Protheragen

Protheragen is a US-based company specializing in the global pharmaceutical and biomedical sectors. Our core services aim to precisely connect innovative pharmaceutical assets with potential partners worldwide, efficiently facilitating diverse strategic collaborations including, but not limited to: licensing-out, financing, co-development, and mergers & acquisitions.

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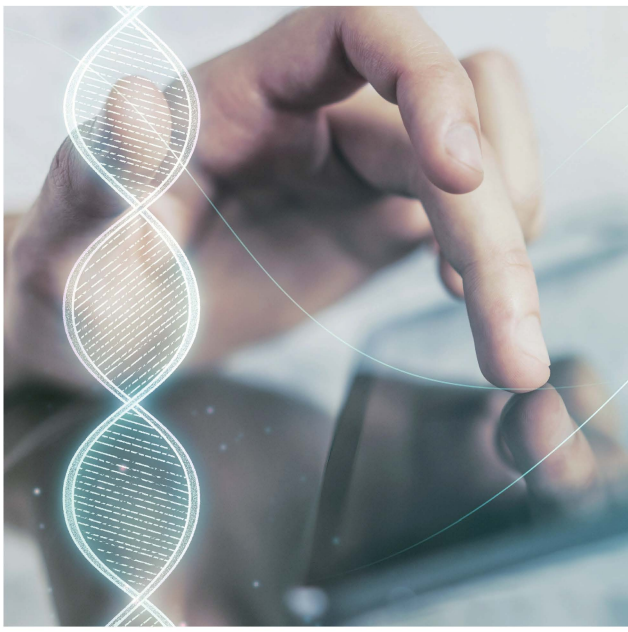
Bridging Global Pharmaceutical Opportunities

Headquartered in New York, Protheragen is a US-based company specializing in the global pharmaceutical and biomedical sectors. We are dedicated to helping biotechnology and pharmaceutical companies expand into international markets, providing exceptional business development and transaction intermediary services.



Professional Team

Protheragen has a dynamic and integrated team that is dedicated to architecting and fostering collaborative opportunities for business development within the global pharmaceutical field, leveraging its strategic footholds in the key markets. Our distinguished team brings a profound depth of specialized knowledge, a keen understanding of industry dynamics, and a forward-thinking approach to identifying and capitalizing on emerging trends.

Core Services

Our core services aim to precisely connect innovative pharmaceutical assets with potential partners worldwide, efficiently facilitating diverse strategic collaborations including, but not limited to:

- Licensing-out
- Equity financing
- Co-development
- Mergers & Acquisitions

Protheragen has collaborated with over 150 pharmaceutical/biotechnology companies, involving more than 500 assets. These assets include new drugs, medical devices, technology platforms, and diagnostic products, among which the majority are innovative drugs. The modalities include antibodies (including mAb, BsAb, and TsAb), ADCs, proteins, cell and gene therapies, etc. The development phases of these assets range from early discovery to late clinical trial phases.

Connecting Innovation

By partnering with us, you gain a direct, facilitated channel to innovation assets with strong scientific merit, competitive differentiation, and clear potential. This is an opportunity to instantly diversify and enrich your development pipeline with therapies targeting high-value therapeutic areas.

Table of Contents

A Novel AAV Gene Therapy for X-Linked Retinoschisis

Name	PTH-0451
Target	Retinoschisin 1
Drug Modality	Gene therapy
Indication	X-linked retinoschisis (XLRS)
Mechanism of Action	Improving the structure and function of the retina by expressing the retinoschisin 1 protein
Status	Phase I/IIa (NMPA); IND (FDA)
Patent	The patents for the core technologies have been granted, and applications for other important patents have also been submitted.

X-linked retinoschisis (XLRS) is an X-linked recessive genetic disease caused by mutations in the retinoschisin 1 (RS1) gene. It is characterized by the formation of schisis cavities within the retina and disorganization of retinal tissue, leading to functional decline. Patients present with varying degrees of visual impairment, and in severe cases, complications such as retinal detachment and vitreous hemorrhage may occur. Clinical treatment mainly consists of follow-up observation for complications and drug therapy, such as carbonic anhydrase inhibitors. There is currently no effective clinical cure.

Due to the clear pathogenic gene for XLRS, gene therapy has emerged as a new direction for its treatment. PTH-0451 is an adeno-associated virus (AAV) gene therapy injection currently under development. Through systematic design of target serotypes and gene expression elements, PTH-0451 can efficiently restore the expression of RS1 protein in retinal cells, thereby improving the retinal structure and function of patients.

Competitive Edge

	rAAV-hRS1	scAAV8-hRs-IRBP	PTH-0451
AAV Serotype	AAV2tYF	scAAV8	scAAV8 Self-complementary AAV, achieving rapid efficacy
Administration	Intravitreal injection	Intravitreal injection	Subretinal injection Achieving efficient infection of photoreceptor cells
Target protein	Wild-type RS1	Wild-type RS1	Independently-designed hRS1 Enhancing the protein expression level and expression specificity
Promoter	CB	IRBP-hRS1	RSP With good safety, strong expression level

Core Technologies

Two-Plasmid Technology

Compared with the three-plasmid system, the two-plasmid system features simplified production process, better batch-to-batch stability, significantly reduced costs, and higher-purity AAV drugs.

Expression Cassette Optimization Technology

Through the engineering modification of tissue-specific promoters, the optimization of target gene codons, and the design of cis-regulatory elements such as introns, the safety of the vector is further improved, and more efficient tissue-specific expression can be achieved.

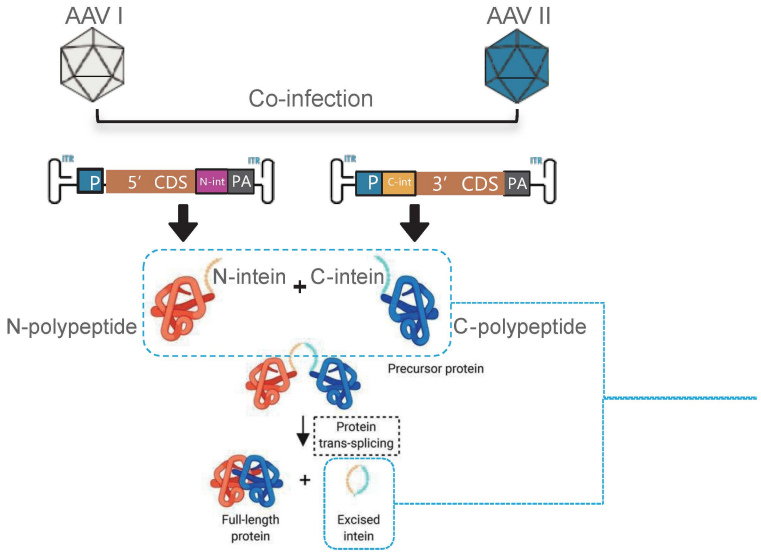
Capsid Screening Technology

AAV capsids with targeting properties and transduction efficiency for specific tissues or cells can be efficiently obtained through novel virus capsid screening and modification technologies.

Dual AAV Vector Delivery Technology

Through the splicing effect of intronic peptides, the peptide fragments delivered by AAV vectors can be spliced together to form complete and functional proteins, thereby overcoming the load limitation of AAV.

Expanding the application scope of AAV therapy through the use of dual-AAV delivery technology



- Through the splicing action of inteins, polypeptide fragments delivered by multiple AAV vectors can be assembled into complete and functional proteins.
- This technology effectively restores the expression of oversized target genes, thereby overcoming the cargo capacity limitations of AAVs.

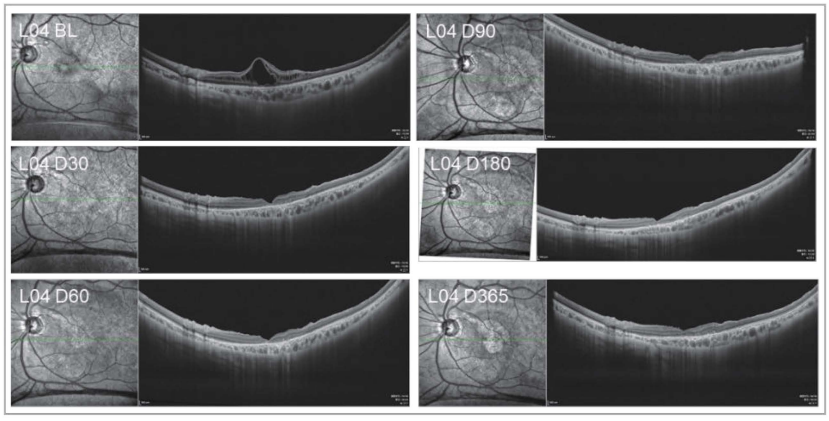
Investigator-Initiated Trial (IIT)

Improving the Retinal Structure and Function

In the investigator-initiated clinical trial, all 12 patients showed good tolerability, with no SAEs or DLTs reported. The results indicated that PTH-0451 had a favorable safety and tolerability profile and was effective at a low dose.

Following a single administration without the need for concomitant therapy, improvements in retinal structure and function were observed, including reduction or even complete closure of the schisis cavity, improvement in best-corrected visual acuity (BCVA), and a significant decrease in central retinal thickness (CRT).

The swept-source optical coherence tomography of the target eye of an IIT subject



A TEAD-YAP Interaction Inhibitor for the Treatment of Advanced Solid Tumors

Name	PKY001
Target	TEAD/YAP transcription complex
Drug Modality	Small molecule
Indication	Advanced solid tumors with abnormal Hippo signaling pathway
Mechanism of Action	Blocking the interaction between TEAD and YAP
Status	IND approval (NMPA)
Patent	Filed in the US, China, and other territories

The small molecule compound PKY001 is a direct YAP-TEAD interaction inhibitor that acts on the Hippo signaling pathway. It is being developed to treat advanced solid tumors caused by abnormalities in the Hippo signaling pathway, such as NF2-deficient malignant pleural mesothelioma, Hippo mutation NSCLC, or tumors with YAP/TAZ fusion.

PKY001 showed reasonable safety profiles in rats and beagle dogs with therapeutic window of about 7-fold. The estimated effective dose in humans ranges from a minimum of 50mg to a maximum of 450mg. In addition, combining PKY001 with an EGFR inhibitor or a G12C inhibitor improved efficacy and prolonged antitumor activity in NSCLC tumor models.

Asset Highlights

- A small molecule inhibitor directly blocking TEAD-YAP interaction
- Showing good druggable profiles with oral bioavailability and target specificity
- Demonstrated dose dependent anti-tumor growth inhibition in Hippo dysregulated tumor models
- Patent protected with international territory filed

Unmet Medical Needs

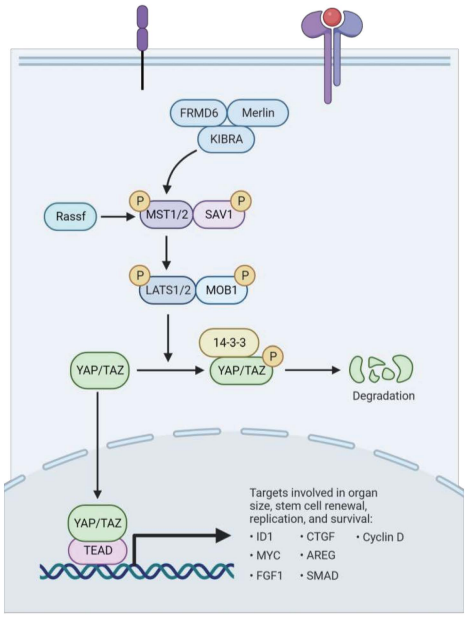
- Genetic deficiency of key hippo component elevates overactivation of TEAD/YAP transcription in cancer.
- TEAD-YAP activation is the key terminal step of Hippo and is the oncogenic driver in many cancers.
- Current lipid binding allosteric pocket has limited clinical efficacy.

