Captor Therapeutics®

Pioneering targeted protein degraders for human health

Corporate Presentation
October 2024

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An experienced leadership team

Tom Shepherd, Ph.D.
Chief Executive Officer

- 30 years in Biotech leadership positions
- Led 12 licensing transactions resulting in > $3 B in sales
- 6 private investment rounds and 3 IPOs.

Michal Walczak, Ph.D.
Co-founder
Chief Scientific Officer

- Ph.D. ETH Zurich,
- Post-doc FMI Basel (Novartis Research Foundation) on TPD
- 10 years in drug discovery and TPD

Anna Pawluk, Ph.D.
VP Operation

- Ph.D. University of Wroclaw
- MBA WSH in Wroclaw
- 15 years of R&D experience

Sylvain Cottens, Ph.D.
Co-founder
SVP Chemistry

- Ph.D. EPFL Lausanne,
- Post-doc Caltech, (USA)
- Scientific expert & leader with 25+ years at Novartis
- Co-inventor of Afinitor and co-developer of Gilenya (both blockbuster drugs)

Andrew Saunders DPM, FFPM
Chief Medical Officer

- MB BCh BAO BA, Medicine, Trinity College, Dublin
- FFPM, Royal College of Physicians, London
- 25 years in oncology clinical development, including global responsibility for Rituximab

EDUCATION

PREVIOUS EXPERIENCE

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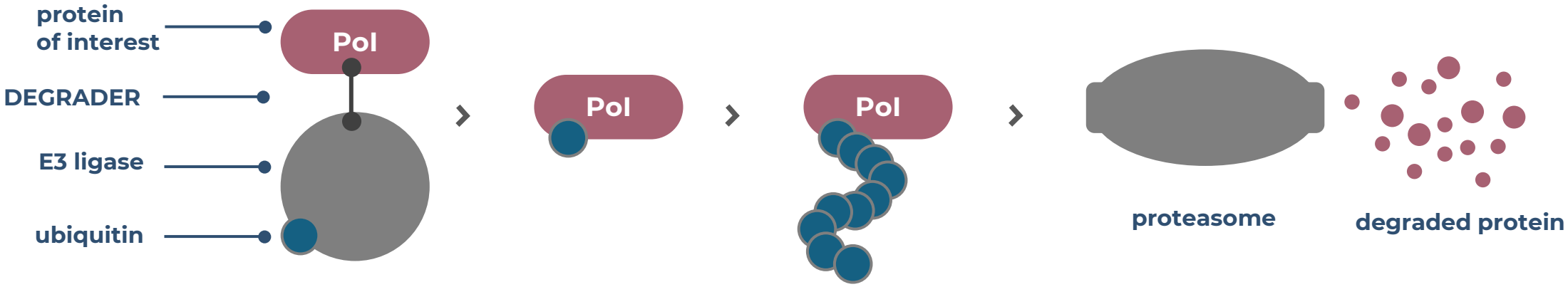
Targeted Protein Degradation expected to unlock $974* bn by 2030



	Degraders	Inhibitors	mAbs	siRNA
Removing multiple pathological functions	✓✓✓	✗	✗	✓✓✓
Oral bioavailability	✓✓✓	✓✓✓	✗	✗
Uncoupling PK from PD = prolonged efficacy	✓✓✓	✗	✗	✓✓✓
Overcoming mutational resistance	✓✓✓	✓	✓✓	✓✓✓
Targeting scaffolding function	✓✓✓	✗	✓✓	✓✓✓
Brain-penetration	✓✓	✓✓✓	✗	✗
Accesing undrugged proteins	✓✓✓	✓	✗	✓✓✓

*Biopharmaceuticals Market by Type and Application: Global Opportunity Analysis and Industry Forecast, 2022-2030

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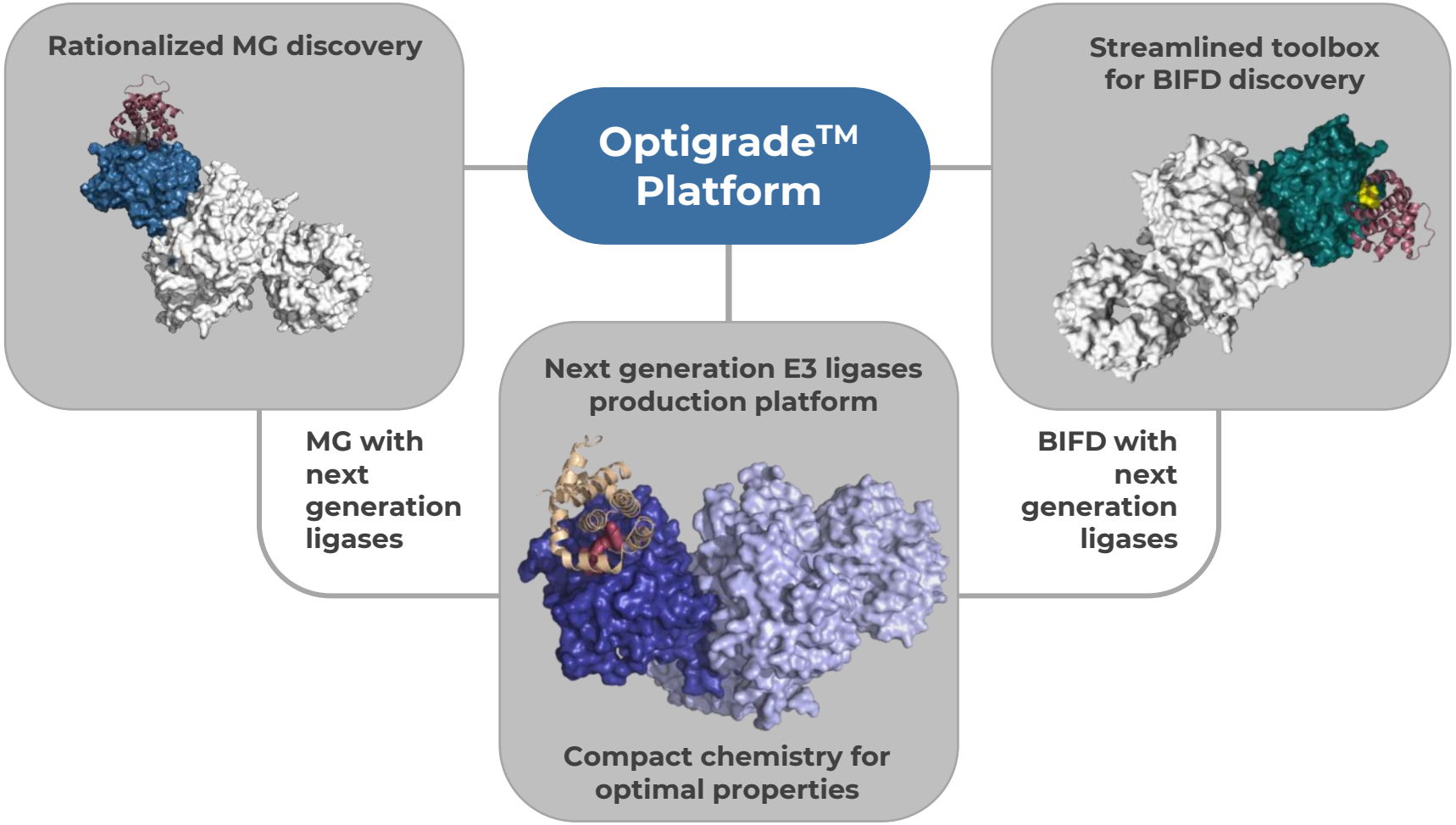
Optigrade™ discovery platform – importance of structure



Optigrade™ – addressing Molecular Glues, Bifunctional Degraders and novel Ubiquitin E3 Ligases

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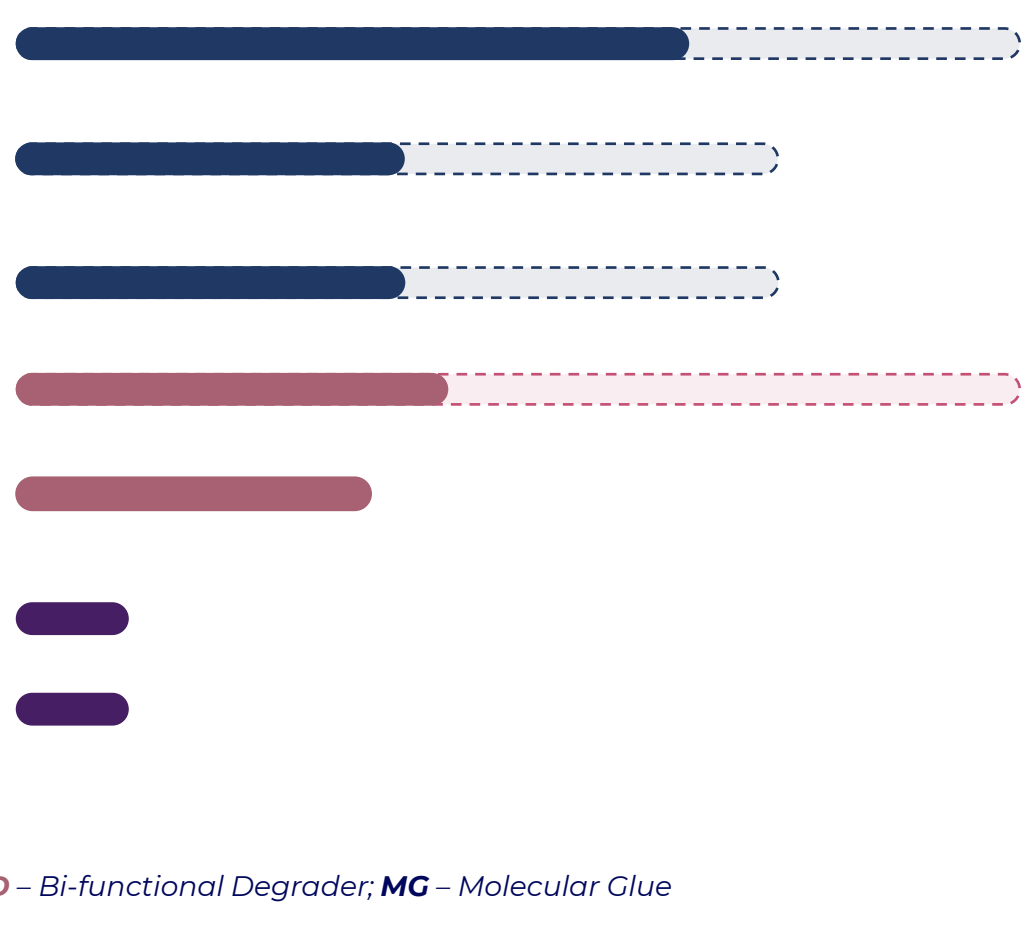
Fully owned pipeline

