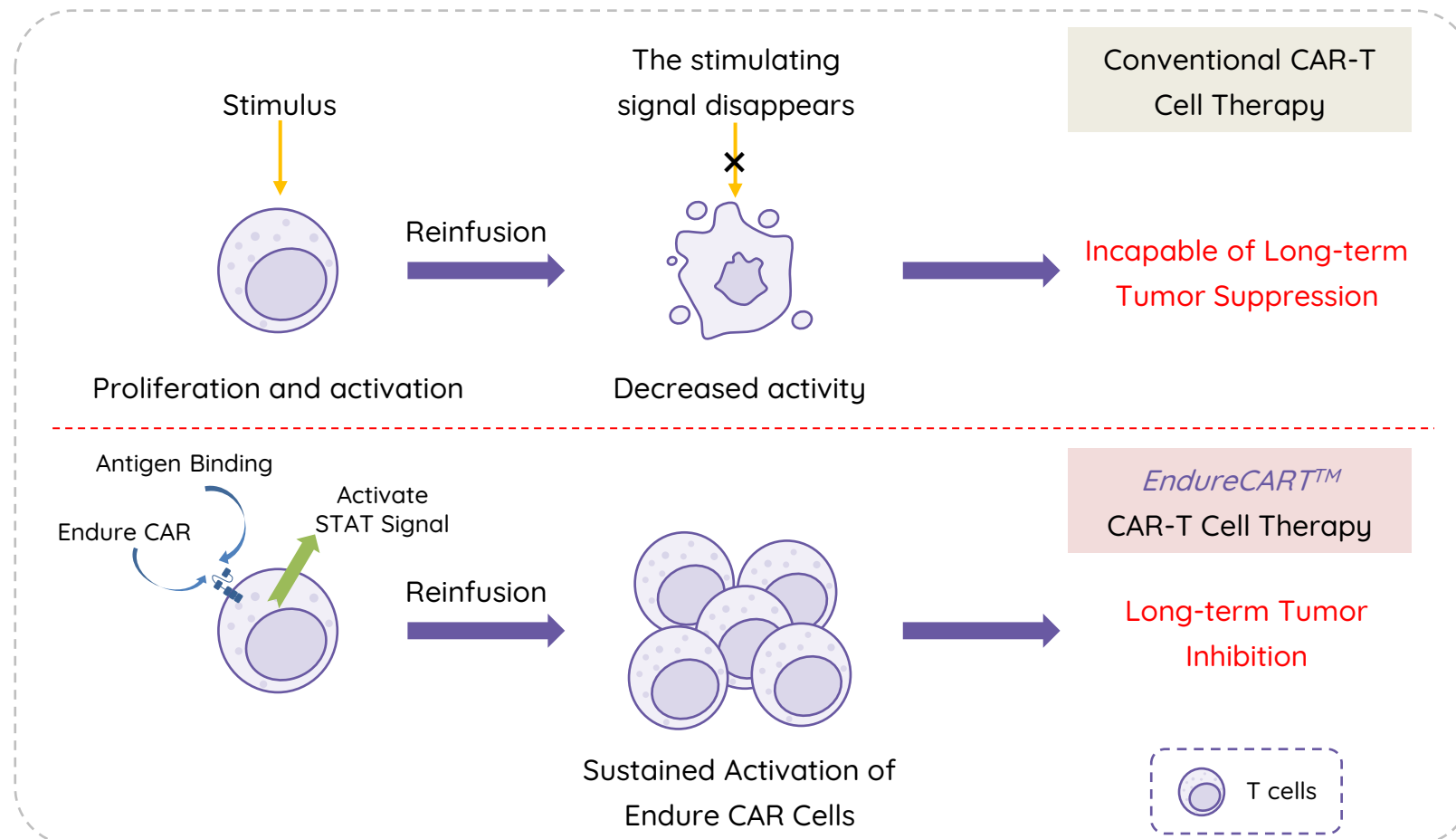


Table. 1 Conventional CAR-T VS Endure CAR-T

Types	Indicators	Conventional CAR-T	Endure CAR-T
In vitro testing	Tonic signal (No antigen exposure)	Elevated IFN-γ and IL-2 expression	Lower tonic signal ↓
	Tumor cell lysis ratio (Repeated antigen exposure)	The cell lysis rate hovers around 45%	The cell lysis rate stays high at 82% ↑
	Proliferation of CAR-T cells with repeated antigen stimulation	Cell numbers changed ~1.35-fold	Cell numbers changed ~2.6-fold ↑
In vivo evaluation	Efficacy validation	Inadequate tumor suppression (TGI: 50%)	Marked tumor suppression (TGI: 95%) and induced memory responses ↑
	Safety assessment	Approximately 10% weight loss	Minimal weight loss, around 1% ↓

## Advantages of EndureCART™



### Long-lasting Effects

Ensuring sustained T-cell activation for enduring therapeutic outcomes.