Hippo Mutation is Common in Many Cancers

Cancer	Mutation	Frequency
Mesothelioma[1,2]	NF2 LATS2	51%
HNSCC[3]	FAT1	29%
ESCC[4,5]	FAT(1-4) YAP^{amp}	37%-48%
NSCLC[6]	FAT(1-4)	57%
LSCC[4,7]	FAT(1-4) LATS(1-2)	71%

[1] Fennell & Maehama, Oncotarget, 2019;[2] Wang et al., Nat Genet 2014; [3] Nature, 2015, 517(7536):576–582; [4] Maehama Cancer Sci. 2021; [5] Li et al., Nature comm. 2022; [6] Feng et al., Cancer Control 2022; [7] Nature, 2012;489: 519-525

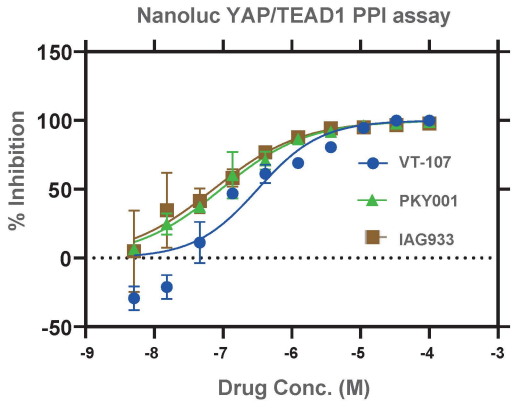
Aberrant TEAD/YAP Transcription Activation is Oncogenic



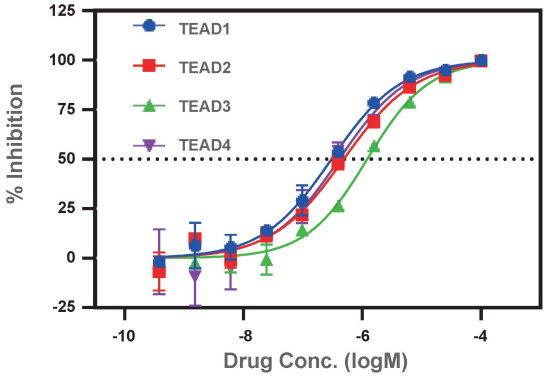
Strong Anti-Hippo Deficient Tumor Growth Inhibition

- PKY001 demonstrated dose-dependent inhibition of tumor growth in Hippo dysregulated tumor models.

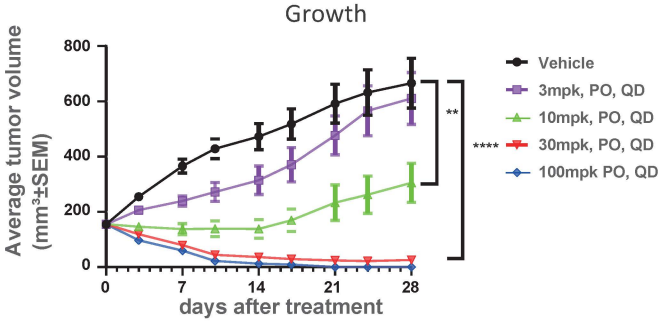
PKY001 Binding to TEAD/YAP Interaction Pocket



PKY001, A Potent pan-TEAD/ YAP/TAZ Inhibitor in Cells

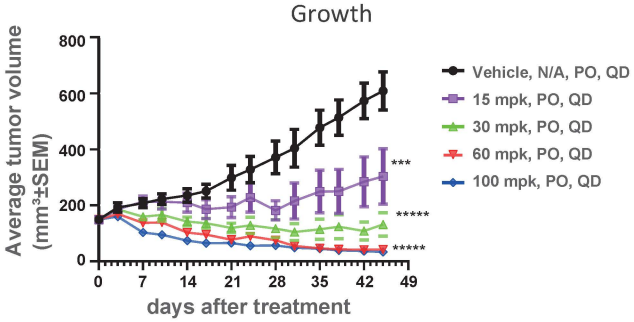


PKY001 Inhibits MSTO-211H (LATS1 Deficient) Tumor Growth



	3mg/kg	10mg/kg	30mg/kg	100mg/kg
TGI (%)	10.8	70.7	125.3	130.4
CR	0/8	0/8	1/8	8/8

PKY001 Inhibits NCI-H226 (NF-2 Deficient) Tumor Growth



	15mg/kg	30mg/kg	60mg/kg	100mg/kg
TGI (%)	66.4	103.9	123.3	125.2
CR	3/8	4/8	8/8	8/8

A Clinically Validated, First-in-Class CAR-T for mCRC

Name	GCC-CART
Target	Guanylate cyclase 2C (GUCY2C2)
Drug Modality	CAR-T cells
Indication	Metastatic colorectal cancer
Mechanism of Action	Modified T cells activated by targeting GUCY2C2 to kill tumor cells
Status	Phase I (FDA); IIT (China)
Patent	PCT patent filed

GCC-CART targets guanylate cyclase 2C (GUCY2C2), a transmembrane protein that is expressed in the metastatic lesions of 70%-80% of subjects with colorectal cancers. Based on a novel and proprietary CAR-T cell platform, GCC-CART pairs GUCY2C2-targeting CAR T-cells with CD19-targeting CAR T-cells to enhance proliferation, activation, and persistence against solid tumors.

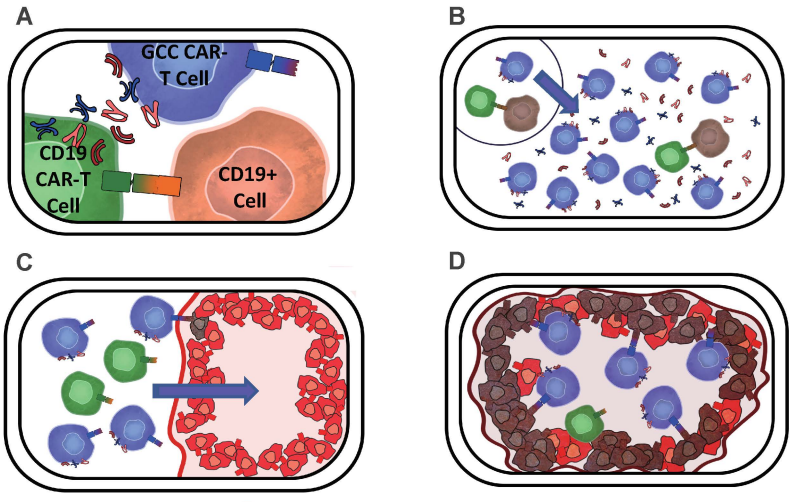
Preliminary data from phase I clinical trials in the US and investigator-initiated trials (IITs) in China shows that GCC-CART has significant efficacy and an acceptable safety profile in patients with mCRC.

Asset Highlights

- Proprietary first-in-class CAR-T technology effective in treating advanced and metastatic solid tumors
- Promising path to accelerated BLA approval based on robust data in a surrogate endpoint
- Broad application potential for earlier colorectal cancer settings (i.e. consolidation in first-line mCRC and high-risk adjuvant settings)
- GMP facility in the United States with 100% production success rate, and the capacity for Phase I studies

Mechanism of Action

As CD19 CAR-T cells kill B cells, signaling molecules are generated (A), resulting in the activation and proliferation of the solid tumor-targeted CAR-T cells WITHOUT engaging the solid tumor antigen (B). Coupled CAR-T cells release cytokines that promote solid tumor CAR-T cell infiltration of the tumor (C) and killing of target cells (D).



Potential Treatment for Metastatic Colorectal Cancer (mCRC)

Consistent results were observed across diverse patient populations based on current data from China and the US. The Chinese trials revealed impressive ORR of 50%, mPFS of 6.3 month, mOS of 26.1 month in the dose of 2E6/kg. Activity was confirmed in the US clinical trial.

The clinical trial results in China (dosage: 2 × 10^6 CAR-T/kg)	The clinical trial results in the US (dosage: 2 × 10^6 CAR-T/kg)
Efficacy • 50% ORR: 4 PR/8 patients • 1 CMR & 5 PMR/8 patients • 100% DCR: 0 PD/8 patients • mPFS=6.3 months • mOS=26.1 month	**Efficacy** • 80% ORR:1 pathCR & 3 PR/5 patients • 1 CMR/2 patients • 80% DCR： 1 PD/5 patients • mPFS 7.8 months • mOS not reached
Safety • No Grade 3 or higher CRS • 1 of 8 (13%) patients had grade 4 neurotoxicity • 4 of 8 (50%) patients had grade 3 diarrhea • 1 of 8 (13%) patients had grade 2 diarrhea • 3 of 8 (38%) patients had grade 1 diarrhea	**Safety** • No Grade 3 or higher CRS • 1 of 5 (20%) patients had grade 3 neurotoxicity • 1 of 5 (20%) patients had grade 3 diarrhea • 1 of 5 (20%) patients had grade 2 diarrhea • 3 of 5 (60%) patients had grade 1 diarrhea • 1 of 5 (20%) patients had grade 5 sepsis

The treatment demonstrated an overall response rate (ORR) of 80%, a median progression-free survival (mPFS) of 7.9 months, and a median duration of response (DoR) of 6.9 months at a dose of 2x10^6 units/kg, which has been established as the projected recommended Phase 2 dose (RP2D).

Unmet Medical Need

- ~47,950 new cases of colorectal cancer and 53,200 deaths in the US in 2020, ranking 4th in incidence and 2nd in mortality among all new cancer cases in the US.[1]
- ~50% of patients develop metastases[2], and mCRC is rarely cured[3].
- The standard of care for mCRC involves successive regimens of combination chemotherapy, as well as anti-VEGF therapy.
- No effective treatment options that provide meaningful clinical benefit after disease progression beyond two lines of treatment.[4]

[1] Howlader N, Cronin KA (eds). SEER Cancer Statistics Review, 1975–2017.
[2] Van Cutsem E, et al. Ann Oncol 2010; 21 (suppl 2):v93-97.
[3] Salvatore Siena, et al. ESMO Open, 2016 Mar 31;1(2).
[4] NCCN Clinical Practice Guidelines for Colon Cancer Version 2. 2021.

A Second-Generation Selective PARP1 Inhibitor for Cancer Therapy

Name	PROTH-021
Target	poly(ADP-ribose) polymerase 1 (PARP1)
Drug Modality	Small molecule
Indication	Advanced malignant solid tumor
Mechanism of Action	Inhibiting PARP
Status	Phase I (NMPA)
Patent	PCT patent filed

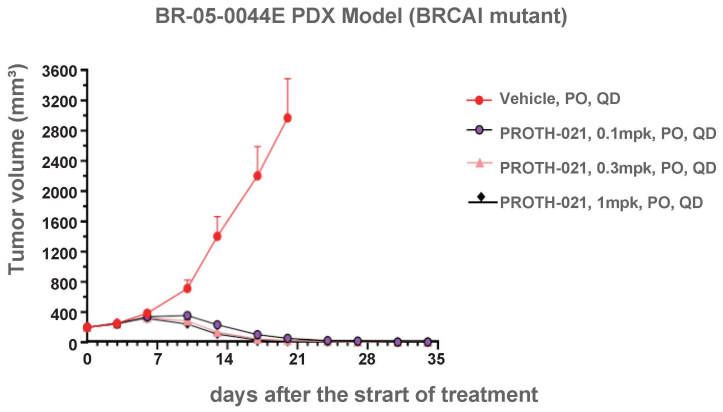
PROTH-021 is a second-generation small molecule PARP inhibitor, which is currently being developed for the treatment of advanced malignant solid tumors with homologous recombination repair deficiency (HRD) or BRCA gene mutations, including breast cancer, ovarian cancer, pancreatic cancer, prostate cancer, etc. PROTH-021 demonstrated good pharmacokinetic and safety characteristics in animal experiments.