Programme	Primary Target	Indications	Modality	Discovery	Preclinical*	IND Filing	Phase IA / IB	Phase II
CT-01	GSPT1	**Hepatocellular carcinoma**, Lung cancer, NET tumours	MG					
CT-02B†	NEK7	Neuroinflammation (Parkinson's Disease, ALS, MS)	MG					
CT-02S‡	NEK7	Systemic autoimmunity	MG					
CT-03	MCL-1	Liquid & solid tumours	BIFD					
CT-05	PKCϴ	Autoimmunity, Oncology, Transplantation, Metabolism	BIFD					
	New target projects	Autoimmunity, Cancer	MG BIFD					
	New E3 ligase degraders	Autoimmunity, Cancer	MG BIFD					



†CT-02B - Brain-penetrant
‡CT-02S - Systemic

Preclinical stage include IND-enabling studies, **BIFD – Bi-functional Degrader; **MG** – Molecular Glue*

Assumed stage at the end of 2025

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CT-01: First-in-Class GSPT1 Targeted Degrader for Hepatocellular Carcinoma (HCC)

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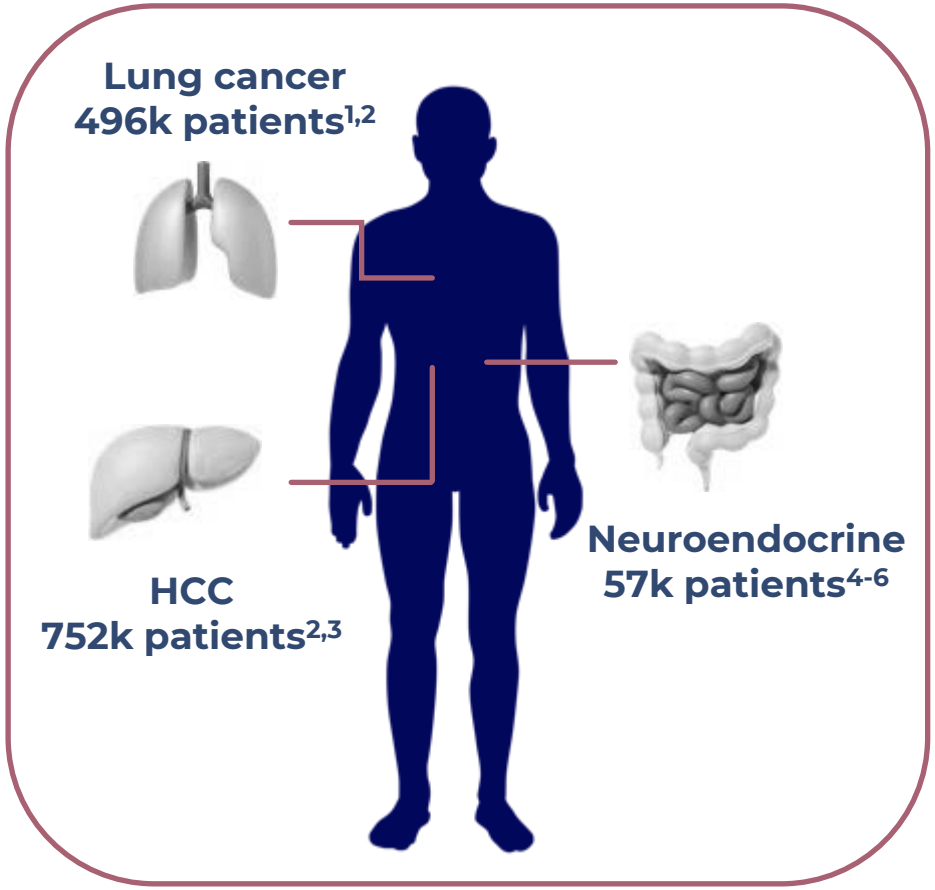
CT-01: first-in-class molecular glue degrader of GSPT1 & NEK7



GSPT1 degradation leads to an Integrated Stress Response (ISR) and induction of apoptosis in HCC cells

NEK7 degradation leads to reduction of IL-1β production – a well-established pro-carcinogenic factor. Reduction of IL-1β levels in the tumor microenvironment enables activation of the immune response

CT-01 is a pro-drug activated by an enzyme present at high levels in the liver, lungs and certain gastrointestinal tumors

A unique degradation profile combined with target tissue pro-drug activation for liver, lung, breast and neuroendocrine cancer

CT-01 (GSPT1)

(1) Semin Cancer Biol. 2006 Aug;16(4):253-64
(2) https://gco.iarc.fr/today/en/
(3) J Hepatol. 2022 Dec;77(6):1598-1606
(4) Semin Cancer Biol. 2006 Aug;16(4):253-64
(5) Endocr Connect. 2023 Nov 23;12(12)
(6) JAMA Oncol. 2017 Oct 1;3(10):1335-1342

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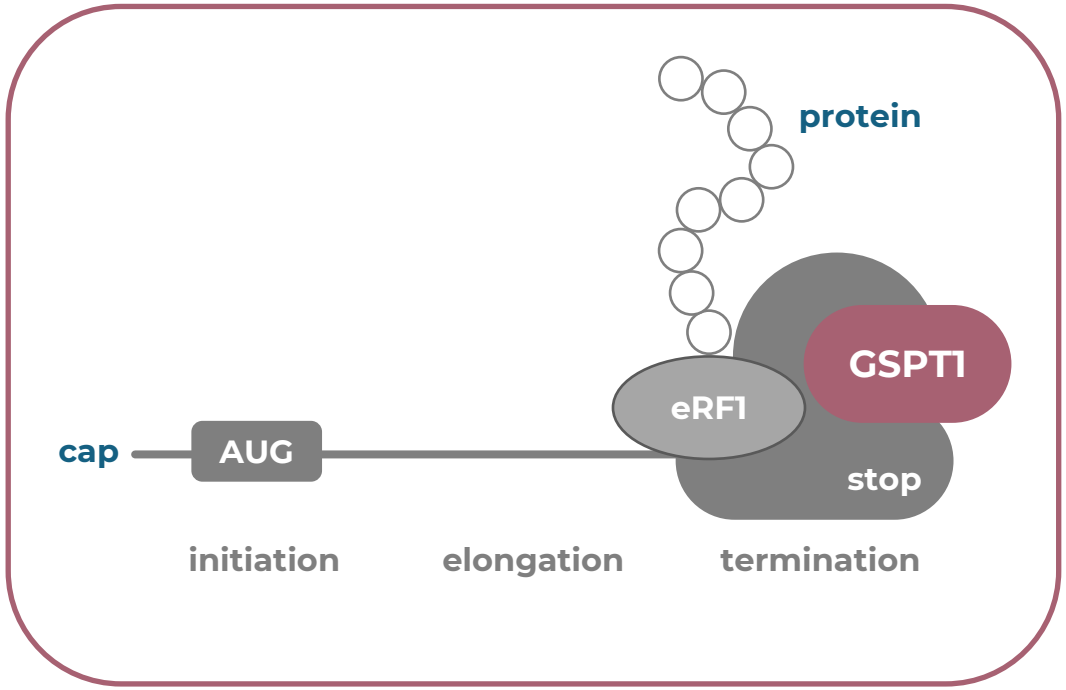
Biology of GSPT1 supports its targeted degradation in cancer treatment



1. Hellen C. U. T., *Cold Spring Harb Perspect Biol*, 2018
2. Salas-Marco, J. & Bedwell, D. M.. *Mol Cell Biol*, 2004
3. Kurosaki, T. & Maquat, L. E., *J Cell Sci*, 2016

Target Biology and Therapeutic Rationale

G1 to S phase transition 1 protein (GSPT1, eRF3a)

is a translation termination factor that regulates mRNA translation[1]

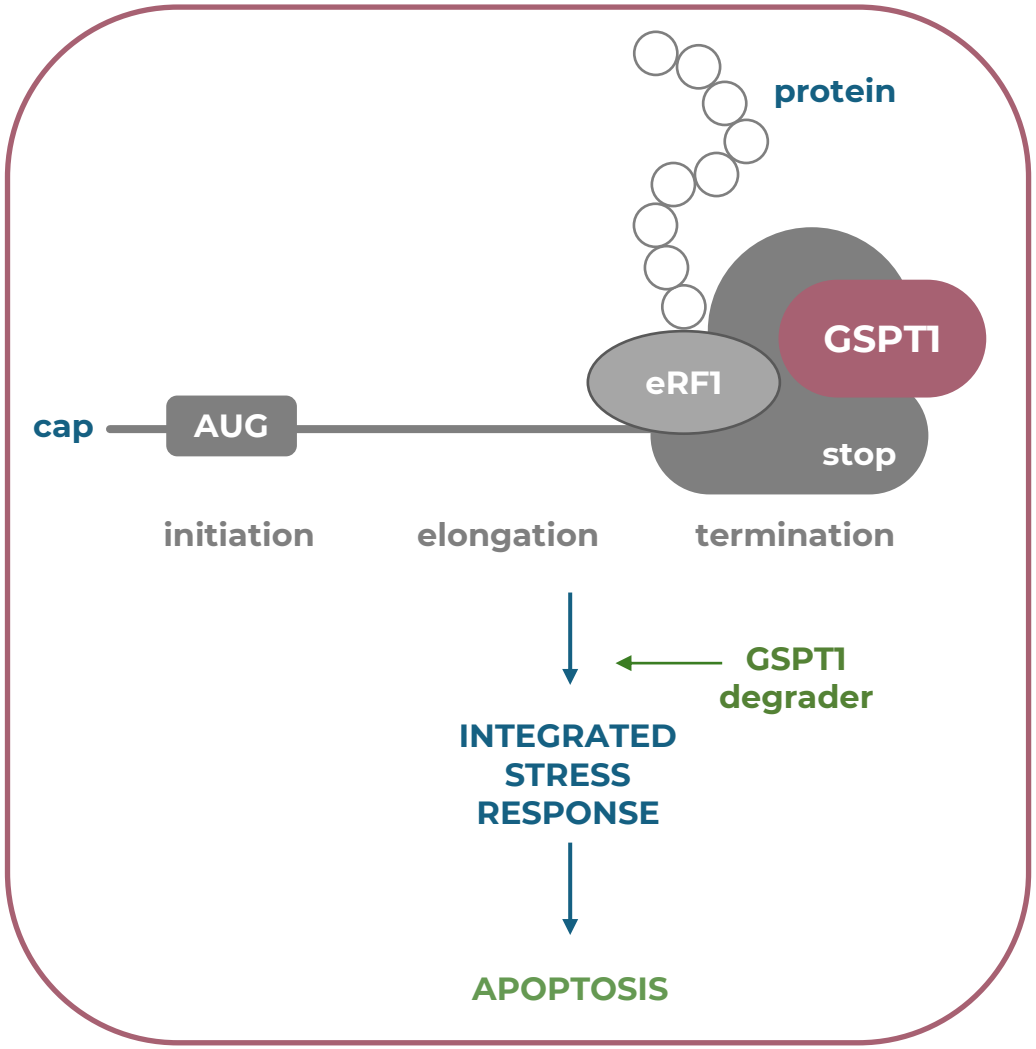
GSPT1 and eRF1 form a translation termination complex that facilitates the nonsense mediated mRNA Decay[2,3]