### Memory Therapy

Boosting T-cell memory capabilities for persistent tumor cell elimination.

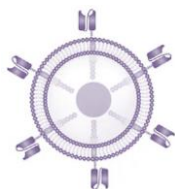


### High safety Standards

Maintaining high safety standards to reduce systemic toxicity and minimize therapeutic risks.

## The Versatility of the *EndureCART™* Platform: Enabling Diverse CAR-T Approaches

Harnessing the potent capabilities of the *EndureCART™* technology platform, **Protheragen** offers a comprehensive portfolio of innovative CAR T-cell therapy development services, encompassing both autologous and allogeneic approaches, to address a wide spectrum of hematological malignancies and solid tumors.



### Autologous CAR-T Cell Therapy Development Services

Utilizing an individual's T cells, engineered to provide a personalized therapy approach. Our *EndureCART™* technology platform is designed to enhance the persistence and anti-tumor activity of these autologous CAR-T cells.



### Allogeneic CAR-T Cell Therapy Development Services

Utilizing T cells from healthy donors, engineered to develop "off-the-shelf" CAR-T therapies for multiple individuals. Our *EndureCART™* technology holds the promise of improving the efficacy of allogeneic CAR-T cells.



# EndureCART™ Platform Applications

Protheragen serves as your dependable partner, fortified by our innovative *EndureCART™* technology platform and comprehensive expertise in CAR-T therapy development. Recognizing the distinct biological attributes and therapeutic complexities of each disease, we are dedicated to delivering precisely tailored CAR-T therapy development services. Regardless of your focus encompassing hematological malignancies, solid tumors, or other therapeutic domains, we possess the proficiency to design and develop the most efficacious CAR-T cell therapies customized to your precise requirements.

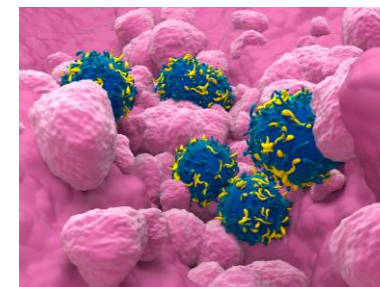


## Extensive Disease Models

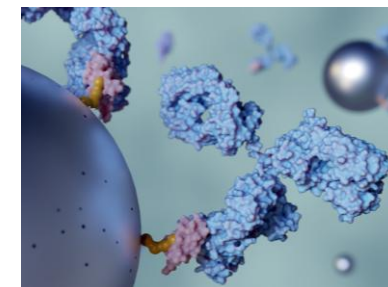
Protheragen's rich disease model serves as a tool for assessing CAR-T therapy *in vitro* and *in vivo*.



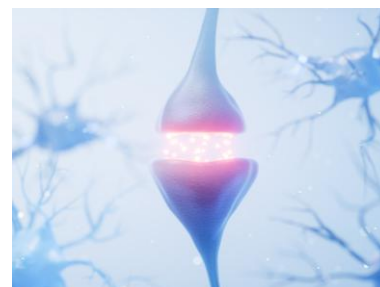
Hematological Malignancies



Solid Tumors



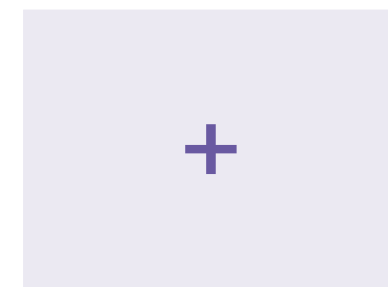
Autoimmune Diseases



Neurological Diseases



Infectious



Other Diseases

Pioneering Customized Cell Therapies: Diverse CAR-T  
Development with the *EndureCART™* Platform

# Case Study of *EndureCART™* CAR-T Therapy

Leveraging the *EndureCART™* platform, we have developed an EDB-targeting CAR-T cell therapy (Endure CAR-T). Compared to second-generation CAR-T cells, Endure CAR demonstrated enhanced T-cell activation and tumoricidal efficacy in both *in vitro* and *in vivo* experiments.