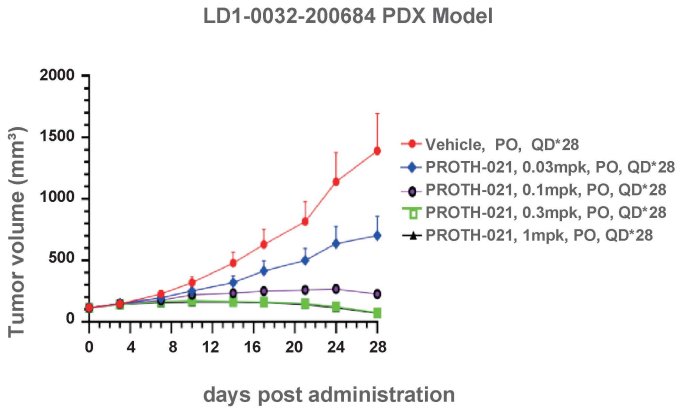
Asset Highlights

- Preclinical studies showed that PROTH-021 could induce PARP1 trapping and it only causes cell death in tumor cells with BRCA1/2 mutations, without affecting the growth of BRCA1/2 wild-type cells.
- In ovarian cancer and breast cancer CDX and PDX animal models, PROTH-021 showed significant tumor suppression effects, and complete tumor regression was achieved in some animals. This effect persists for 2 to 7 weeks after stopping the administration.
- Compared with the first-generation PARP inhibitors, the second-generation PARP inhibitors have better safety characteristics with alleviated hematological toxicities such as anemia. Their clinical applications as single drugs and in combination therapy are expected to expand.

Evaluation of the Efficacy in Animal Models

PROTH-021 showed a dose-dependent inhibitory effect on tumor growth in the breast cancer PDX mouse tumor model, as well as the ovarian cancer PDX mouse tumor model.





Other Nonclinical Pharmacological Studies

Study Topics		Details
Major Therapeutic Effects	In vitro	• PROTH-021 selectively traps PARP1 with an EC50 of 1.3nM, while its trapping ability for PARP2 is weaker, with an EC50 of 164.4nM. • PROTH-021 exhibits dose-dependent inhibitory effects on the proliferation of BRCA gene mutant tumor cell lines MDA-MB-436 and UWB1.289, with IC50 values of 0.984nM and 2.891nM, respectively. It does not have any inhibitory effect on the cell proliferation of BRCA gene wild-type tumor cell line MDA-MB-231, with an IC50 greater than 1000nM.
	In vivo	• PROTH-021 exhibited a dose-dependent inhibitory effect on tumor growth in the MDA-MB-436 (BRCA1 MUT) mouse tumor model. • PROTH-021 demonstrated a dose-dependent inhibitory effect on tumor growth in the ovarian cancer PDX mouse tumor model LD1-0032-200684. • PROTH-021 showed a dose-dependent inhibitory effect on tumor growth in the breast cancer PDX mouse tumor model BR-05-0044E.
Secondary Pharmacology	In vitro	• In experiments evaluating the functions of 44 safety-related enzymes and receptors, PROTH-021 (10μM) only inhibited Phosphodiesterase (PDE3A) by more than 50% (79%). • PROTH-021 increased the levels of the DNA damage response protein pH2AX in MDA-MB-436 cells, inhibiting DNA repair. • PROTH-021 showed dose-dependent inhibition of PARylation in MDA-MB-436 cells with an IC50 of 6.75nM.
	In vivo	• The study of the PD and PK relationship of PROTH-021 in the MDA-MB-436 mouse tumor model showed that with an increase in the plasma free drug concentration, the inhibition rate of PARylation in tumor tissue also increased. • PROTH-021 at doses of 1mg/kg and 3mg/kg had a mild and transient inhibitory effect on SD rats' reticulocyte count and significantly lower inhibitory effect compared to Olaparib (100mg/kg).
Safety Pharmacology	hERG	IC50>0.8749μM (0.40μg/mL) (highest tested concentration)
	Cardiovascular system (Canine)	No adverse effects were observed at the doses of 3, 10, and 30 mg/kg.
	Respiratory system (Rat)	No adverse effects were observed at the doses of 20, 60, and 200mg/kg.
	Central nervous system (Rat)	

A Novel Water-Soluble TRPM8 Agonist for the Relief of Dry Eye Discomfort

Name	PTH-I001
Target	TRPM8
Drug Modality	Small molecule
Indication	Dry eye disease
Mechanism of Action	Activating TRPM8
Status	Phase I/II (FDA)
Patent	PCT patent filed

Transient receptor potential melastatin 8 (TRPM8) is the principal receptor protein of cold-sensitive nerve fibers associated with the detection of cooling sensations on body surfaces such as the skin. PTH-I001, a novel water-soluble TRPM8 agonist, is a promising candidate for relief of dry eye discomfort. PTH-I001 affects the ophthalmic nerve and central nervous system through selective activation of TRPM8 and effectively promotes tear secretion to directly alleviate dry eye symptoms while simultaneously improving both symptoms and clinical signs.

Asset Highlights

- A unique, simpler route of administration using an eyelid wipe on the upper eyelid that provides longer duration of action, and improved safety and efficacy.
- Rapid onset of action, breaking through the slow efficacy limitations of current dry eye medications.
- Innovative eyelid wipe administration with Unit Dose packaging, offering clear differentiation in clinical and commercial applications.
- Globally patented, with exclusive worldwide compound patents and a comprehensive IP portfolio of over 50 invention patents.

Unmet Clinical Needs in Dry Eye Disease

The global dry eye disease market is poised for significant expansion, driven by an aging population and increasing digital screen exposure. However, a substantial gap remains between the growing patient population and the effectiveness of current therapeutic options. A primary unmet clinical need lies in the slow onset of action of existing treatments. First-line prescription anti-inflammatory therapies can take weeks or even months to demonstrate noticeable symptomatic relief. Furthermore, complex administration regimens significantly hinder patient compliance. The management of dry eye disease frequently requires the frequent, long-term application of multiple types of eye drops. The physical burden of self-administration coupled with common side effects like transient stinging or blurred vision, creates a high barrier to adherence.

Competitive Advantages

PTH-I001: Potential for Best in Class for Dry Eye Disease

- Right Molecule: Cooling Sensation instead of Cold (no irritation), symptoms improved significantly and rapidly
- Right Delivery: Target on eyelid margin (better safety & efficacy)
- Right Time: < 5 min onset

	PTH-I001	AR-15512/WS-12
Status	Phase II completed Positive topline data	Phase III topline data Met primary endpoint
Target	TRPM8	TRPM8
Administration route	Eyelid wipe	Eye drop
Sensation	Cool feeling (Comfort)	-
API (Drug Substance)	Clear liquid	White powder (crystals)
API Solubility	Soluble in water up to 50 mg/ml	Insoluble in water

Phase I/II Clinical Trial Topline Data

The phase I/II clinical trial enrolled 150 patients with dry eye disease in the United States.

Safety Results Confirming Favorable Tolerability Profile

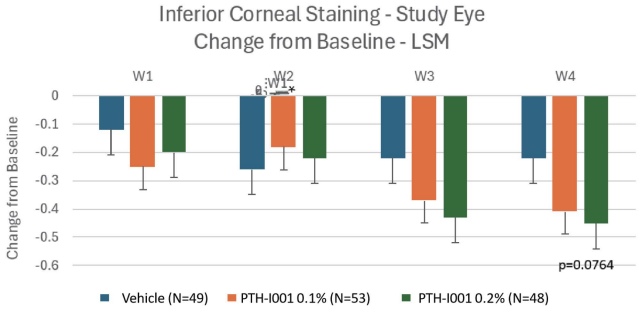
- PTH-I001 was well-tolerated across all treatment groups, with the majority of adverse events (AEs) being mild or moderate in severity.
- Ocular irritation was the most commonly reported AE, observed slightly more frequently in the PTH-I001 treatment groups (3%) compared to vehicle (0%).
- No serious adverse events (SAEs) related to the investigational product (IP) were reported.
- No patients discontinued the study due to IP-related AEs.

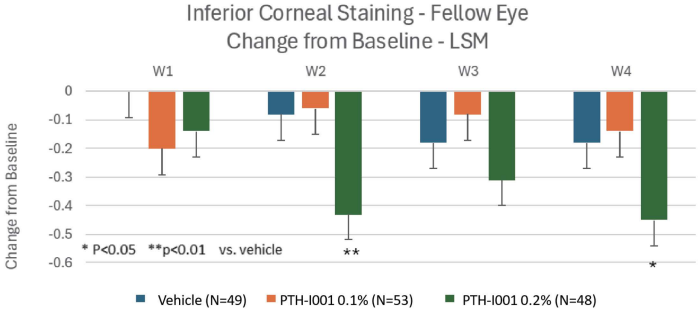
Preliminary Efficacy Results Identifying Potential Endpoints for Future Trials

The trial achieved statistically significant and clinically meaningful improvements in key signs and symptoms of dry eye patients at the final timepoint (Week 4), including reductions in corneal fluorescein staining (total and inferior zones) and significant reductions in symptom scores, including Eye Dryness Score and SANDE (frequency and severity). There were also positive trends in both basal (anesthetized) and reflex (unanesthetized) tear production. Moreover, the data demonstrated a dose-response relationship, with the higher dose (0.2%) consistently showing greater efficacy across multiple endpoints.

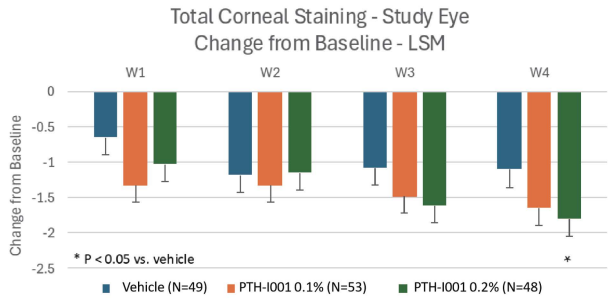
- Total / Inferior CFS – Corneal Health- Key Sign Improvement

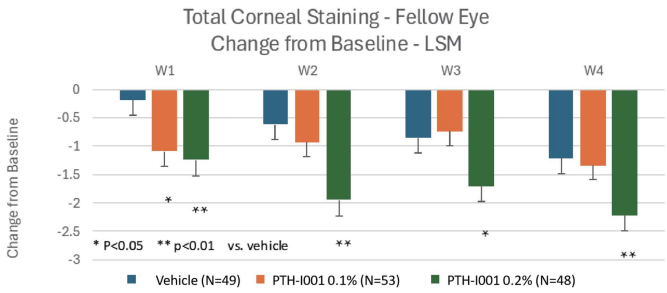
Inferior Corneal Fluorescein Staining: PTH-I001 0.2% improved staining significantly (week 4:-0.45 vs.-0.18, p=0.0318) over vehicle.





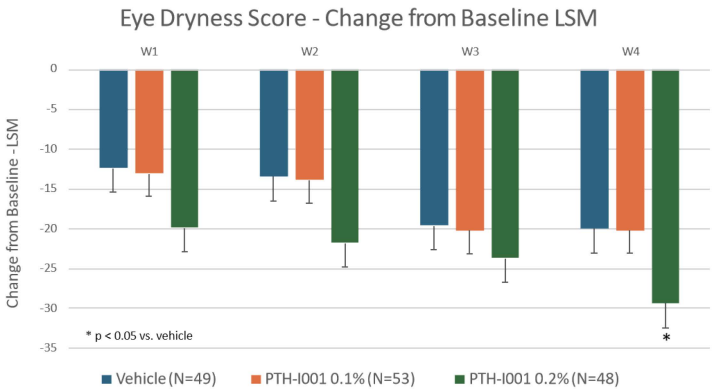
Total Corneal Fluorescein Staining (Zones 1-5): PTH-I001 0.2% reduced staining (-1.7 vs.-1.3, p=0.0097) over vehicle.