Clinical opportunity

Targeting protein translation GSPT1 degradation offers treatment options of:

1. Hepatocellular Carcinoma (HCC)
2. Lung cancer
3. Breast cancer
4. Gliomas
5. Rare cancers, e.g.: hepatoblastoma, angio- and liposarcomas

GSPT1 degrader



GSPT1 degradation leads to apoptosis via induction Integrated Stress Response (ISR)

An excellent opportunity for targeting of cancer cells that require translational adaptations and efficient protein synthesis

CT-01 degrader is a pro-drug converted by an enzyme elevated in the inflammed liver, lungs and blood-brain barrier.

The active molecule is released in HCC and features:

1) poor cell membrane penetration and

2) fast clearance, both of which significantly expand the therapeutic window.

CT-01 degrades also NEK7, whose pro-carcinogenic role is manifested in stabilization of MDSCs and TAMs in Tumor Micro-Environment (TME)

CT-01 (GSPT1)

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HCC: current standard of care and opportunity

Line of therapy	Therapy	Survival Benefit *vs* Sorafenib [months]	FDA Approval
1	Tecentriq + Avastin	+5.8[1]	uHCC / mHCC
1	Imfinzi + Imjudo	+2.7[2]	uHCC
1/2	Nexavar	0.0[3]	uHCC
2	Optivo	+1.7[4]	uHCC (Post sorafenib)
2	Cabometyx	+2.2[5]	uHCC (Post sorafenib)

Market Research Provider	Base (Year / $B)	Future (Year / $B)	CAGR (%)
Vision Research Reports[6]	2024: $3.2	2033: $11.6	15%
SNS Insider[7]	2022: $2.9	2030: $12.9	20%
Skyquest[8]	2022: $2.7	2030: $11.4	20%
Research and Markets[9]	2022: $2.4	2030: $7.8	15%
Polaris[10]	2021: $2.2	2030: $10.4	20%

Global market reports forecast **15-20% CAGR**

uHCC – unresectable HCC
mHCC – metastatic HCC

CT-01 (GSPT1)

(1) J Hepatol. 2022;76(4):862-873 | (2) NEJM Evid 2022;1(8) | (3) N Engl J Med 2008; 359:378-390 | (4) Lancet Oncol 2022 Jan;23(1):77-90 | (5) N Engl J Med 2018 Jul 5;379(1):54-63
(6) https://www.visionresearchreports.com/liver-cancer-drug-market/40952 | (7) https://www.snsinsider.com/reports/liver-cancer-therapeutics-market-3215 | (8) https://www.skyquestt.com/report/liver-cancer-drugs-market
(9) https://www.researchandmarkets.com/reports/5899559/liver-cancer-drug-market-size-share-and-trends | (10) https://www.polarismarketresearch.com/industry-analysis/global-liver-cancer-market

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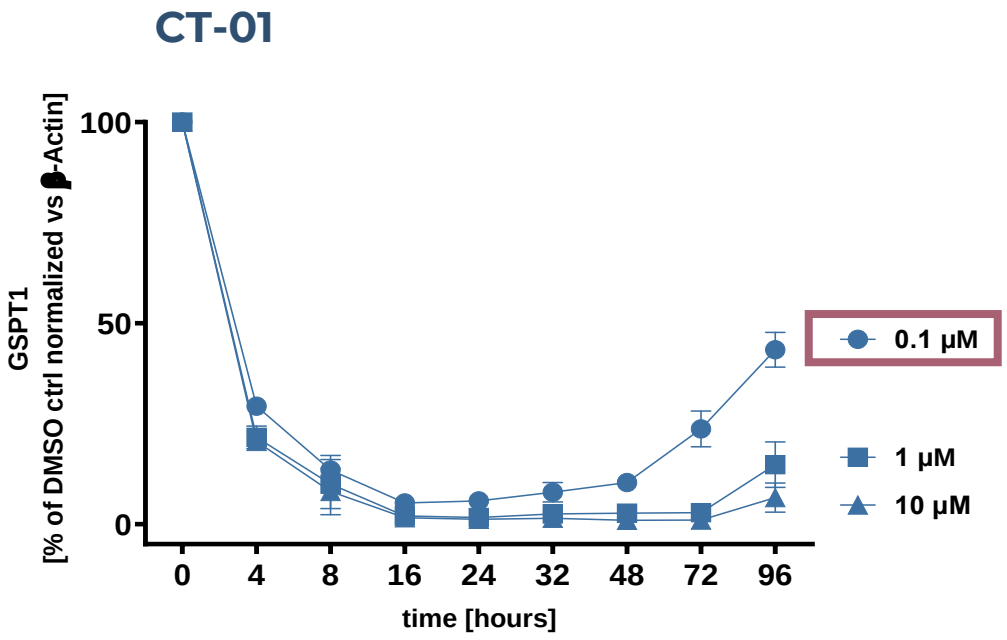
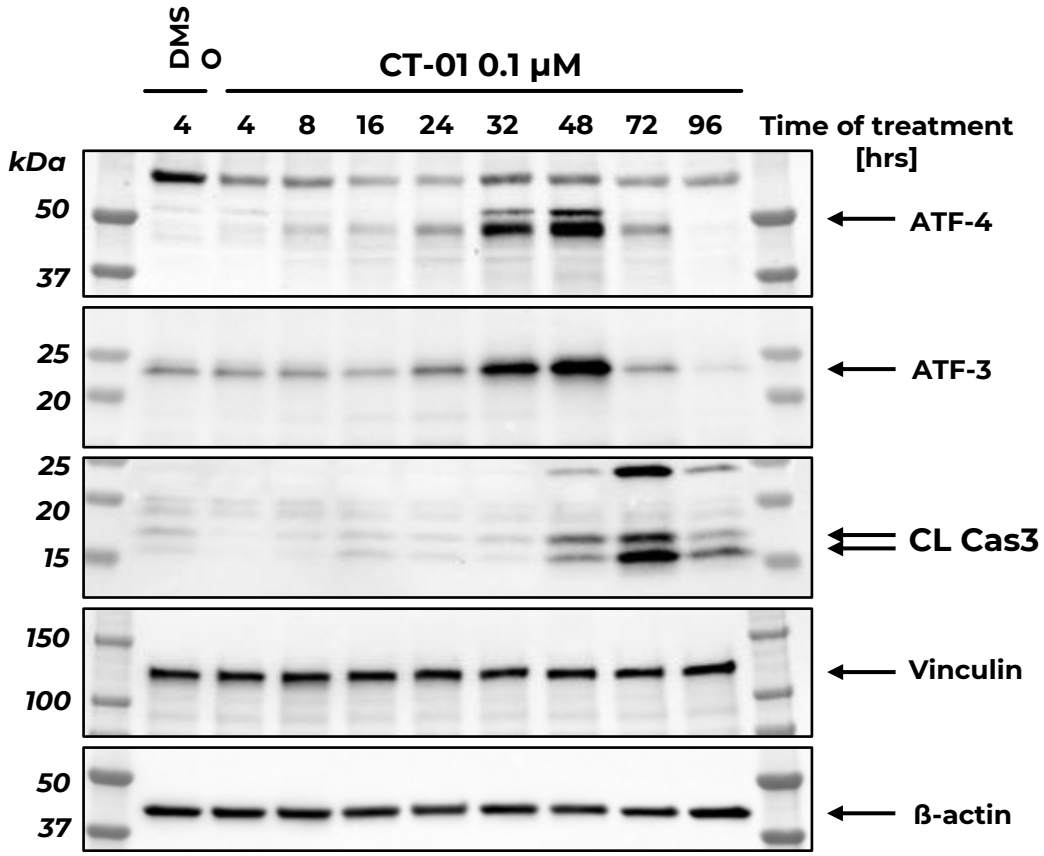
Induction of ISR-dependent cell death in Hep3B tumor cells

Degradation of GSPT1 in the function of time (WB densitometry)



ISR markers during CT-01 treatment



Hep3B cells, 96h treatment with 0.1 , 1 and 10 µM compound

CT-01 (GSPT1)

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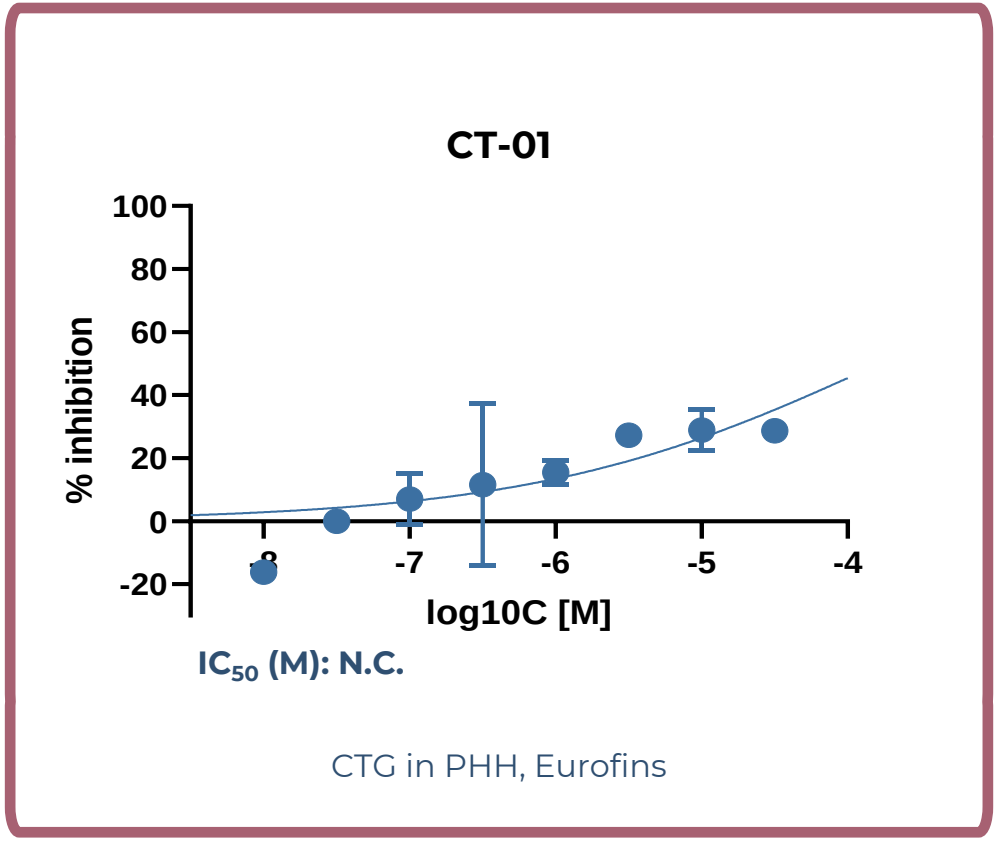
Lack of cytotoxicity to primary human hepatocytes provides extra safety level