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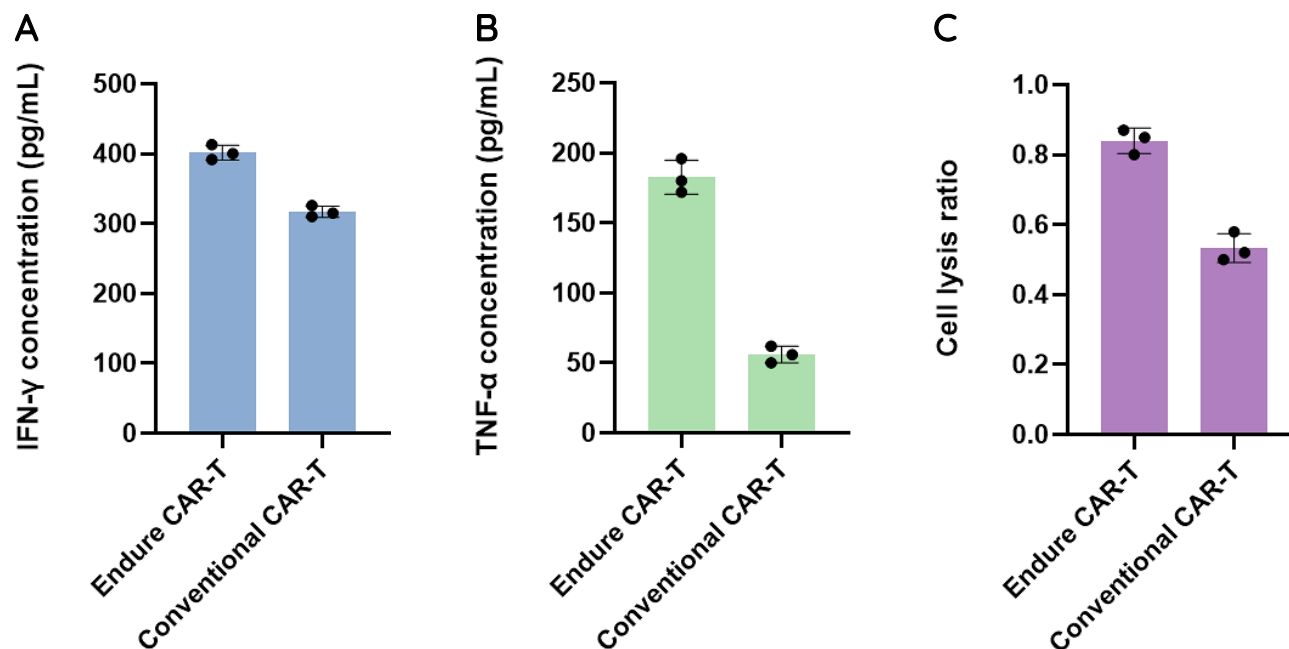


Fig.1 Cytotoxic activities of EDB-targeting second-generation CAR or Endure CAR T cells *in vitro*. After two rounds of tumor cell challenges, TNF- $\alpha$ , IFN- $\gamma$  expression, and cytotoxicity of the Endure CAR were superior compared to second-generation CAR.