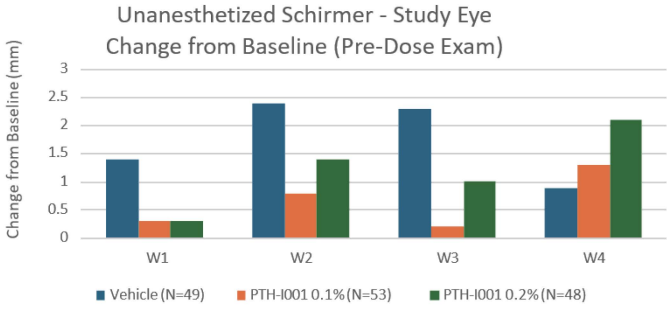
- Significant Eye Dryness Score Improvement

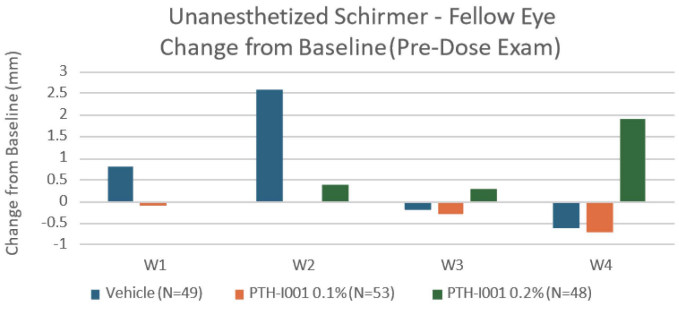
Eye Dryness Score is the most sensitive symptomatic endpoint for PTH-I001's efficacy. The significant improvements observed at Week 4 justify prioritizing this measure in future studies. Significant reductions with PTH-I001 0.2% (-22.8 vs.-18.3, p=0.0315) compared to vehicle at Week 4 highlight its symptomatic efficacy.



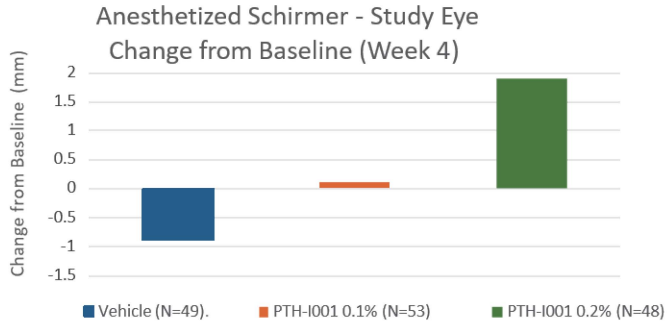
- Tear Production Schirmer's Tests

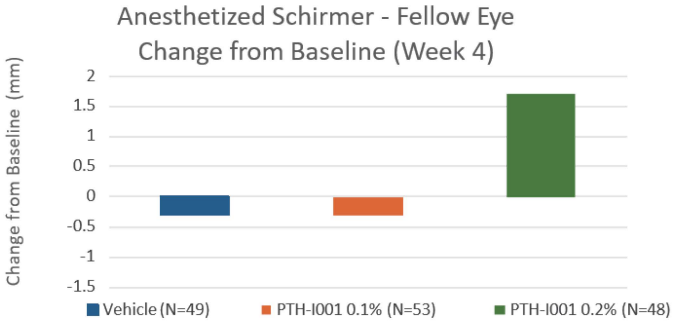
Schirmer's Test (Unanesthetized): PTH-I001 0.2% demonstrated the greatest improvement in tear production (+2.1 mm), though statistical significance was not achieved. Dose-dependent trends were evident.





Schirmer's Test (Anesthetized): PTH-I001 0.2% improved basal tear production (+1.9 mm). Responder rates favored PTH-I001 0.2% (8.5%) over vehicle (4.3%).





A First-in-Class Bispecific ADC Targeting HER2/Trop-2 for the Treatment of Solid Tumors

Name	PTH-I0201
Target	HER2; Trop-2
Drug Modality	Bispecific ADC
Indication	Solid tumor
Mechanism of Action	Delivering a new DNA topoisomerase I inhibitor specifically into tumor cells expressing HER2/Trop-2
Status	Preclinical
Patent	Granted

PTH-I0201 is a novel antibody-drug conjugate (ADC) consisted of a novel bispecific anti-HER2/Trop-2 antibody conjugated with a proprietary potent DNA topoisomerase I inhibitor via a cleavable linker. This DNA topoisomerase I inhibitor exhibits similar characteristics with DXd, including in vitro and in vivo anti-tumor activities and safety profile. PTH-I0201 was demonstrated to have enhanced cell binding and internalization, and to exhibit strong cytotoxicity against cancer cells that co-express HER2and Trop-2.

PTH-I0201 was fully characterized, and in vitro and in vivo anti-tumor activity of PTH-I0201 was assessed using preclinical models. PTH-I0201 may be expected to have a similar clinical activity to Enhertu or Trodelvy but treat more patient sub-populations and indications.

Asset Highlights

Potency and Efficacy

- Comparable in vivo anti-tumor activities toward HER2 and Trop-2, ensuring a similar clinical efficacious dose range against tumors expressing either of these two targets

Minimizing Trop-2 Associated On-Target Toxicity

- Lower binding affinity to Trop-2 than that to HER2
- Higher binding off-rate to Trop-2 binding

In-House Developed Payload and mAb

- Proprietary topoisomerase I inhibiting toxin with proven clinical efficacy
- Anti-Trop-2 mAb developed in house; Anti-HER2 mAb: Trastuzumab

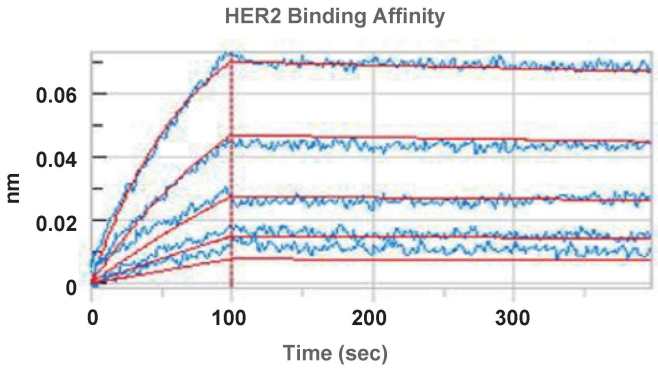
Addressing the Challenge of Trop-2 ADC On-Target Toxicity

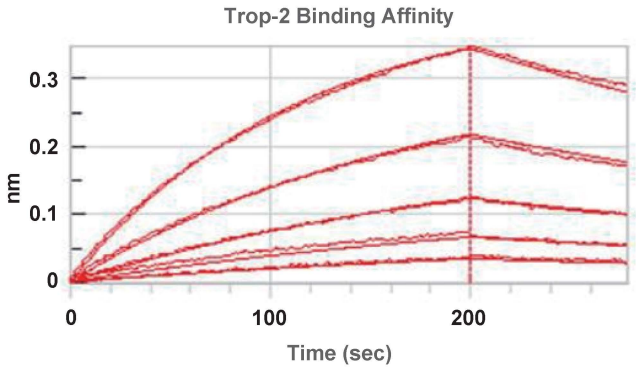
The expression level of Trop-2 is relatively high in some normal tissues, which leads to on-target toxicity.

Product	Company	Target	DLT
PF-06664178	Pfizer	Trop-2	• Mucosal inflammation • Rash • Toxic epidermal necrolysis
SKB264	Merck/Kelun	Trop-2	• Stomatitis • Rash

DS-1062	Daiichi Sankyo/AstraZeneca	Trop-2	• Mucosal inflammation • Stomatitis • Rash

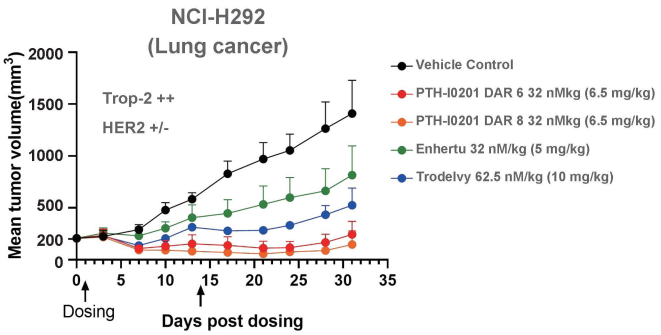
PTH-I0201 exhibits a higher binding affinity to HER2 than to Trop-2, and has a faster dissociation rate from Trop-2. Therefore, it can minimize the target associated toxicity.

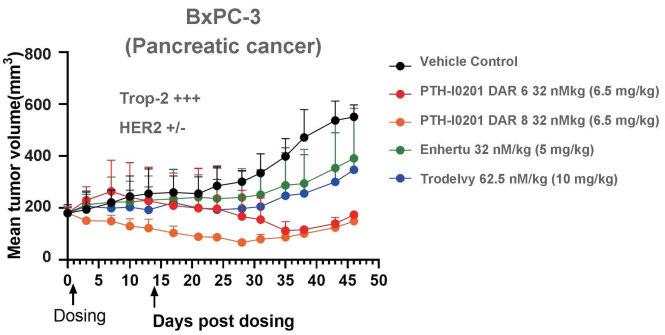


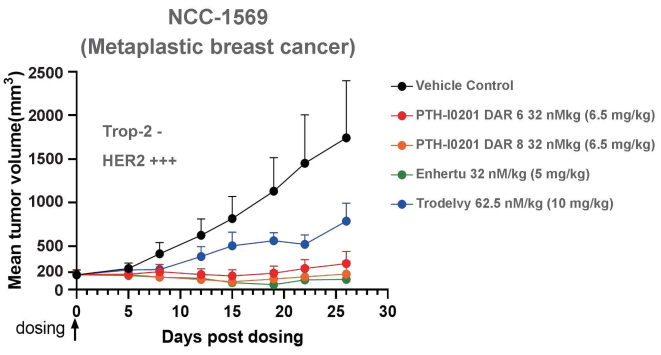


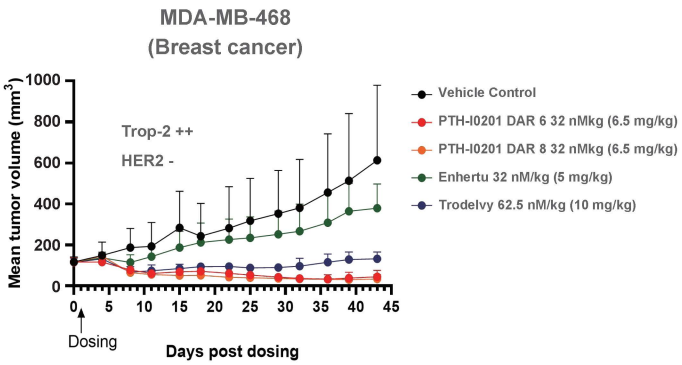
Potent Anti-tumor Activity in Tumor Xenograft Models

In xenograft models with HER2- or Trop-2-positive tumors, PTH-I0201 showed robust anti-tumor effects, implying broader spectrum of tumor coverage compared to ADCs targeting a single target. Particularly in tumor models that were insensitive to Enhertu and Trodelvy, PTH-I0201 demonstrated potent anti-tumor activity.









A First-in-Class MyD88 Inhibitor for the Treatment of Psoriosis

Name	PROTH-007
Target	MyD88
Drug Modality	Small molecule
Indication	Psoriasis
Mechanism of Action	Inhibiting the dimerization of MyD88, thereby interrupting or attenuating associated signaling pathway
Status	Phase 2 (psoriasis, China); IND (multiple indications, the US and China)
Patent	International patents grated

PROTH-007 is a first-in-class small molecule that inhibits MyD88, which specifically binds to the TIR domain of MyD88 and prevent its dimerization, thereby interrupting the transmission of immune signals. PROTH-007 is currently undergoing phase 2 clinical trials in China for the treatment of psoriasis. Other indications currently under development include autoimmune diseases, chronic inflammation, neurodegeneration, transplant rejection, inflammatory tumors, metabolic inflammatory diseases, etc.