CTG in PHH, Eurofins

CT-01 (GSPT1)

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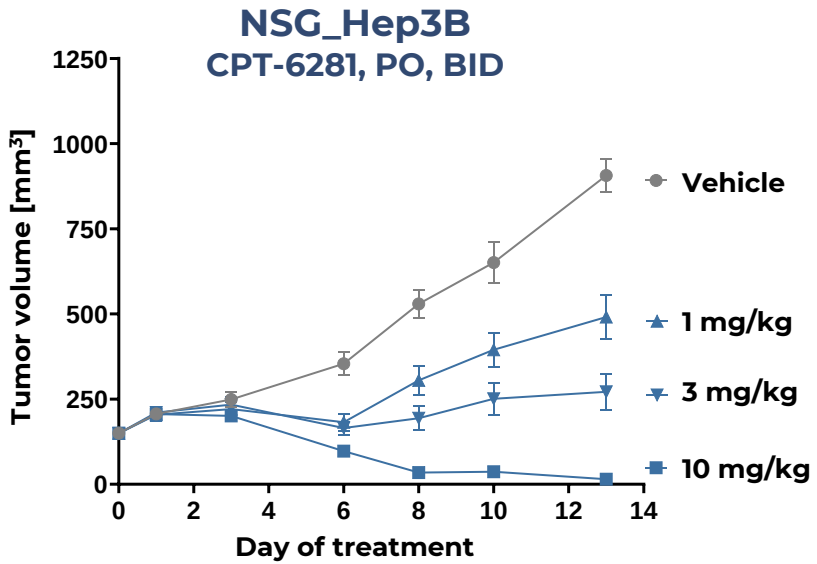
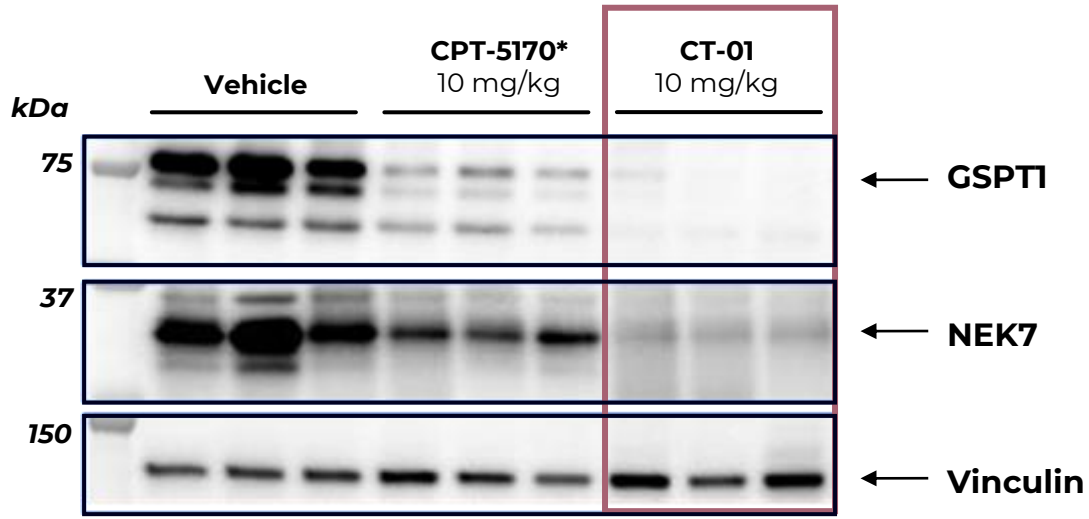
Highly potent CT-01 regresses tumors in mice





Regression of large tumors (~ 150 mm²) observed at doses as little as 10 mg/kg BID administered orally
*CPT-5170: an early lead compound in the CT-01 project

CT-01 strongly regresses liver cancer in Hep3B model at 10 mpk

CT-01 (GSPT1)

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Convincing tumor growth inhibition in HCC PDX models

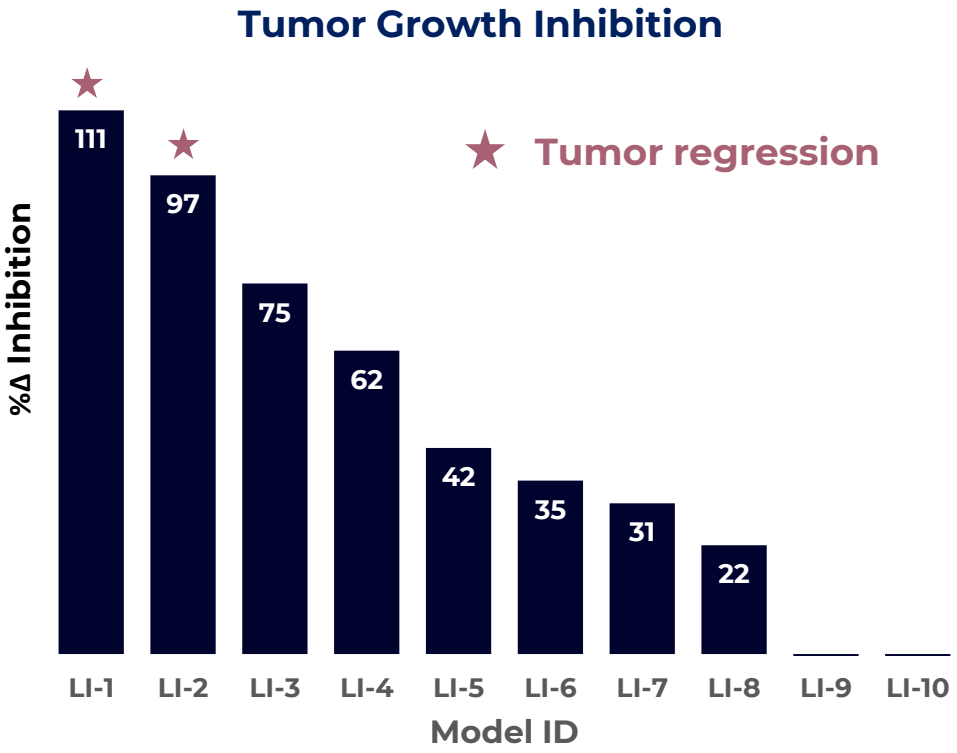
CrownBio
CONNECTING SCIENCE TO PATIENTS

PDX Models/

10 random HCC patient samples (no selection for drug target)

CT-01, 100mg/kg, BID

3 animals per vehicle & treatment groups



Efficacy demonstrated in 8/10 PDX models; TGI>50% in 4 models, 2 models with regression

CT-01 (GSPT1)

Captor Therapeutics®

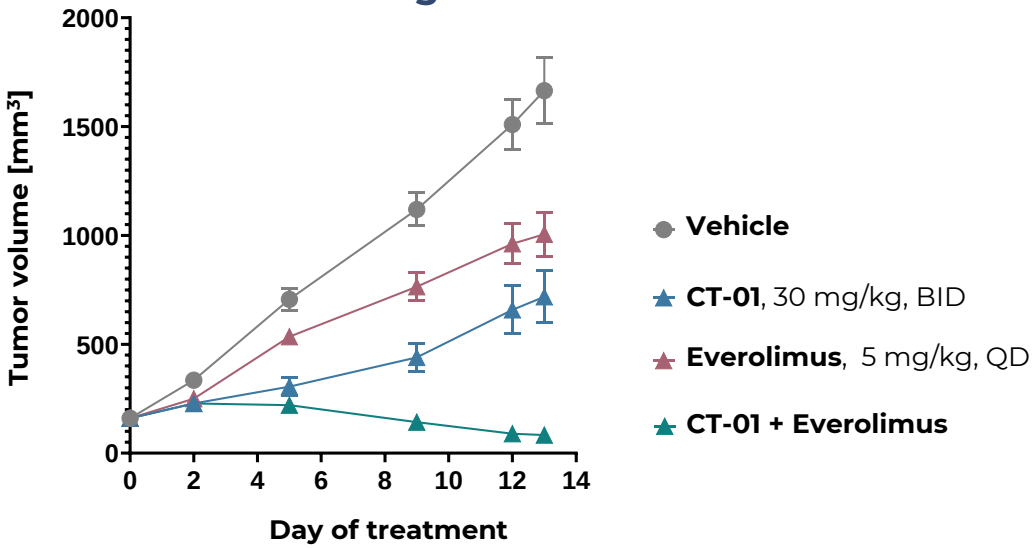
Strong synergy of CT-01 in combination with everolimus