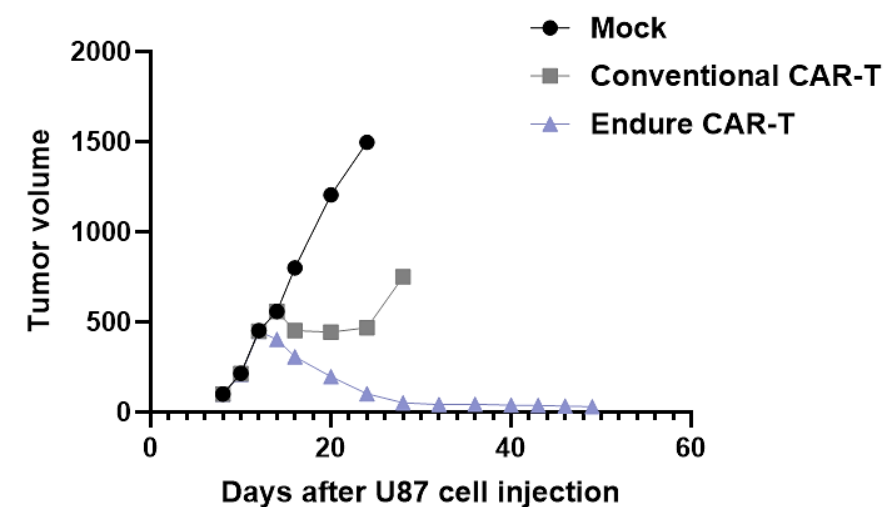


Fig.2 *In vivo* Anti-tumor efficacy of Endure CAR T-cells. In a large tumor model (>100 mm<sup>3</sup>), the rate of complete responses in PBMC-reconstituted NSG mice treated with Endure CAR T-cells approached 100%, demonstrating a significant advantage over both the control group and traditional CAR T-cells.

# Case Study of *EndureCART™* CAR-T Therapy

Expanding the application of our proprietary *EndureCART™* platform, we have successfully engineered a novel chimeric antigen receptor T-cell therapy targeting Claudin18.2 (CLDN18.2), designated as CLDN-Endure CAR-T. To evaluate the memory response and long-term protection, mice that achieved complete responses following the initial CLDN-Endure CAR-T therapy were subjected to a secondary tumor challenge (2X tumor challenge) with the same tumor line at a later time point, without any further CAR-T cell infusion.

02

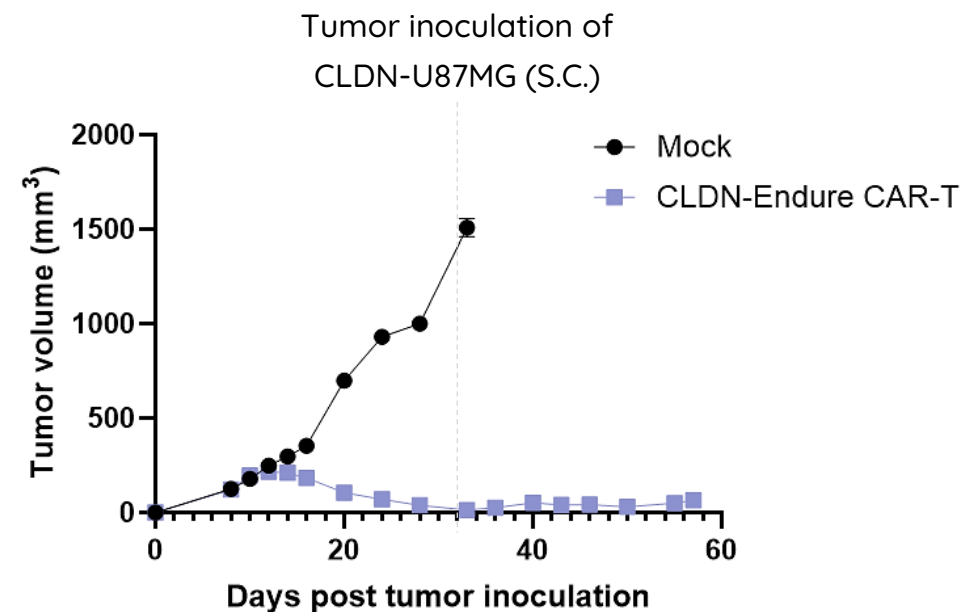
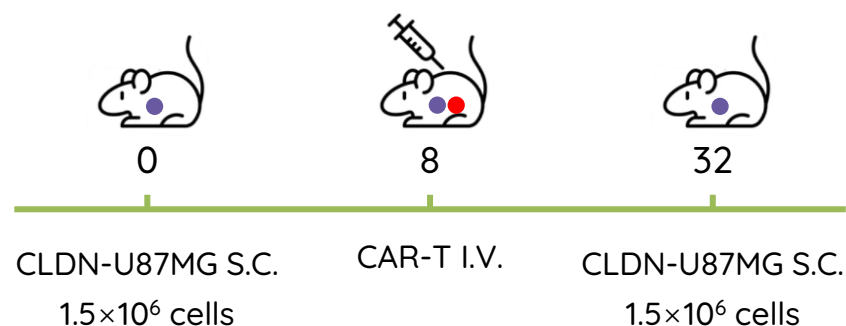
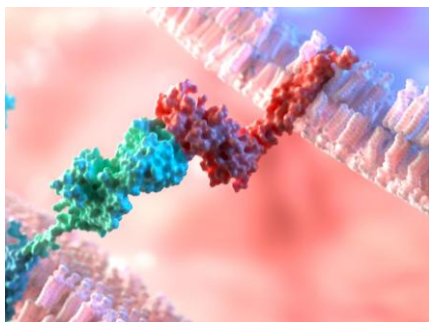


Fig.3 The anti-tumor efficacy and long-term memory response of CLDN-Endure CAR-T cells were evaluated in a stringent *in vivo* large tumor model. The mice that achieved complete responses following the initial CLDN-Endure CAR-T therapy exhibited a robust and durable memory response. Upon rechallenge with tumor burden, these animals demonstrated rapid and complete tumor eradication, with no evidence of tumor engraftment or growth.