Asset Highlights

- A innovative MyD88 inhibitor at the clinical stage
- Broad range of indications, including various severe inflammatory diseases

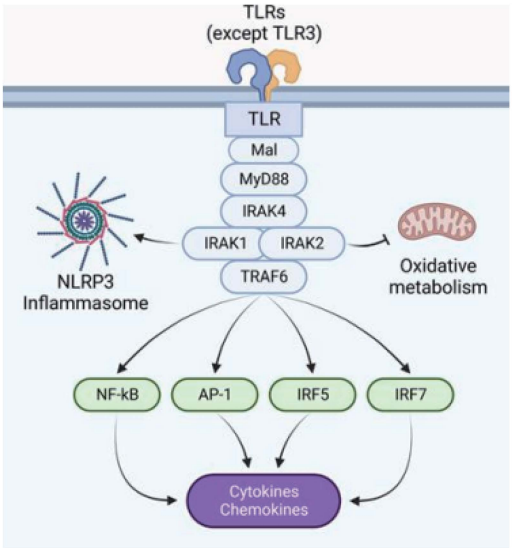
Formulation	Indication	Development Phase
PROTH-007, Ointment	Psoriasis	Phase II in China
	Eczema	IND Applied in the US and China
	Nervous dermatitis, etc.	
PROTH-007, IV Injectable	Acute myocardial infarction	
	Acute cerebral infarction	
	Organ transplantation	
	Limb replantation	

Scientific Rationale for the Target

MyD88 – A Key Molecules in TLR Signal Pathway

Under pathological conditions, the persistent stimulation of Toll-like receptors (TLRs) by pathogen-derived signals induces hyperactivation of the TLR/MyD88 signaling pathway, thereby triggering various immune inflammatory disorders. Within the TLR signaling cascade, MyD88 plays as the central signaling transducer. Except for TLR3, the other TLR subfamily members propagate downstream signals through MyD88-dependent mechanisms.

MyD88 functions as a critical nodal hub for signal transduction in the innate immune system. Inhibiting the dimerization of MyD88 shows therapeutic potential by attenuating or disrupting associated immune signaling cascades.



The Efficacy of PROTH-007 Ointment in Clinical Trials

The Investigator-Initiated Trials (IIT)

Indication	Number of Cases	Outcome
Psoriasis	15	All cured
Neurodermatitis	11	9 cases cured
Atopic Dermatitis	7	3 cases cured
Allergic Dermatitis	12	All cured
Ulceration from insect bites	15	All cured

PROTH-007 ointment demonstrated excellent efficacy in the IIT, with the following highlights:

- Quick effect in minutes
- >90% Radical cure
- 100% Complete remission
- Reduced scar tissue
- Reduced pigmentation, whitened skin

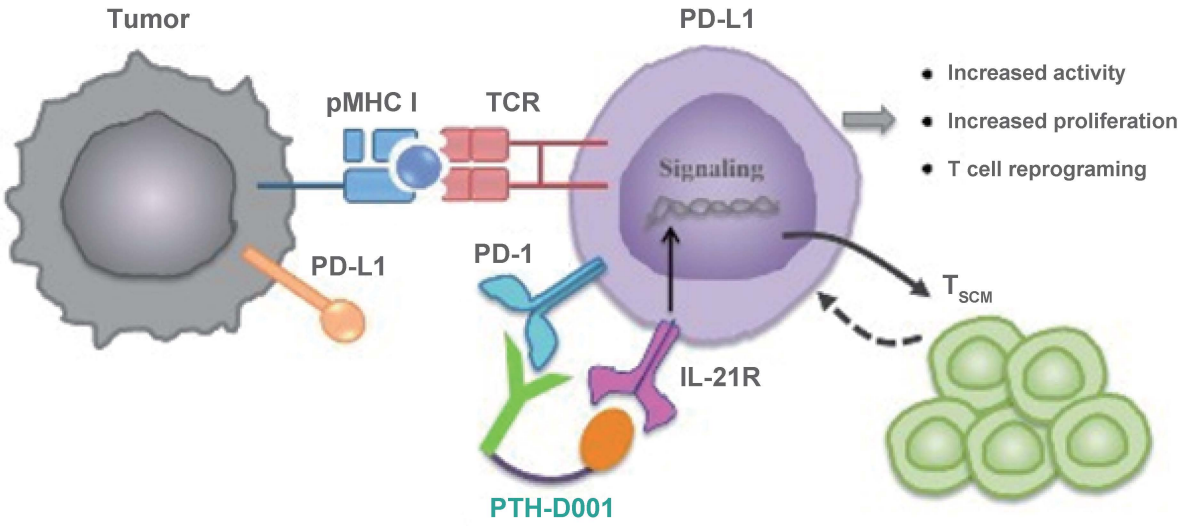
The Phase I Clinical Trial (Completed)

PROTH-007 ointment demonstrated good safety and tolerability in healthy subjects, and its pharmacokinetic characteristics showed a dose-dependent pattern. No serious adverse reactions were observed.

A Novel Fusion Protein Targeting IL-21 to PD-1+ T Cells for Tumor Therapy

Name	PTH-D001
Target	PD-1; IL-21
Drug Modality	Fusion protein
Indication	Solid tumors
Mechanism of Action	Enhancing tumor-specific immune responses
Status	IND (FDA and NMPA)
Patent	Granted

PTH-D001 is a recombinant humanized IgG4 fusion protein consisting of an anti-PD-1 antibody and two mutated IL-21 molecules, which are fused to the C-terminus of the heavy chains of the antibody via a linker. This dual-targeting strategy can simultaneously block the PD-1/PD-L1 axis and deliver IL-21 specifically to PD-1+ T cells, aiming to enhance tumor-specific immune responses while minimizing systemic adverse effects.

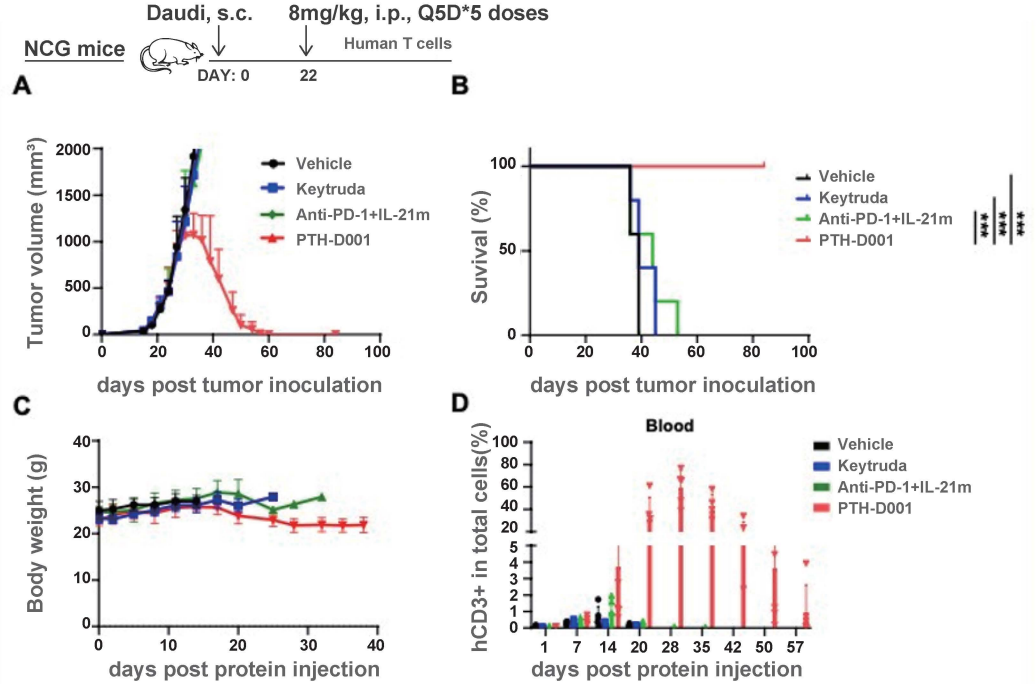


Asset Highlights

- PTH-D001 is a recombinant humanized IgG4 fusion protein consisting of:
  - An anti-PD-1 antibody with similar properties to Keytruda
  - An IL-21 mutant with comparable efficacy to the wild type
- In in vivo experiments, PTH-D001 demonstrated superior anti-tumor activity compared to anti-PD-1 monotherapy or its combination with IL-21.
- In preclinical studies, PTH-D001 demonstrated a favorable safety profile and potent anti-tumor activity, supporting its future development as a therapeutic candidate for advanced solid tumors.
- PTH-D001 has received IND approval for solid tumors in the United States and China, and for hematologic malignancies in China.

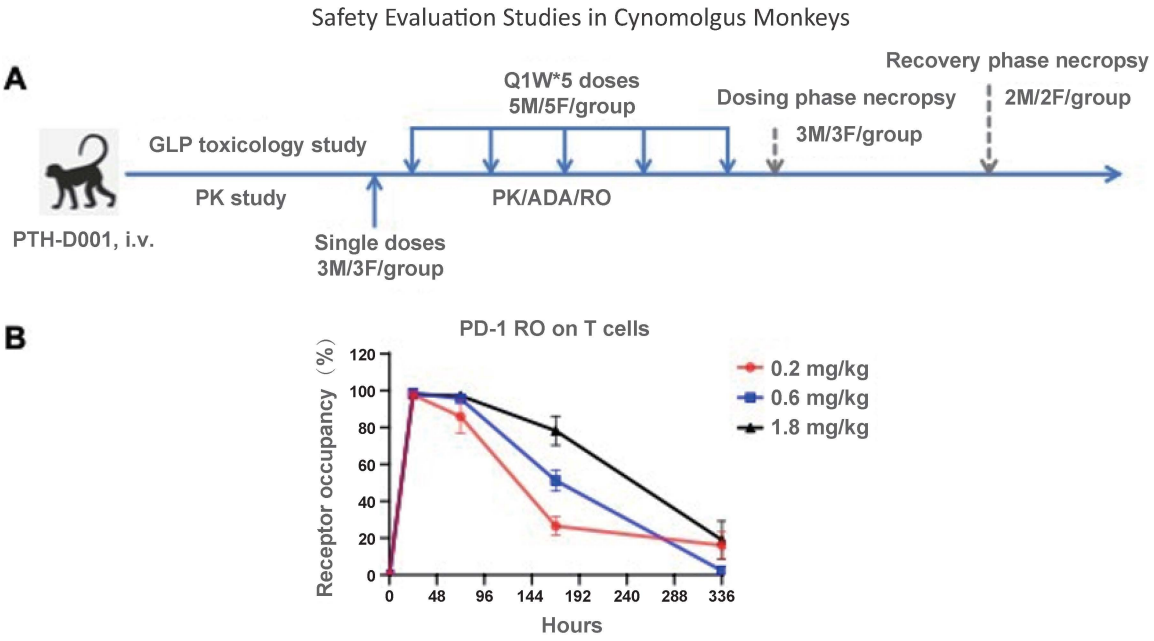
Superior Antitumor Efficacy in Humanized Lymphoma Model

Compared to the anti-PD-1 monotherapy and combination therapy, PTH-D001 treatment significantly inhibited tumor growth and led to complete tumor regression, resulting in cure (A and B). No significant decrease in body weight was observed in the mice during treatment (C). In peripheral blood, a significant expansion of T cells was observed in PTH-D001-treated mice, which significantly diminished after tumor regression (D).



Well-Characterized Safety Profile

- GLP toxicity studies demonstrated a favorable toxicity profile, with no significant cardiovascular or neurological dysfunctions observed. Immunotoxicity observed in the GLP study tended to resolve or was fully resolved by the end of the recovery period.
- PK studies showed dose-proportional systemic exposure of PTH-D001 with no significant accumulation after repeated dosing in cynomolgus monkeys, and receptor occupancy results illustrated more than 30% of target engagement within 7 days (B).