CrownBio
CONNECTING SCIENCE TO PATIENTS

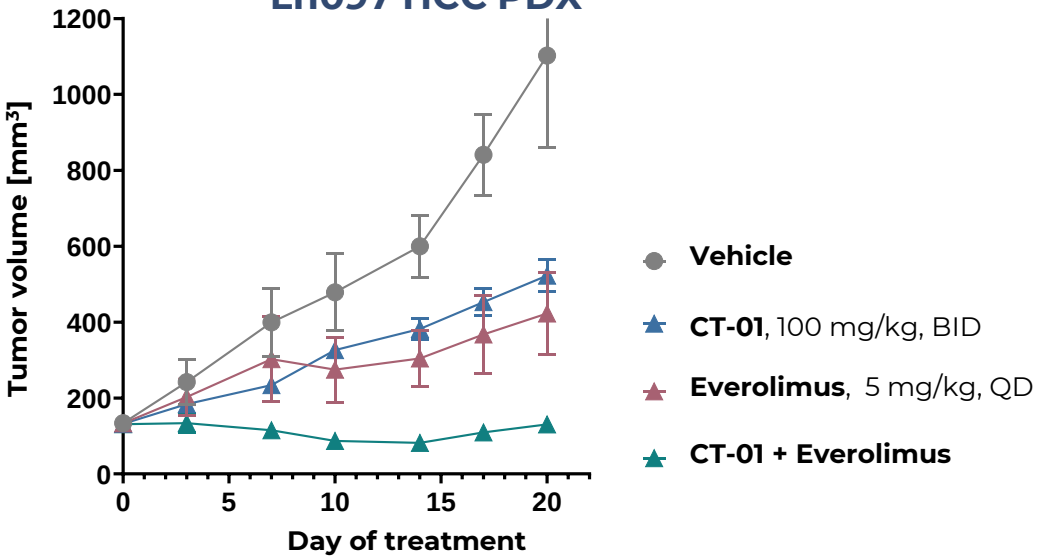
PDX Models/

Everolimus is an approved anticancer drug (kidney, breast & brain cancers), and shows clear synergy with CT-01 in combination

HUH-7 Xenograft Model



LI1097 HCC PDX



Combination with everolimus sensitizes poorly or non-responding tumor models

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CT-01 is highly differentiated among GSPT1 degraders

Assay	CT-01 (Captor)[1]	CC-90009 (BMS)[2]	MRT-2359 (Monte Rosa)[3]
Selectivity (Px, WB)	**GSPT1, GSPT2, NEK7**	GSPT1, GSPT2, SALL4, FIZ1, RNF166, ODC1 (1)	GSPT1, GSPT2
CYP DDI (2B6, 1A2, 2D6, 3A4, 2C8, 2C9, 2C19)	**>50 µM**	CYP2C19 at 1.5 µM	>30 µM
hERG	**>30 µM**	5.3 µM	>30 µM
CEREP, % inhibition	**Protein panel <20% at 10 µM**	M1/M2 > 50% at 10 µM	a1A>50% at 10 µM
Caco2 (Efflux Ratio) of active drug	**1.0**	>100	9
Route of Administration	**PO**	IV	PO
Metabolic activation	**Yes**	No	No
Cell permeability of the active drug	**Very low**	High	High
Clearance of the active drug	**Fast; >300 ml/min/kg**	Medium; ~70 ml/min/kg	N/A
Tissue specificity	**Yes**	No	No
Potential weaknesses	**Unknown (No hypocalcemia or thrombocytopenia seen in GLP-tox)**	Hypocalcemia and thrombocytopenia	Dose-limiting thrombocytopenia

(1) Internal profiling
(2) DOI: 10.1021/acs.jmedchem.0c01489
(3) Monte Rosa Corporate Presentation

CC-90009 = BMS / Celgene GSPT1

CT-01 (GSPT1)

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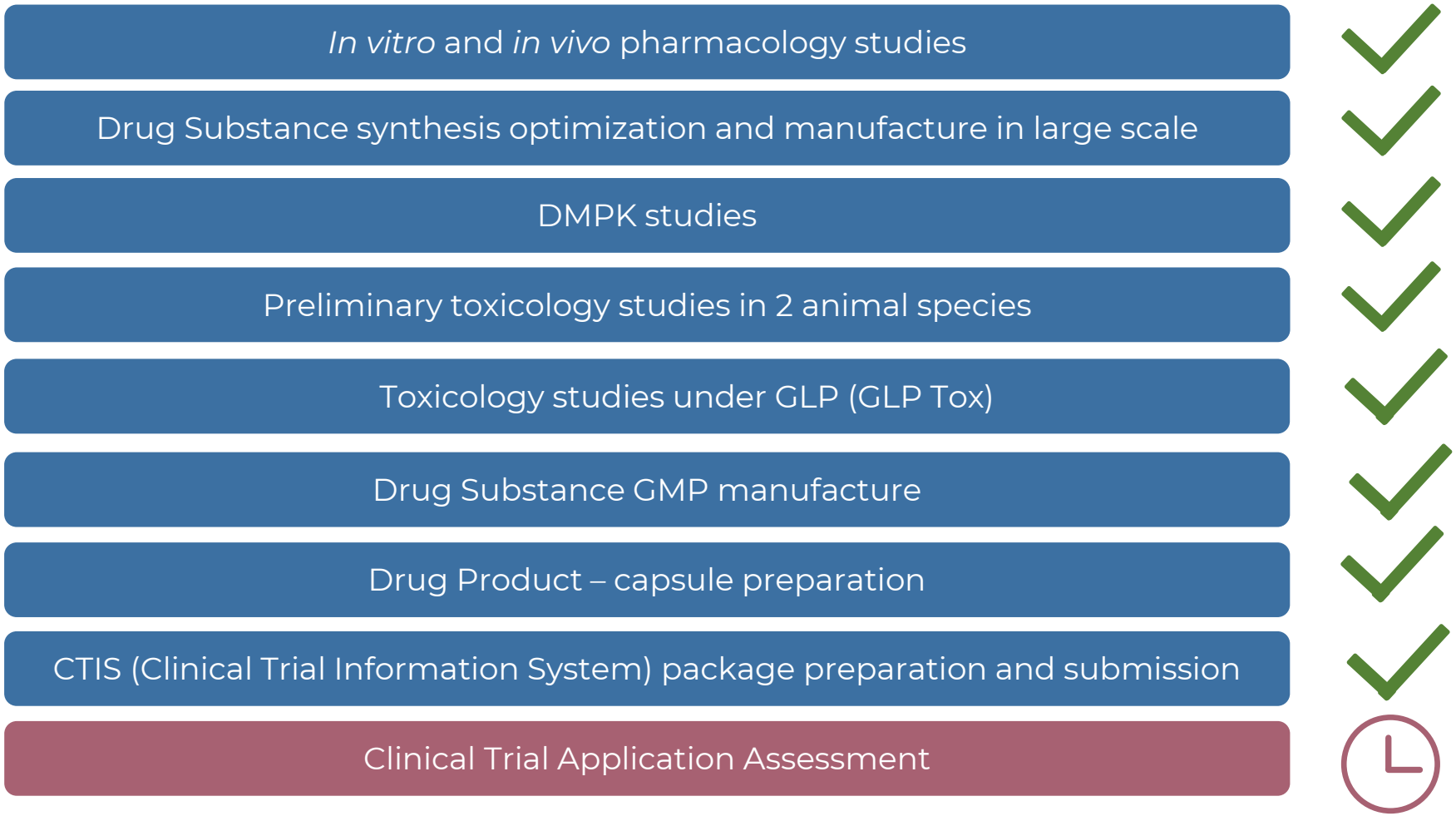
CT-6281: CTA submission status



CT-01 (GSPT1)

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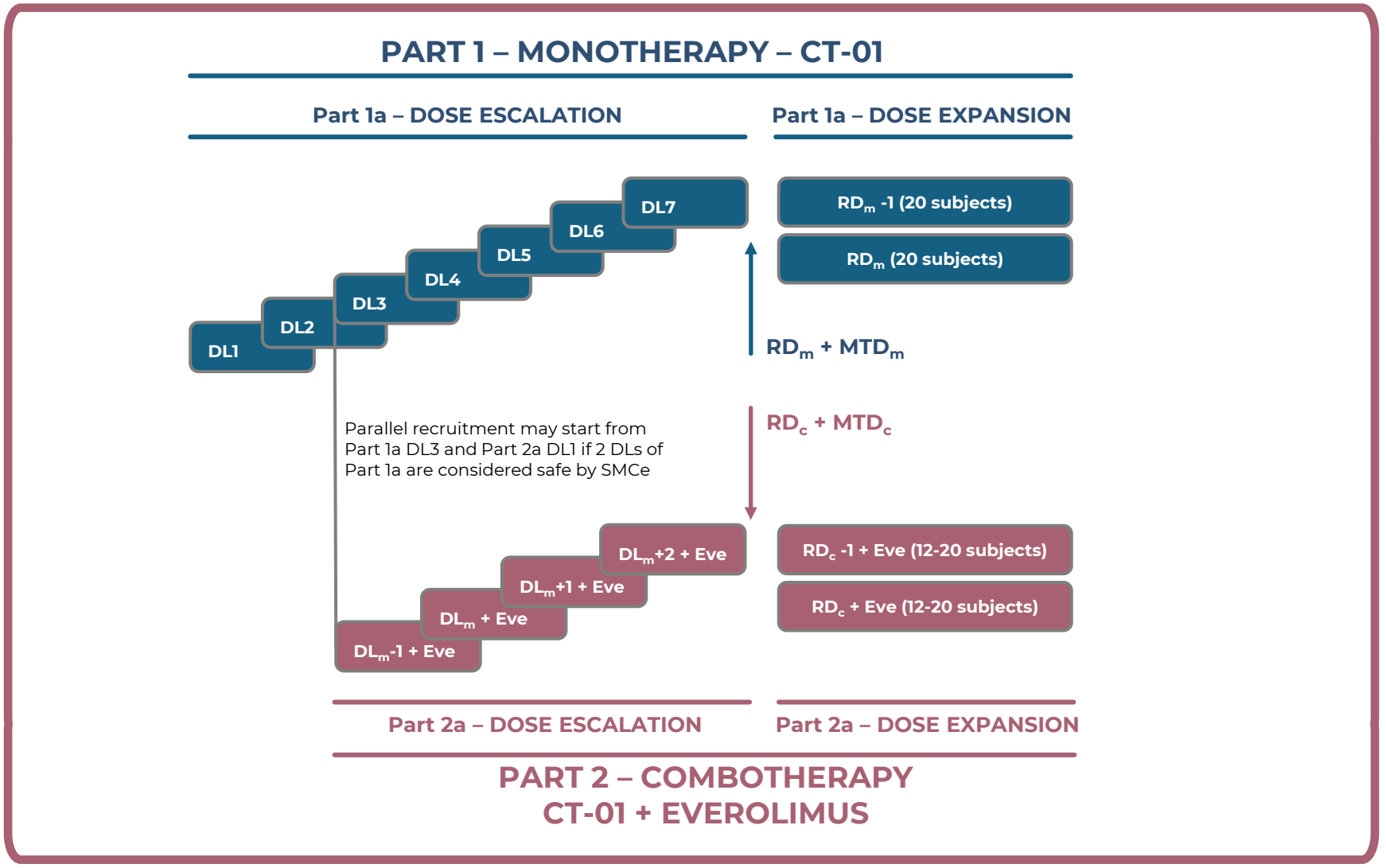
Study design