# One-stop CAR-T Therapy Development

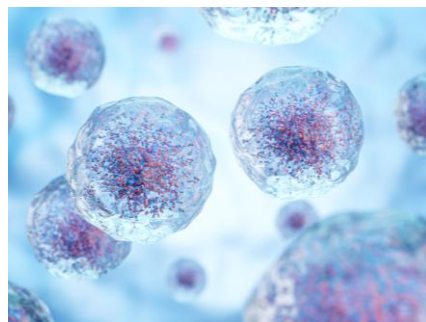
## Comprehensive Preclinical Research Services

Owing to our experience and know-how in developing cell therapies and with the availability of the advanced *EndureCART™* technological platform, **Protheragen** renders a full range of Preclinical services to the developers of CAR-T cell therapy, including the design of CAR molecules, preparation of cells, and conducting phenotypic analysis, cell and animal model generation, and *in vitro/in vivo* efficacy studies.



### CAR Design and Construction

- Target recognition and antibody development
- Design and construction of CARs
- CAR lentivirus preparation



### CAR-T Cell Preparation

- T cell isolation and activation
- Viral or non-viral gene delivery



### *In Vitro* Assay Services

- CAR expression validation
- CAR-T cell proliferation
- CAR-T cell cytotoxicity
- Cytokine detection



### *In Vivo* Analysis Services

- Animal model construction
- Pharmacodynamics
- Viability and bio-distribution study of CAR-T cells
- Toxicity evaluation



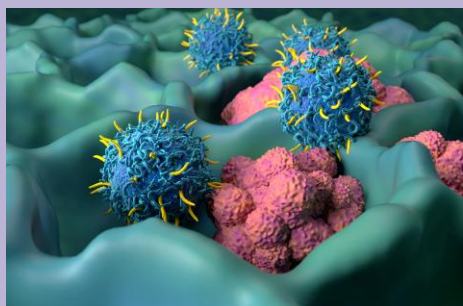
## Customized Clinical Research Services

Building upon our robust preclinical development expertise and the innovative *EndureCART™* technology platform, **Protheragen** offers comprehensive and specialized clinical research services designed to efficiently and effectively translate your CAR-T therapy candidates from preclinical success to impactful individual outcomes. Our dedicated team possesses deep experience in cell therapy, ensuring the highest standards of individual safety, data integrity, and regulatory compliance throughout all phases of development.



Access to the Cutting-Edge *EndureCART™* Technology Platform: Develop superior CAR-T therapies with enhanced efficacy and persistence.

Project	Modalities	Diseases	Discovery	Preclinical	IND	Phase I	Phase II	Phase III
ECAR01	EndureCAR-T	CRC, HCC						
ECAR02	EndureCAR-T	Sarcoma, HNCC						
ECAR03	EndureCAR-T	Solid Tumor						



Encompassing initial target validation and preclinical investigations, with a forward-looking perspective on upcoming clinical evaluations, each endeavor within our pipeline exemplifies our commitment to providing transformative CAR-T therapy development services. Collaborate with us to strategically advance projects within our pipeline or harness our technology platform and innovative solutions to accelerate your project's progression, collectively forging the future of cellular immunotherapy.

Should our project pipeline and technology platform pique your interest, we encourage you to contact us for comprehensive information.

# Collaboration Opportunities

Flexible collaboration models are tailored to meet your specific needs and objectives

- **One-stop Development:** End-to-end service from target discovery to clinical trial.
- **Modular Services:** Choose specific services to complement your in-house capabilities.
- **Technology Licensing:** Access and utilize the *EndureCART™* platform for your development programs.
- **Joint Development Programs:** Collaborative partnerships to co-develop innovative CAR-T therapies.
- **Customized Solutions:** We are open to discussing tailored collaborations to achieve your unique goals.



# Your Trusted Partner in CAR-T Therapy Development

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