A First-in-Class Dual-Action Peptide-Drug Conjugate for Acute Ischemic Stroke

Name	PTH-M006
Drug Modality	Peptide-drug conjugate
Indication	Acute ischemic stroke
Mechanism of Action	Thrombolysis, anti-inflammation, and free radical clearance
Status	Biological testing
Patent	Granted

Thrombosis can induce cerebral ischemic injury, leading to cerebral ischemia-reperfusion injury. PTH-M006 is a conjugate comprising borneol and a thrombolytic peptide, which can cross the blood-brain barrier (BBB) into the brain and undergo self-cleavage to release its components. Borneol, a bicyclic monoterpene compound, exhibits strong lipophilicity that facilitates its penetration through the BBB, enabling anti-inflammatory and neuroprotective effects. Borneol suppresses the expression of inflammatory cytokines and proteins, activates GABAa receptors, and reduces apoptosis and necrosis, to alleviate cerebral edema and ischemia-reperfusion injury. The peptide of PTH-M006 dissolves blood clots and neutralizes free radicals generated during ischemia-reperfusion, thereby mitigating cerebral ischemic damage and ischemia-reperfusion injury.

Core Innovations

- **Dual Mechanism of Action:** High-efficiency thrombolysis and neuronal protection are simultaneously achieved, addressing critical challenges in stroke treatment in one step.
- **High Diffusibility Across the BBB:** The conjugate design utilizes the strong lipophilicity of borneol to transport the entire molecule across the BBB.
- **Extended Therapeutic Time Window:** The conjugated neuroprotective agent is expected to protect the nerve cells in the ischemic penumbra while thrombolysis, potentially prolonging the effective treatment time window.

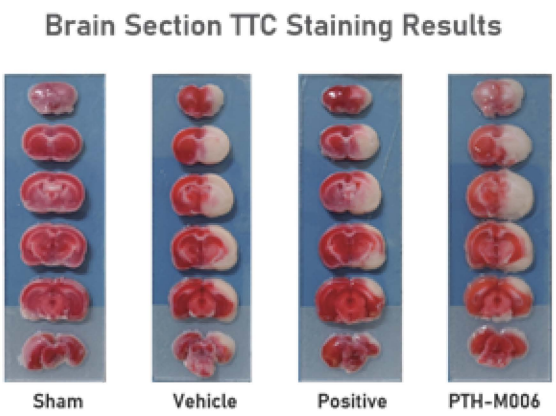
Superior Restorative Effect on Cerebral Infarction

In an efficacy evaluation study using the rat middle cerebral artery occlusion (MCAO) model, PTH-M006 demonstrated significant improvement in neurological symptoms in rats with acute cerebral ischemia, outperforming the positive control group. TTC staining results of brain slices revealed reduced proportions of visible ischemic areas in both the PTH-M006 group and the positive control group. Comparative analysis of infarct volumes across groups further indicated cerebral infarction conditions in rats with acute cerebral ischemia were ameliorated in the PTH-M006 group and the positive control group.

Research system	Species	SD rat, 250-280g, male
	Model	MCAO rat model (2 hrs occlusion of medial carotid artery followed by 7 days of reperfusion)
	Number	6-10 rats/group, 8 groups, 76 in total

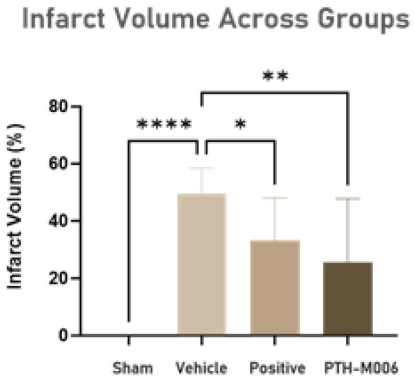
	Group	Treatment	Dosage	R.o.A	Frequency	Animal No.
Grouping	Group 1-Sham	Vehicle: 20% propylene glycol aqueous solution	N/A	i.v.	6 doses, 1h after ischemia (Day0), each day (Day1-Day5)	6
	Group 2-Vehicle	Vehicle: 20% propylene glycol aqueous solution	N/A	i.v.		10
	Group 3-Positive	Positive-Edaravone + Dexborneol	8:2 mg/kg	i.v.		10
	Group 4-PTH-M006	PTH-M006	5 umol/kg	i.v.		10
Model Establishment	All mice were established as the tMCAO models on Day 0 except the mice of Group 1.					
General Observation	• Both the Model group and the Positive Drug group showed a significant downward trend in animal body weight over time, with weights decreasing by over 25% by Day 4. • In contrast, the PTH-M006 group's animal body weight remained largely stable after an initial decrease on Day 1. Its decrease was significantly less pronounced than that observed in both the Model group and the Positive Drug group.					
Neurological Function Evaluation	• Both the Positive Drug group and the PTH-M006 group showed a gradual decrease in neurological function scores with increasing doses and time. While the PTH-M006 group's scores decreased slightly more than the Positive Drug group's, this difference was not statistically significant.					

Infarct Size Evaluation



- TTC staining of 2mm brain coronal sections was performed to observe cerebral infarction, with ischemic areas appearing white.
- The Model group showed clear and significant cerebral infarction and ischemia.
- The Positive group and PTH-M006 group demonstrated an improvement in the proportion of ischemic areas.

Infarct Volume



- There was a significant difference between the Model group and the Shamoperated group, confirming successful model establishment.
- There was a significant and highly significant statistical difference in infarct volume when comparing the Positive group and the PTH-M006 group to the Model group, respectively.

A Long-Acting Anti-Myostatin Antibody Fused with GLP-1RA for Obesity Therapy

Name	PTH-0244
Target	Myostatin; GLP-1R
Drug Modality	Fusion protein
Indication	Obesity
Mechanism of Action	Blocking the binding of myostatin and its receptor ActRII, and increasing insulin secretion and decreasing glucagon production through mimicking the effects of the GLP-1
Status	Biological testing

Myostatin (GDF-8) is a TGF-β family ligand secreted mainly by skeletal muscle. It binds Activin type II receptors (ActRIIA/B) and activates SMAD2/3 signaling, which suppresses muscle growth and promotes atrophy. Elevated circulating myostatin is seen in obesity, and is thought to inhibit fatty-acid oxidation, suppress browning of adipose tissue, and worsen insulin sensitivity. An anti-myostatin antibody neutralizes myostatin, preventing it from binding ActRII receptors on muscle. This relieves SMAD2/3-mediated inhibition of anabolic pathways, leading to increased muscle fiber size, increased muscle strength and contractility, enhanced satellite cell activation and regeneration.

PTH-0244 is expected to offer a convenient, long-acting single biologic with fixed stoichiometry and potentially lower required GLP-1 RA dose. The fusion of anti-myostatin antibodies with GLP-1 RA can suppress appetite, slow down gastric emptying, improve glucose control, and maintain or establish skeletal muscle by acting on GLP-1. At the same time, it can block the myostatin/activin-ActRII signaling pathway to counter muscle atrophy, thereby driving robust fat loss.

In Vitro/Vivo Study of the Anti-Myostatin mAb in PTH-0244

In Vitro Study Summary

Affinity KD	Binding ELISA EC50	ActRIIA	ActRIIB		Animal Efficacy
		Cell Function IC50	ELISA IC50	Cell Function IC50	
11.1 nM	0.2566 nM	0.1274 nM	6.68 nM	0.158 nM	100% weight loss from fat

DIO Mouse Animal Study Summary

The anti-myostatin mAb in PTH-0244 showed muscle improvement capability. It can be combined with semaglutide for the treatment of obesity, off-setting the side effect of muscle loss also with other GLP-1R products.

- The anti-myostatin mAb showed muscle enhancer performance (lean mass increased by 7% at day 27).
- When the anti-myostatin mAb combining with Semaglutide at day 27, the anti-myostatin mAb+Semaglutide increased 2.5% lean mass, similar to the performance of Trevogrumab+Semaglutide. Semaglutide alone lost 5% lean mass.
- At day 27, Semaglutide showed 17% weight loss from lean mass. Similar to Trevogrumab + Semaglutide, the anti-myostatin mAb+Semaglutide showed 100% weight loss from fat mass.

PROJECT11

A Novel Anti-Trop-2 ADC

Name	PTH-I0106	Category	ADC
Target	Trop-2	Indication	Solid tumors
Phase	Phase I (FDA)		

Clinical Study Summary

- PTH-I0106 demonstrated good tolerability and safety with typical adverse events (TEAE) aligned with those caused by chemotherapy and DM-1 ADC treatment at effective doses.
- PTH-I0106 exhibited typical pharmacokinetic characteristics of ADC in patients.
- PTH-I0106 showed a favorable patient benefit rate.

  √ Achieved an 82% disease control rate (DOR) in 11 evaluable patients with tumors.

  √ A breast cancer patient who had previously received treatment with Trop-2 ADC (Trodelvy) and HER2 ADC (Enhertu) achieved a partial response (PR), suggesting the potential effectiveness of PTH-I0106 in nonresponsive cases to Trodelvy and Enhertu.

PROJECT12

A Novel Anti-Claudin 6 ADC

Name	PTH-I0110	Category	ADC
Target	Claudin 6	Indication	Solid tumors
Phase	Lead optimization		

Design Highlights of the Anti-Claudin 6 ADC

- The antibody that generated by mice immunization specifically binds to Claudin 6 with high affinity, but not to Claudin 9.
- A topoisomerase-1 inhibitor as payload, DAR8.
- Cleavable linker with strong bystander effect to address multiple major indications with high unmet need.

PROJECT13

A Novel Anti-B7H4 ADC

Name	PTH-I0109	Category	ADC
Target	B7H4	Indication	Solid tumors
Phase	Lead optimization		

B7H4: A Promising Target for the Treatment of Multiple Solid Tumors

Highly expressed in multiple major tumors with high unmet need, such as breast cancer, ovarian cancer, endometrial carcinoma, and cholangiocarcinoma

Design Highlights of the Anti-B7H4 ADC

- The antibody that generated by mice immunization specifically binds to B7H4 with high affinity and good developability.
- A topoisomerase-1 inhibitor as payload, DAR8.
- Cleavable linker with strong bystander effect to address multiple major indications with high unmet need.

PROJECT14

A Promising ADC Targeting FGFR2b for the Treatment of Gastric Cancer

Name	PTH-I0112	Category	ADC
Target	FGFR2b	Indication	Gastric cancer
Phase	Lead optimization		

FGFR2b is highly expressed in gastric cancer with high unmet need. The high expression of FGFR2b is often associated with poorly differentiated and diffuse histological features, which contributes to a decrease in overall survival rate.

Highlights of PTH-I0112

- The antibody that generated by mice immunization specifically binds to FGFR2b with high affinity and good developability.
- A topoisomerase-1 inhibitor as payload, DAR8.
- Superior PK properties compared to FGFR2-DXd.

PROJECT15

A Re-Designed CD20 TCE with Superior B Cell Depletion Activity and Good Safety Profile

Name	PTH-0353	Category	Bispecific antibody
Target	CD20; CD3	Indication	CD20+ DLBCL; Autoimmune diseases
Phase	Phase II (NMPA); IND (FDA)		

A 1:1 CD20xCD3 Bispecific T-cell Engager Within an IgG1 Scaffold

- PTH-0353 is designed with a low-affinity CD3 binding (194 nM) to minimize cytokine release, while maintaining high-affinity binding to CD20 (2.8 nM) for robust anti-tumor efficacy.

Promising Results for Patients Who Failed Prior CD19-Targeting Treatments

- In patients who failed prior CD19 CAR-T therapy (n=14), the ORR and CRR were 71.4% and 35.7%, respectively.
- In patients with prior treatment of CD19×CD3 TCE therapies (n=2), the ORR and CRR were 100% and 50.0%, respectively.
- In patients who failed ASCT therapies (n=7), 2 patients reached CR, 4 patients reached PR, and the ORR was 85.7%.

Good Safety Profile from Phase I/II Clinical Study for the Treatment of CD20+ DLBCL

- MTD had not been reached. No DLTs were observed.
- No cases of ICANS or other clinically significant neurologic AEs were observed.

- CRS was manageable. Most CRS events were grade 1. Only 1 patient (1.1%, 1/93) had grade 3 CRS, lower than Glofitamab (4.1%), Epcoritamab (2.5%), and CN201 (3.9%).
- A safety profile similar to peer molecules, and no extra pretreatment for toxicity reduction.