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Best-in-class potential of highly differentiated CT-01

- **Strong differentiation from other GSPT1 degraders (BMS, Monte Rosa)**
  - Best-in-class degradation profile
  - Active degrader lingers inside cancer cells after activation (poor cell penetration after prodrug conversion)
  - Active degrader is rapidly cleared from systemic circulation
- **Degradation profile**
  - GSPT1, NEK7
  - Activated in diseased liver, lung, adipocytes and inflamed blood-brain barrier
- **Initial indications**
  - hepatocellular carcinoma (HCC)
  - lung cancer
  - brain tumors
  - rare cancers (hepatoblastoma, lipo- and angiosarcoma)
- **Development activities**
  - Clinical Trial Authorization Application submitted in Europe
  - Initiation of Phase 1 clinical trials in hepatocellular carcinoma Q1 2025

CT-03: First-in-Class MCL-1 Degraders for Liquid & Solid Tumors

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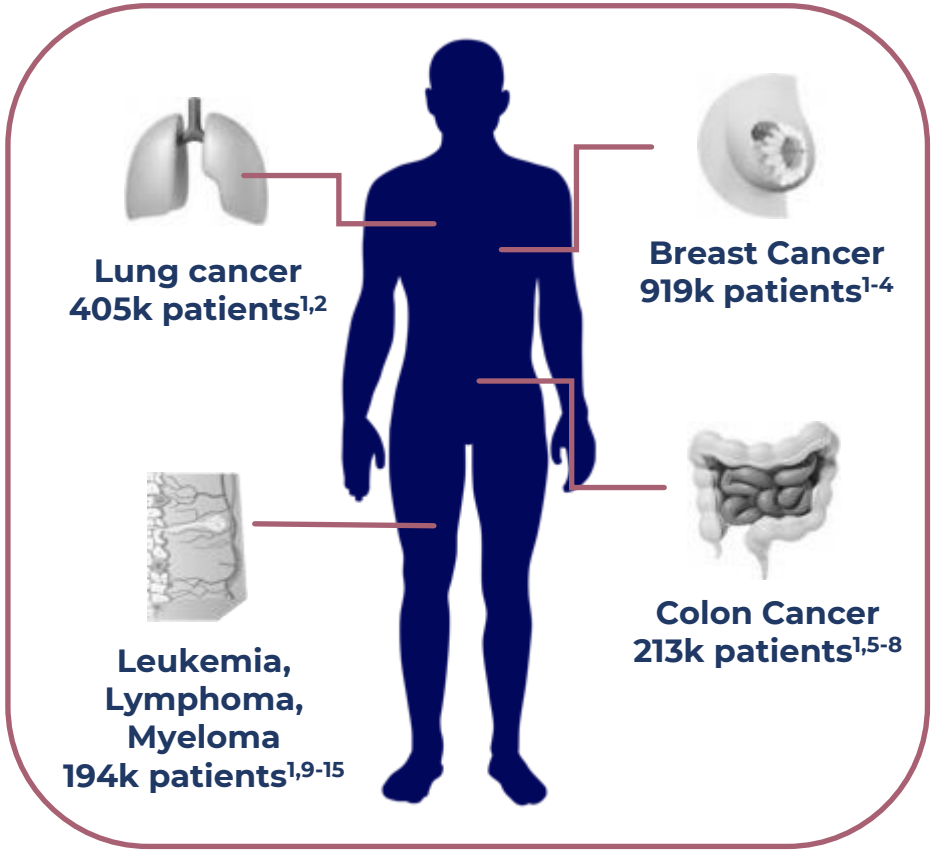
CT-03: MCL-1 – a critical pathway for cancer resistance



MCL-1 is one of the most amplified proteins in cancer†

A critical resistance mechanism in hematological and solid tumors‡, cancer cells require very high levels to avoid induction of apoptosis

Degradation or inhibition of MCL-1 protein directly attenuates tumors in vivo as monotherapy & sensitizes tumors for other therapies

Inhibitors require prolonged, almost 100% of target coverage and cause accumulation of MCL-1†, cardiotoxicity through necrosis§

Short-term degradation of ≈70% of MCL-1 irreversibly induces apoptosis in cancer cells

This, together, with optimized clearance expands the therapeutic window of degraders

1. https://gco.iarc.fr/today/en/
2. Semin Cancer Biol. 2006 16(4):253-64
3. Cell Death Dis 2018 9(2): 19
4. Breast Cancer Res. 2016 18(1): 125
5. Int J Mol Sci. 2019 20(3): 5999
6. Cell Death Dis. 2022 13(1): 63
7. Colorectal Dis 2022 24(11): 1295-1307
8. Ann Fam Med. 2016 14(3): 215-20
9. Exp Hematol Oncol. 2020 Jun 19;9:14
10. Hum Pathol. 2004 Sep;35(9):1095-100
11. ACS Key Statistics for AML, CLL, Lymphoma
12. Curr Treat Options Oncol. 2020 Jun 29;21(8):66
13. Int J Mol Sci. 2024 Jan 27;25(3):1589
14. Blood Rev. 2020 Nov;44:100672
15. Leukemia. 2013 Jun;27(6):1381-90

†Front Oncol. 2023 Jul 31;13:1226289
‡Apoptosis. 2023 Feb;28(1-2):20-38
§iScience. 2020 April; 23(4): 101015

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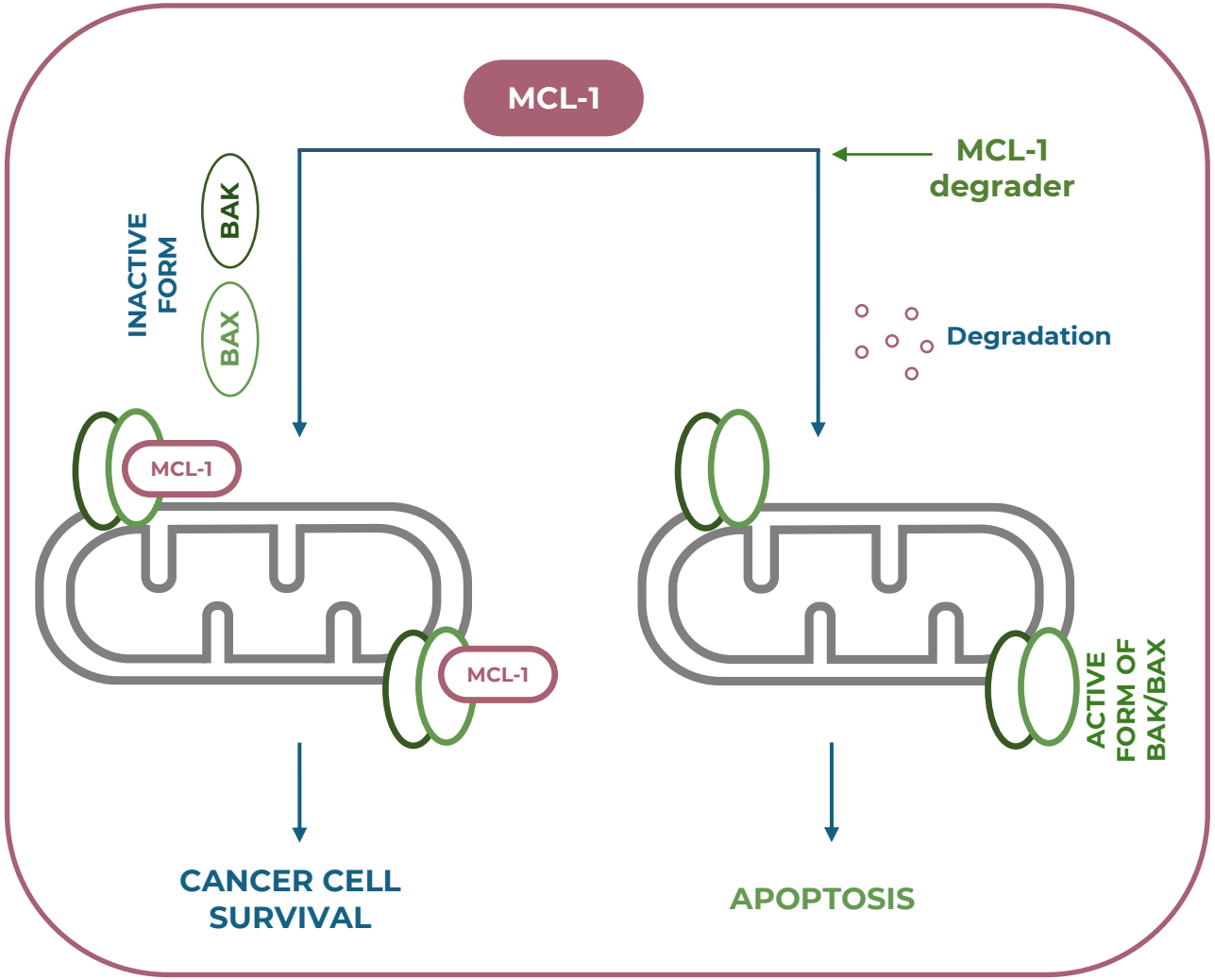
CT-03: MCL-1 – a critical pathway for cancer resistance



MCL-1 biology and clinical relevance

MCL-1 is a well-characterized oncogenic protein with a key role in **evading apoptosis** and **promoting the survival of cancer cells**[1].

Studies show cell growth dependency of MCL-1 levels in liquid (leukemia, lymphoma, myeloma) and solid tumors (breast and lung cancers[2]).

Monoallelic KO of MCL-1 in mice is viable and do not show signs of cardiac damage[3] or gross phenotype, and show resistance to selected liquid tumors.

Numerous systemic and targeted therapies drive the clonal selection of cells towards increased levels of MCL-1, like in AML refractory to venetoclax[4].