PROJECT16

A Potent Next-Generation TCE Targeting MSLN

Name	PTH-0359	Category	Bispecific antibody
Target	MSLN; CD3	Indication	Ovarian cancer
Phase	Preclinical		

MSLN Expressed on a Wide Spectrum of Solid Tumors

Mesothelin (MSLN) is overexpressed in many cancer indications, including pancreatic, mesothelioma and ovarian, and the medical needs for these cancers have not yet been met.

Highlights of the MSLN-Targeting T-cell Engager

- PTH-0359 was constructed using a proprietary heterodimeric platform, with optimized binding to two different epitopes of MSLN.
- The 2:1 TCE format showed superior anti-tumor activity compared to the 1:1 format.
- PTH-0359 demonstrated high selectivity and more potent anti-tumor activity for MSLN high expressed tumor cells, compared to benchmark molecule HPN536.

PROJECT17

A Trispecific Antibody with High Affinity for BCMA and Low Affinity for CD3

Name	PTH-0361	Category	Trispecific antibody
Target	CD19; BCMA; CD3	Indication	Autoimmune disease
Phase	PCC		

Asset Overview

PTH-0361 is a trispecific antibody developed to target multiple biomarkers on human B cells by using a proprietary technology. It binds to CD3 with low affinity and to BCMA with high affinity. PTH-0361 showed improved B cell cytotoxicity compared to benchmark BCMA TCE and CD19 TCE, but with much lower T cell activation and cytokine release to ensure better safety.

PROJECT18

A Fully Human Long-Acting Fibroblast Growth Factor 21

Name	PTH-P0025	Category	Protein
Target	FGF21	Indication	MASH; SHTG
Phase	Phase II (NMPA); IND (FDA)		

Asset Overview

PTH-P0025 is a fully human long-acting fibroblast growth factor 21 (FGF21) analog. In China, it is being developed for the treatment of metabolic dysfunction-associated steatohepatitis (MASH) and severe hypertriglyceridemia (SHTG) in the phase II clinical trials. In the United States, IND has been approved for the treatment of MASH.

Phase I clinical results showed that PTH-P0025 has a favorable safety and tolerability profile, with no safety-related immunogenicity identified. PK and PD data indicated that PTH-P0025 had a mean circulating half-life of approximately 8-11 days in humans, which was substantially longer than that of competing agents targeting the same pathway. This could support a convenient once-weekly or once-every-two-weeks dosing regimen, greatly improving patient compliance.

PROJECT19

A Rationally Designed Long-Acting FGF21–GLP-1 Fusion Protein

Name	PTH-P26	Category	Fusion protein
Target	FGF21; GLP-1	Indication	Type 2 diabetes; MASH; Obesity
Phase	IND (NMPA)		

Asset Overview

PTH-P26 is a fully human long-acting FGF21 fusion protein incorporating a GLP-1 moiety, engineered to attenuate the molecular activity of GLP-1 while enhancing that of FGF21. Currently marketed GLP-1 therapies offer the advantage of rapid onset of action but have notable drawbacks, including reduced gastrointestinal motility, decreased appetite, and suppression of various motivational drives. In contrast, FGF21 can increase gastrointestinal motility and promote appetite. By combining FGF21 and GLP-1 and modulating their respective activities, PTH-P26 is designed to harness the strengths of both pathways while effectively compensating for their individual limitations.

PROJECT20

A Gut-Acting and Gut-Restricted Peptide Targeting Vagus Nerve

Name	PTH-0202	Category	Peptide
Target	Vagus nerve/AVPR1a	Indication	Major depression; Alzheimer's disease
Phase	Phase I (TGA)		

Summary of Preclinical Studies

- PK/PD studies showed that PTH-0202 was gut-restricted and gut-acting, with a favorable safety/tolerability profile.
- Robustness of preclinical data with PTH-0202, the in vitro/in vivo DMPK, and clean toxicology data provided solid rational to initiate the phase I study.
- In the rat PK study, PTH-0202 was only detected in the stomach. Therefore, the exposure time was the gastric emptying time. PTH-0202 may affect the gastric emptying time.

Safety and Good Tolerance Shown in Phase I studies

- All safety assessments (vitals, ECGs) and physical exams were normal across the dose cohorts.
- The adverse event profile showed no safety and tolerability issues, no SAEs, some minor gastro-intestinal events (e.g., dry mouth, abdominal discomfort) in 60 mg and 540 mg, and none in 180 mg.

PROJECT21

An In-Situ Gel-Forming Solution for the Treatment of Conjunctivitis

Name	PTH-1201	Category	Small molecule
Phase	Phase II (completed)	Indication	Conjunctivitis

Innovative, Proprietary Extended-Release Formulation

A povidone-iodine extended-release ophthalmic solution is developed based on the patented i-Gel in-situ gel technology, which can effectively kill bacteria, viruses, fungi, and other pathogens.

- Sol-to-gel in-situ gel formation
- Long acting antibacterial and antiviral efficacy
- Minimum irritation and toxicity
- No drug resistance

Both Bacterial and Viral Conjunctivitis Phase II Trials Demonstrated Good Safety and Tolerability

- Phase II trial for bacterial conjunctivitis: Primary endpoint of non-inferiority to Ofloxacin achieved (prespecified endpoint: cure rate at day 8) and PTH-1201 showed superior clinical cure results to Ofloxacin in subjects with negative bacterial culture.
- Phase II trial for viral conjunctivitis: Primary endpoint of superiority to Placebo achieved on day 8 and PTH-1201 showed superior clinical cure results to Placebo in subjects with confirmed adenoviral conjunctivitis.

PROJECT22

A Potential Best-in-Class Pan-RAS(ON) Inhibitor

Name	PTH-0317	Category	Small molecule
Target	RAS proteins	Indication	Solid tumors
Phase	IND-enabling		

Asset Highlights

- **Exceptional High and Broad-Spectrum in Vitro Potency:** Significantly more potent inhibition of cell growth across KRAS mutant and EGFR mutant cell lines vs RMC-6236 (Daraxonrasib); remarkable activity in inhibiting ERK phosphorylation across various mutant KRAS cell lines

- **Superior in Vivo Efficacy:** > 25x vs RMC-6236; ~3-10x vs ERAS-0015 in KRAS-mutated CDX models
- **Superb PK Profile:** Higher exposure, much longer T1/2, and preferential drug distribution in tumor tissues in CDX models vs RMC-6236 and ERAS-0015
- **Potentially Brain-Penetrable:** Caco-2 efflux ratio = 1.8 (RMC-6236 ER = 11.2; ERAS-0015 ER = 18)
- **Great Safety Profile:** Higher hERG window and well tolerated in all test doses in-vivo models
- **Much Lowered Predicted Human Dose (< 1 mg) vs RMC-6236:** Potentially reduced off-target toxicities, better GI tolerability and reduced CMC/API cost

PROJECT23

A MRGPRX2 Antagonist with Superior PK/PD Properties

Name	PROTH-028	Category	Small molecule
Target	MRGPRX2	Indication	Chronic urticaria; Atopic dermatitis
Phase	Preclinical		

MRGPRX2 Receptor in Mast Cell-Mediated Inflammatory Diseases

Mast cells are primarily activated through two pathways: IgE-dependent and IgE-independent. The IgE-independent pathway is triggered by the activation of the Mas-related G protein-coupled receptor X2 (MRGPRX2). This activation leads to mast cell degranulation and the release of inflammatory mediators, contributing to the development and progression of mast cell-mediated diseases, such as chronic urticaria and atopic dermatitis.

Summary of In Vitro and In Vivo Findings for PROTH-028

- Effectively inhibited cortistatin-14-induced-Ca^{2+} influx in cells overexpressing the MRGPRX2.
- Demonstrated robust inhibition of mast cell degranulation triggered by a variety of stimulants in LAD2 human mast cell lines.
- Inhibited cortistatin-14-induced extravasation in an in vivo model, suggesting a functional anti-inflammatory effect.
- Exhibited a superior PK profile when benchmarked against comparable compounds, specifically EP262 and EVO756.
- Showed a high tolerance in a single-dose rat toxicity study, with the MTD exceeding 500 mpk.

PROJECT24

A Potent and Selective Menin-MLL Inhibitor

Name	PTH-0316	Category	Small molecule
Target	Menin	Indication	Acute myeloid leukemia; Acute lymphocytic leukemia
Phase	Preclinical		

Menin is widely expressed in human tissues and regulates a variety of functions in key signaling pathways. The menin-MLL (KMT2A) complex plays a critical role in acute leukemias with MLL rearrangements or NPM1 mutations. PTH-0316 is a small molecule disrupting the menin-MLL interaction, and is a potential and effective therapeutic strategy for these actue leukemias.

Asset Highlights of PTH-0316

- **High Potency:** PTH-0316 demonstrated exceptional binding affinity to the wild-type menin and the menin bearing T349M and G331R mutations; 6-8x greater potency vs the competition (SNDX-5613) against leukemia cell lines with MLL rearrangements or NPM1 mutations.
- **High Specificity:** PTH-0316 showed approximately 2000-fold selectivity over MLL-WT cell line (HL-60).
- **Superior In Vitro Efficacy:** PTH-0316 exhibited 10-fold greater potency compared to the competitor (SNDX-5613) in MV-4-11 (containing MLL-AF4 fusion) CDX model.
- **Favorable PK Profile:** PTH-0316 exhibited a superb pharmacokinetic profile, characterized by excellent bioavailability, extended half-life (T1/2), supporting a very low predicted and once-daily dosing in human.
- **Strong Safety Profile:** PTH-0316 presented high hERG IC50 value, high therapeutic index and well tolerated in test doses in in-vivo models.

PROJECT25

A Brain Penetrant Inhibitor Targeting FGFR2/3 Gatekeeper Mutants

Name	PTH-24422-03	Category	Small molecule
Target	FGFR2/3	Indication	Cancer
Phase	Preclinical		

Superior Pharmacokinetic and Safety Profiles

PTH-24422-03 with a novel chemical structure is a potent inhibitor for many cancer-related tyrosine kinases / drug-resistant mutants. It showed good PK profiles and brain penetrant in animal models.

- Demonstrated good efficacy in SNU-16 CDX model
- No significant inhibitory effects on hERG and CYPs observed
- Well-tolerated in mice at 100 mpk, BID for 10 days
- No hyperphosphatemia in mice after 10-day 100 mpk, BID (related to FGFR1 inhibition)

PROJECT26

A Breakthrough Combined Therapy for Alzheimer's Disease

Name	PTH-0203	Category	Combinational therapy
Target	Multiple	Indication	Alzheimer’s disease
Phase	Preclinical		

Asset Overview

PTH-0203 is a combination of two existing drugs, sodium phenylbutyrate and taurursodiol, which act to prevent nerve cell death by blocking stress signals and stabilizing mitochondria in cells. Targeting core mechanisms such as neural plasticity, neuroinflammation and protein aggregation holds promise for the treatment of Alzheimer’s disease, and this therapeutic strategy can be developed for more indications.

PROJECT27

A Brain Active PDE4 Inhibitor for CNS Diseases

Name	PTH-0201	Category	Small molecule
Target	PDE4	Indication	Major depression; Alzheimer's disease
Phase	PCC		

A Clinical Validated Target

Phosphodiesterase 4 (PDE4) is predominantly responsible for hydrolyzing cAMP within both immune cells and cells in the central nervous system and it influences cell signaling particularly in inflammation and neuroplasticity.

Asset Highlights of PTH-0201

- PTH-0201 is a non-selective PDE4 inhibitor with potential for multiple indications, including chronic inflammatory arthritis syndrome (CIAS), fragile X syndrome (FXS), and Alzheimer's disease (AD), among others.
- This highly specific pan-PDE4 inhibitor can penetrate the brain.
- The deuterated analog of PTH-0201 showed the improvement of memory and cognitive function in the phase II clinical development in the United States.

PROJECT28

An AAV Gene Therapy for Durable Anti-VEGF Control in Retinal Disorders

Name	PTH-0565	Category	Gene Therapy
Target	VEGF	Indication	nAMD; DR; DME
Phase	Phase I/II a (NMPA)		

Asset Overview

Neovascular age-related macular degeneration (nAMD), diabetic retinopathy (DR), and diabetic macular edema (DME) are common retinal disorders characterized by a lack of spontaneous recovery and continuous progression. Current treatment is dominated by monoclonal antibodies and fusion proteins, including ranibizumab, aflibercept, and conbercept. However, these therapies require long-term administration, and frequent intravitreal injections reduce patient convenience, adherence, and persistence. In addition, repeated antibody dosing may induce immune tolerance, leading to diminished long-term efficacy.

AAV gene therapy can provide sustained, stable expression of anti-VEGF proteins at an effective low concentration, achieving an optimal balance between efficacy and safety, enabling a single administration with durable benefit. PTH-0565 was developed using a multi-target strategy, featuring an innovative expression cassette design and coordinated codon optimization, resulting in markedly improved expression efficiency. Compared with similar treatment strategies, PTH-0565 could achieve up to a 19-fold increase in anti-VEGF protein expression, supporting substantial clinical improvements in dosing and safety while reducing overall treatment costs.

PTH-0565 is being evaluated for the nAMD indication in a multicenter Phase I/IIa clinical trial, with available data

demonstrating clinically meaningful efficacy. The first treated patient has been followed for more than one year, showing an improvement of over 10 letters in BCVA; the second patient has been followed for more than 40 weeks, with a BCVA gain of over 15 letters.

PROJECT29

A Muscle-Targeted AAV Gene Therapy Delivering Dystrophin for DMD

Name	PTH-0567	Category	Gene Therapy
Target	Dystrophin	Indication	DMD
Phase	IIT		

Asset Overview

Duchenne muscular dystrophy (DMD) is caused by mutations in the dystrophin gene and is characterized by progressive muscle weakness and muscle wasting. Gene therapy has the potential to provide a treatment with durable benefit, representing an optimal clinical solution.

PTH-0567 features a unique gene therapy architecture that integrates a muscle-tropic AAV capsid, a muscle-specific promoter, and a truncated dystrophin transgene. This “mini” dystrophin construct retains the key functional domains of dystrophin and is designed for expression in both skeletal and cardiac muscle. Compared with the AAV capsids selected by competing companies, PTH-0567’s engineered AAV capsid enables more efficient muscle transduction and higher expression, while offering lower immunogenicity.

To date, three patients have been enrolled and dosed. Trial data indicate that PTH-0567 has demonstrated a favorable safety profile and encouraging efficacy, with significant improvements in patients’ motor function and quality of life.

PROJECT30

An mRNA Therapeutic Vaccine for EBV-Positive Tumors

Name	PTHC-043	Category	mRNA vaccine
Phase	Phase I (FDA and NMPA)	Indication	EBV-positive cancers

Asset Overview

The Epstein-Barr virus (EBV) persists and spreads after infection in humans, leading to the occurrence and metastasis of a variety of cancers, posing great challenges in the treatment of cancer. Conventional cancer therapies tend to have limited success and significant side effects.

PTHC-043 is an mRNA vaccine targeting EBV-positive tumor associated antigens. It was evaluated for safety, tolerability, and immunogenicity in a prospective, single-center, investigator-initiated study. In this study, PTHC-043 showed the safety and potential efficacy, demonstrating its ability to induce specific immune responses and achieve substantial disease control in a

challenging patient population. These results support the advancement of PTHC-043 as a candidate for immunotherapy in EBV-positive cancers, and highlight the translational potential of mRNA vaccine technology in the oncology landscape.

PROJECT31

An mRNA Therapeutic Vaccine for HBV-Induced HCC

Name	PTHC-201	Category	mRNA vaccine
Phase	IND (FDA and NMPA)	Indication	HBV-induced hepatocellular carcinoma

Asset Overview

PTHC-201 is an mRNA therapeutic vaccine developed for hepatitis B virus (HBV), constructed based on a proprietary mRNA sequence design and an lipid nanoparticle delivery platform. It encodes multiple antigens/epitopes, aiming to induce a dual immune response against both the virus itself and the liver cancer it drives. In an Investigator-Initiated Trial completed in China, PTHC-201 demonstrated favorable safety and immunogenicity, as well as potential clinical therapeutic efficacy.

As an mRNA immunotherapy with a defined mechanism and clear immune characteristics, PTHC-201 can be used as a monotherapy or be compatible with combination therapies, such as with antiviral drugs and immune checkpoint inhibitors. It is expected to potentially enhance the efficacy of liver cancer treatment, reduce recurrence risk, and facilitate a true clinical cure for hepatitis B.

Modality	Asset	Phase	Description	Indication	Target
ADC	PTH-0375	Preclinical	An anti-CD98hc (SLC3A2) ADC	Cancer	CD98hc
	BI0107 ADC	Preclinical	A novel ADC with an undisclosed payload	Acute myeloid leukemia	CLEC12A
Antibody	PTH-0339	Phase II (NMPA, TGA); IND (FDA)	A first-in-class humanized monoclonal IgG antibody that blocks Cx43 hemichannels	Acute spinal cord injury; Stroke; Osteoarthritis; Parkinson's	Cx43
	PTH-0354	Phase I (NMPA)	A novel anti-HER2xCD3 bispecific antibody	Breast cancer	HER2; CD3
	PTH-0377	Phase I (NMPA); IND (FDA)	The VHH construct targeting CD33/CD47/HSA/CD16A	Acute myeloid leukemia; Myelodysplas-tic syndrome	CD33; CD47; HSA; CD16A
	PTH-0356	IND (NMPA)	A novel anti-B7-H3xCD3 bispecific antibody	Solid tumors	B7-H3; CD3
	PTH-0376	Preclinical	A dual-tumor-antigen-specific T-cell engager and conditional CD28 agonist	Solid tumors	PD-L1; EGFR; CD28
	PTH-0288	Preclinical	An innate cell engager targeting EGFR/CD16A	Lung cancer; Colorectal cancer; Oher epithelial-origin tumors	EGFR; CD16A
	PTH-0348	Preclinical	A potential best-in-class IL-13/TSLP bispecific antibody	Asthma; Atopic dermatitis	IL-13; TSLP
	PTH-0357	Preclinical	A anti-GPC3xCD3 bispecific antibody	Hepatocellular carcinom	GPC3; CD3
	PTH-0249	Discovery	A potential first-in-class T-cell engager with long action	B cell-related autoimmune diseases	BAFF-R; CD3
	PTH-0411	Discovery	A directed immunosuppressant bivalent bispecific antibody	Inflammatory diseases;	IL-1β; IL-1R
	PTH-0250	Discovery	A potential first-in-class long-acting trispecific antibody	B cell-related autoimmune diseases	BAFF-R; CD3; CD20
Protein	PTH-0366	Phase I (NMPA)	A recombinant kallikrein 1 protein	Acute ischemic stroke	KLK1
	PTH-0370	Phase I (NMPA)	A bifunctional fusion protein	Metabolic dysfunction-associated steatohepatitis	GLP1; FGF21
	PTH-0415	IND (NMPA)	A Lutetium-177 radiotracer (radioactive peptide)	Sarcoma	CD13; αvβ3

	PTH-0414	IND (NMPA)	A Gallium-68 radiotracer (radioactive peptide)	Sarcoma	CD13; αvβ3
	PTH-0285	Preclinical	A cytokine/antibody fusion protein	Cancer	PD-1; IL2
	PTH-0410	Preclinical	A long-acting triple agonist	Obesity; Type 2 diabetes	GLP-1R; GIPR; GCGR
Small Molecule	PTH-0423	Phase II (NMPA)	A novel SSRI and 5-HT modulator with excellent BBB permeability and PK properties	Major depressive disorder	5-HTT; 5-HT_3 receptor
	PTH-0379	Phase II (NMPA)	A KCNQ2/3 potassium ion channel opener	Epilepsy; Amyotrophic lateral sclero-sis; Major depressive	KCNQ2/3 channel
	PTH-0412	Phase II	A first-in-class PRMT1 inhibitor	Advanced/ metastatic solid tumors	PRMT1
	PTH-0413	Phase I/II (FDA/NMPA)	A brain-penetrable MTA-cooperative PRMT5 inhibitor	MTAP-deleted solid tumors	PRMT5
	PTH-0387	Preclinical	A NMT1 inhibitor	Solid tumors	NMT1
	PTH-0390	Preclinical	A miR-124 modulator	Inflammatory bowel disease; Crohn's disease; Rheumatoid arthritis; Allergic rhinitisdisorder; Bipolar	miR-124
	PTH-0424	Preclinical	A rapid-acting antidepressant candidate based on NMDA receptor antagonism	Major depressive disorder	NMDA receptor
	PTH-0422	Preclinical	A highly active MAT2A small molecule inhibitor	MTAP-deleted solid tumors	MAT2A
	PTH-0389	Discovery	An inhibitor of RNA helicase A	Solid tumors	DHX9
	PTH-0391	Discovery	A VAV1-targeting molecular glue degrader	Autoimmune diseases	VAV1
Cell and Gene Therapy	PTH-0332	Phase II (NMPA); IND (FDA)	An in vivo CRISPR-based investigational therapy to inactivate the TTR genes	ATTR Amyloidosis	Transthyretin
	PTH-0105	Phase I (NMPA)	siRNA targeting ANGPTL3, using the proprietary GalNAc delivery system	Metabolic diseases	ANGPTL3
	PTH-0232	Phase I (NMPA)	iPSC-derived EPCs to repair damaged vasculature	Acute ischemic stroke	-

	PTH-0200	Preclinical	Intracranial gene therapy targeting TRPM7	Alzheimer's disease	TRPM7
	PTH-0426	IIT (China)	Targeting BCMA/NKG2DL/FAP TCR-T cells that possess the characteristics of TCR-T and the 4th-generation CAR-T cells	Multiple myelomadisor-der; Bipolar	BCMA; NKG2DL; FAP
	PTH-0427	IIT (China)	Super-effective TCR-T cells	B/T cell malignancies; Leukemia	CD19; CD37; FAP
	PTH-0428	IIT (China)	Super-effective TCR-T cells	Solid tumors	Nectin4; NKG2DL; FAP
	PTH-0429	IIT (China)	Super-effective TCR-T cells	Solid tumors	Nectin4; B3H7; TROP2; FAP
	PTH-0430	IIT (China)	Super-effective TCR-T cells	Lupus erythematosus	CD19; BCMA
	PTH-0089	IIT (China)	NK cell therapy derived from induced iPSCs through the programming and modification with the CD16 gene (vCD16)	Solid tumors	CD16
	PTH-W0301	IIT (China)	in vivo CAR-T cells	Solid tumors	CD19
	PTH-0091	Preclinical	iPSC-Derived CAR-NK cells	Solid tumors	-
	PTH-0092	Preclinical	iPSC-Derived CAR-NK cells	Autoimmune diseases	-
	PTH-0096	Preclinical	Anti-CD19/CD22 CAR-T cells	Lymphoma	CD19; CD22
	EDB-TCR-T	Preclinical	T cells equipped with duraCAR demon-strated antigen-induced metabolism profile suitable for sustained in vivo efficacies	Solid tumors	Fibronectin extra domain B
	PTH-0097	Discovery	Autologous/Allogeneic CAR-T cells	Acute and chronic graft-versus-host disease (GVHD)	-
	TCR-T012	Discovery	TCR-T cells	Blood tumors; Ovarian cancer	WT1
	TCR-T013	Discovery	TCR-T cells	Nasopharyn-geal cancer; Gastric cancer	EBV
	TCR-T016	Discovery	TCR-T cells	Melanoma; Non-small cell lung cancer	NY-ESO-1
Others	PTH-W0101	Phase I	Proprietary LNP	-	-
	PTH-W01	BLA	Novel nano adjuvants	-	-

WELCOME TO CONTACT US

We have more assets available for partnership. These assets span from the early discovery stage to clinical phases, focusing on key therapeutic areas such as oncology, autoimmune diseases, and metabolic disorders. They are actively open for out-licensing, co-development, or other forms of collaboration.

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