1. Singh R et al. Nature Reviews, 2019; 20: 175-193
2. Kotschy A et al. Nature, 2016; 538(7626): 477-482
3. Brinkmann K et al. Cell Death Differ, 2017; 24(12): 2032-2043
4. Garciaz S et al. Cancers, 2024; 16(6): 1091

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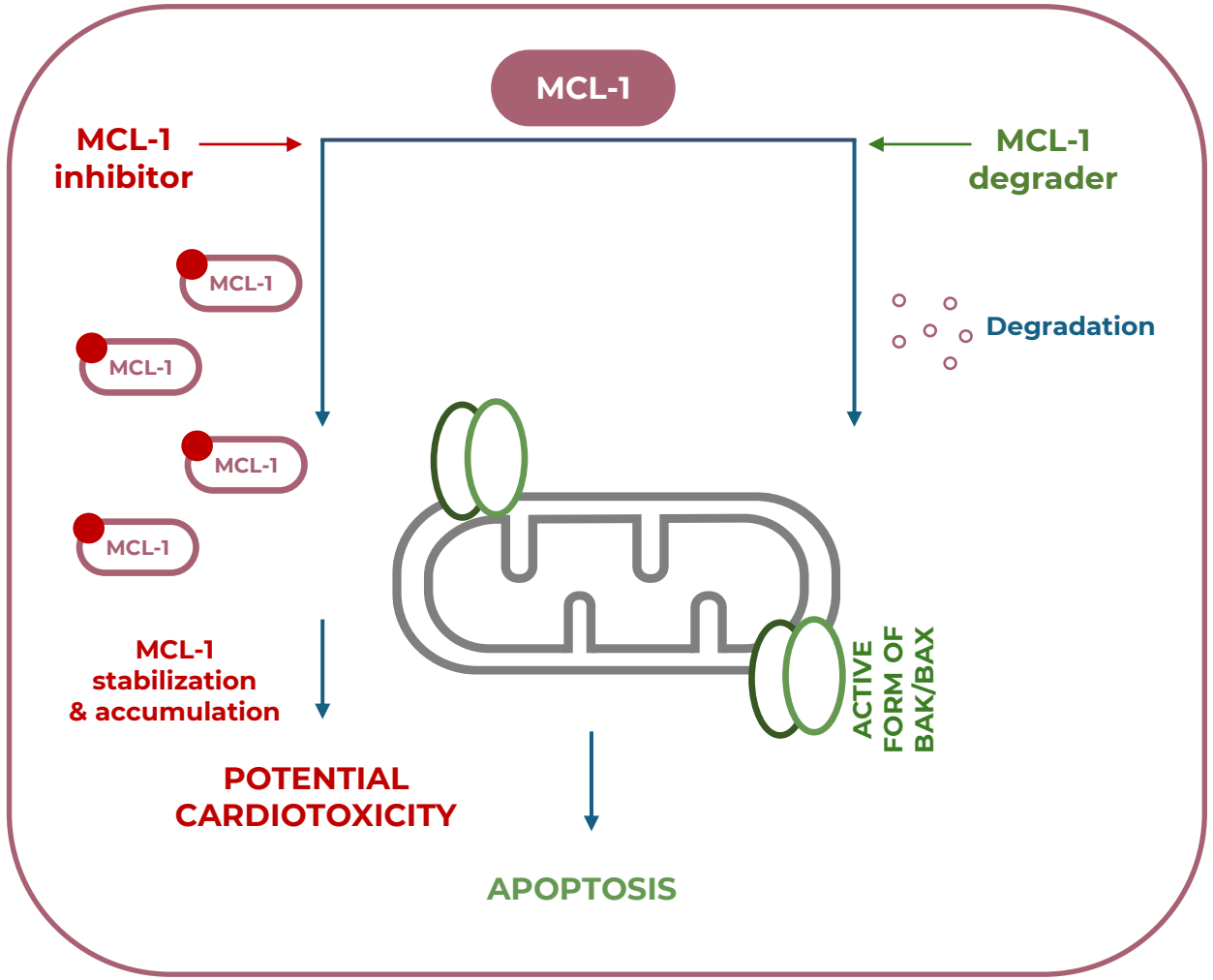
CT-03: MCL-1 – a critical pathway for cancer resistance



MCL-1 degraders advantage over inhibitors

MCL-1 inhibition increases its stability, through its aberrant phosphorylation and consequent accumulation[1].

The result of MCL-1 accumulation is a cellular rewiring that affects cardiomyocyte viability *via* necrosis, not apoptosis[2].

None of the MCL-1 inhibitors progressed significantly in clinical development due to safety issues, i.e. cardiotoxicity.

Since degraders induce rapid apoptosis of cancer cells via reduction of MCL-1 levels and provide homeostatic levels of MCL-1 in cardiac myocytes, they are expected to avoid toxicity seen with the class of inhibitors.

1. Singh R et al. Nature Reviews, 2019; 20: 175-193
2. Kotschy A et al. Nature, 2016; 538(7626): 477-482

CT-03 (MCL-1)

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MCL-1: a high potential cancer target

Highly attractive target with application in numerous cancer markets

Hematological malignancies

Multiple Myeloma (MM)
Est. $53B by 2030[1]

Acute Myeloid Leukemia (AML)
Est. $6B by 2028[2]

Non-Hodgkin Lymphoma (NHL)
Est. $16B by 2032[3]

Selected solid tumors

Small cell lung cancer (SCLC)
Est. $6.5B by 2031[4]

Non-small cell lung cancer (NSCLC)
Est. $36.9B by 2031[5]

Triple-negative breast cancer (TNBC)
Est. $1.5B by 2030[6]

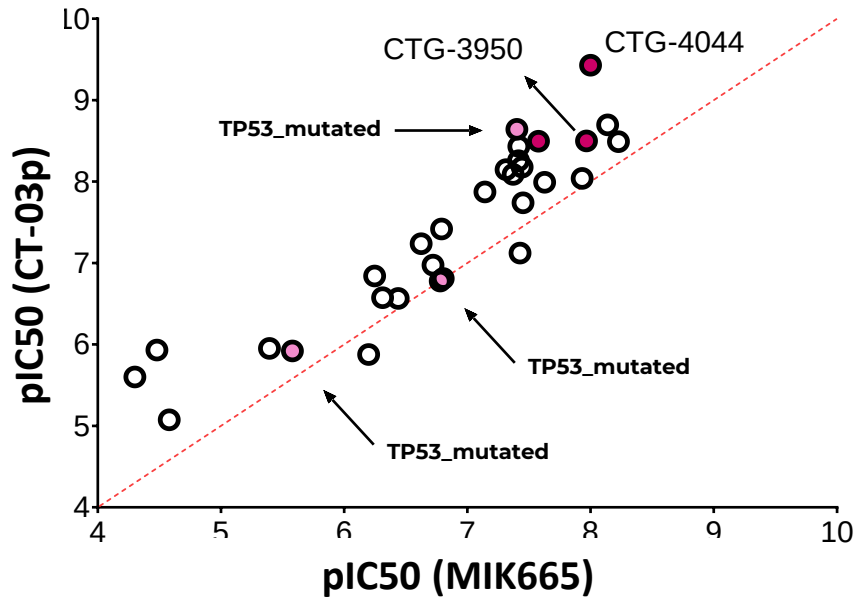
Despite years of effort, no MCL-1 targeting drug has been approved and several inhibitors have been associated with toxicity

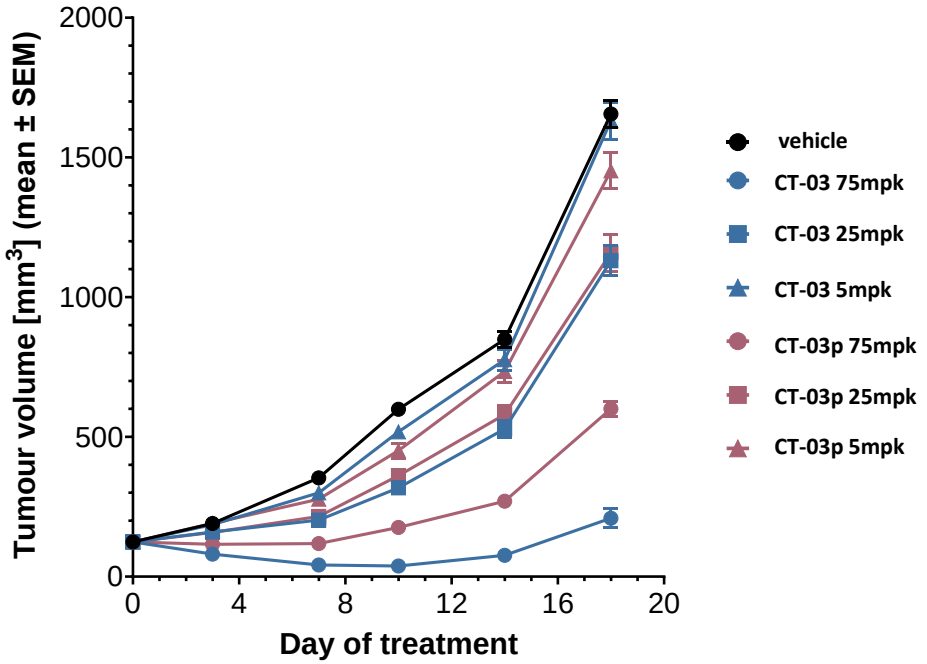
Captor has nominated a candidate, CT-03p (prodrug); neither has shown any evidence to date of cardiotoxicity in keeping with their different mode of action

[1] Allied Market Research
[2] BCC Research
[3] Spherical Insights
[4] iHealthcareAnalyst
[5] Allied Market Research
[6] Databridge Market Research

High potency of MCL-1 degraders in AML patient samples *ex vivo* & in-vivo leukemia model

MCL-1 degrader is more potent than MIK665 (Novartis) in patient-derived AML cells





Q3D, IV
N=7-10/group

CT-03 – active compound; CT-03p – produg of CT-03

CT-03p (prodrug) is more potent than MIK665 (Novartis) in a panel of 30 PDC cell lines and shows nM activity in cells refractory to gilteritinib and venetoclax

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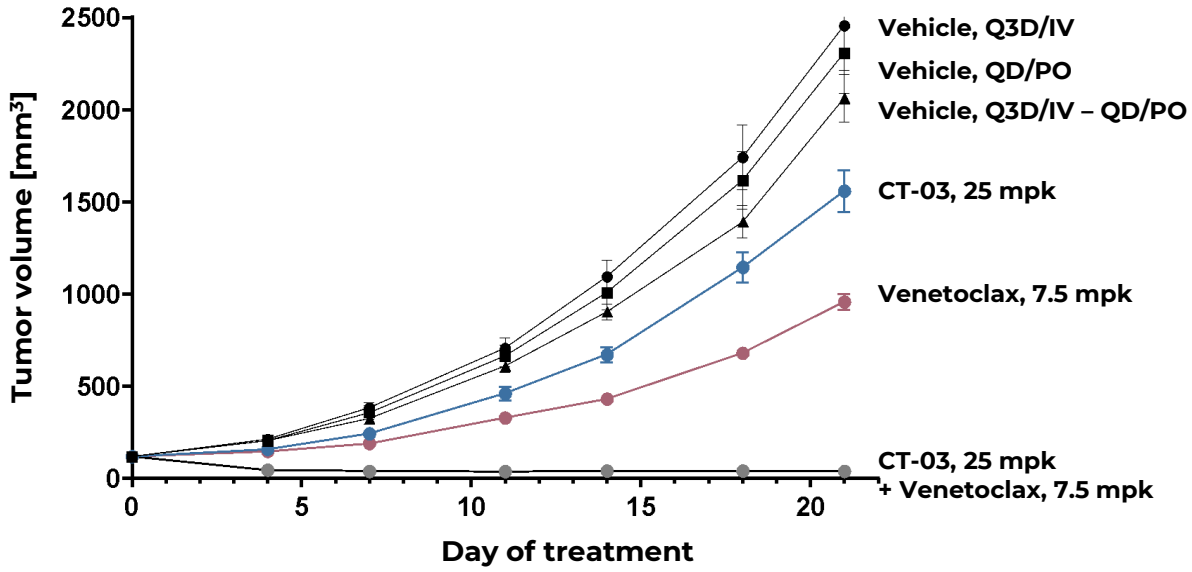
Combined of MCL-1 degrader with venetoclax regresses AML tumors in mice

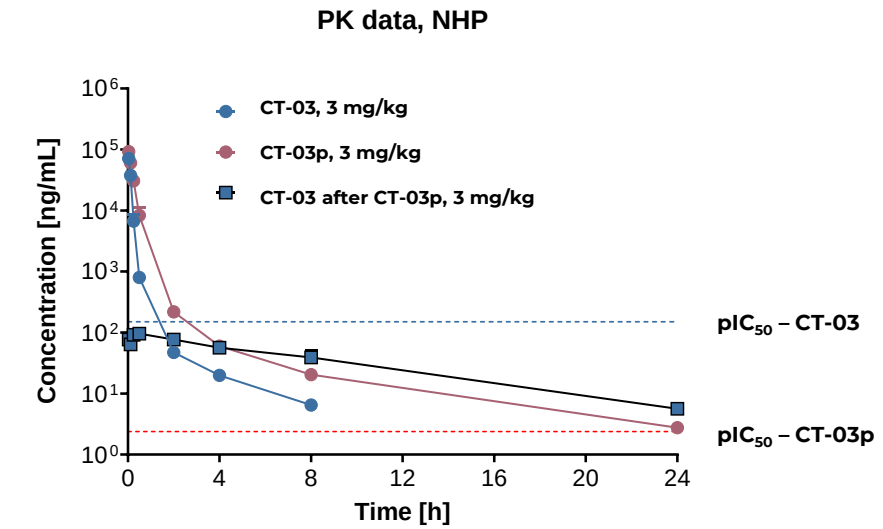


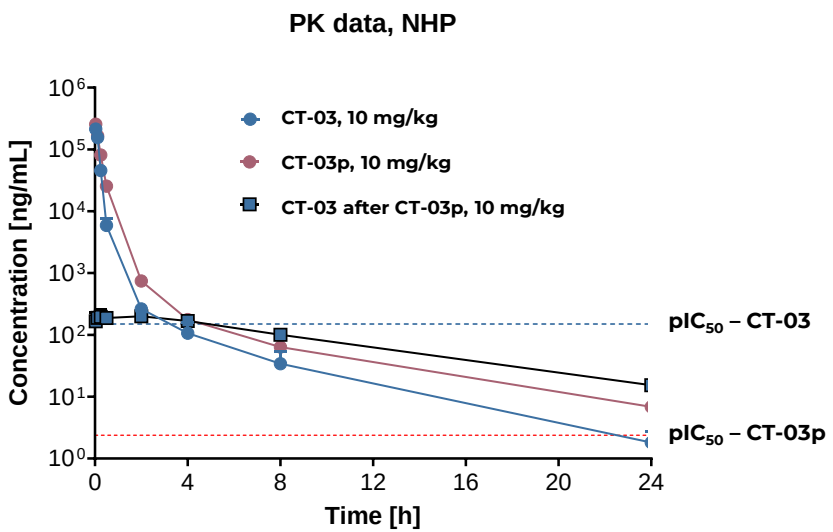
Regression of large tumors was observed for both CT-03 and venetoclax, with the combination providing the best outcome

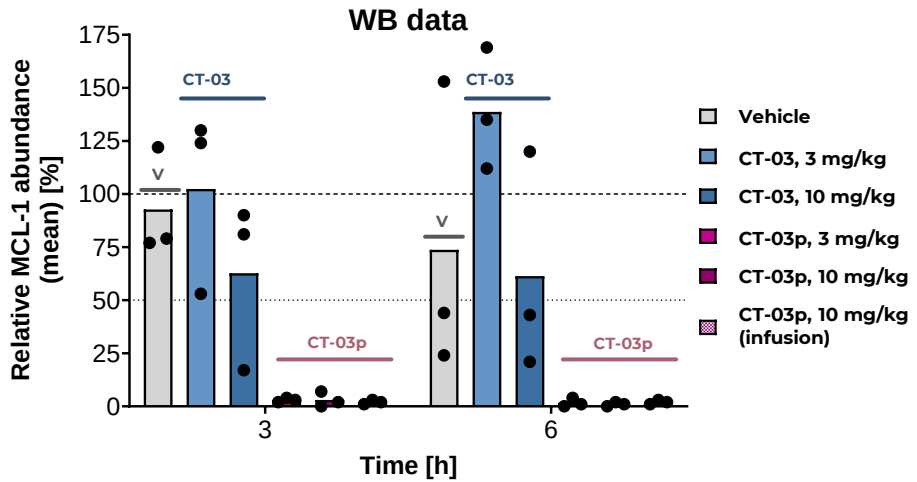
CT-03 was administered 8 times, every 3 days (Q3D) intravenously and venetoclax was administered daily (QD) orally

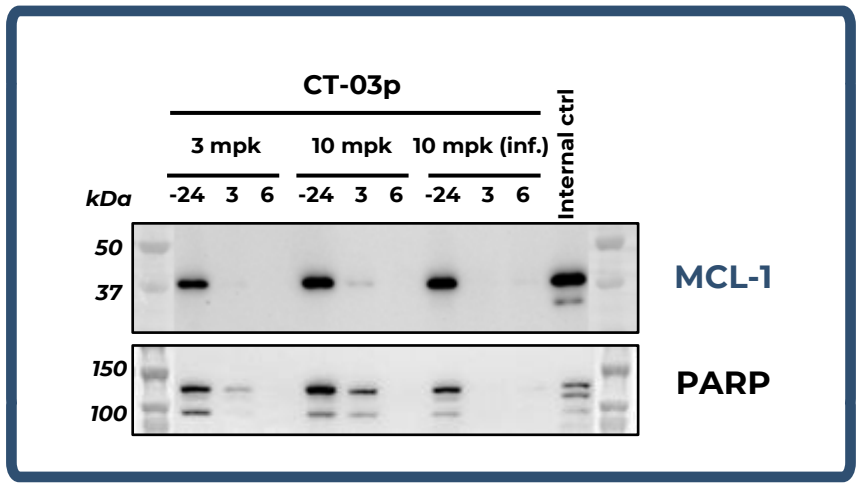
CT-03 in combination with venetoclax strongly inhibits cancer growth in MV4-11 Human Leukaemia Xenograft Model

Degradation of MCL-1 in NHP after single IV dose of degraders









CT-03 (MCL-1)

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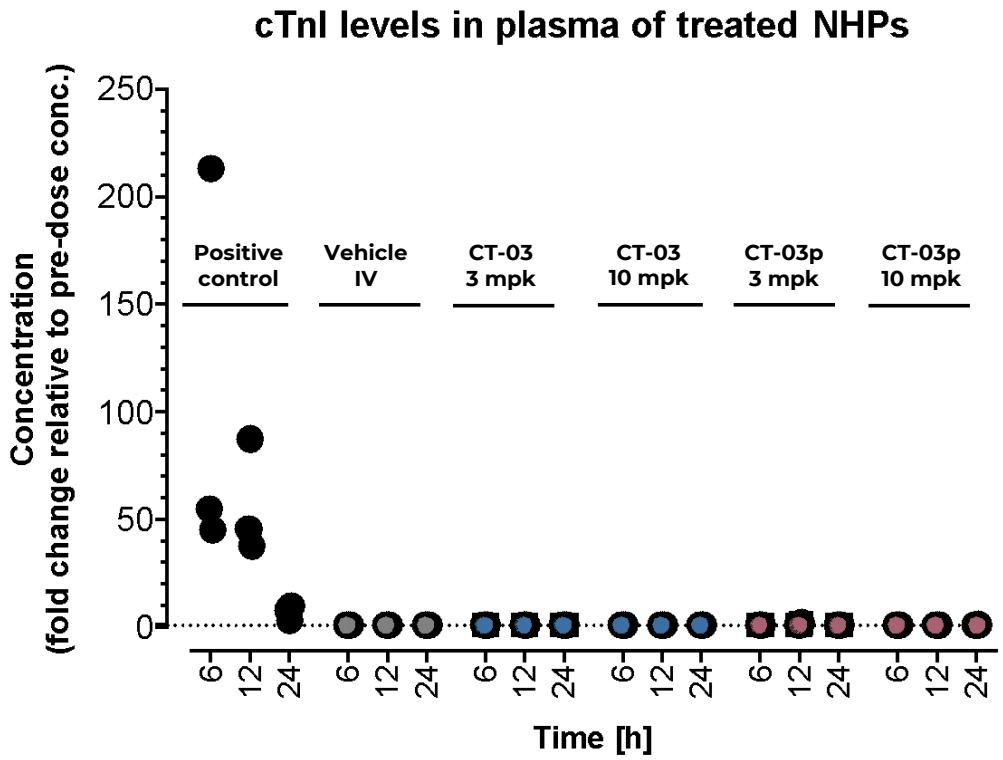
Cardiotoxicity marker Troponin I in plasma of NHPs after CT-03 dosing



CT-03 & CT-03p: no observed increase in troponin-I levels

***Cardiotoxic positive control - Isoproterenol 3mg/kg, Vasopressin 0.3mg/kg**

CT-03 – active compound; CT-03p – produg of CT-03

Captor Therapeutics®

CT-03 candidate drug with unmatched therapeutic window

- **Strong differentiation from MCL-1 inhibitors**
  - Pharmacology of MCL-1 degradation vs. pharmacology of accumulation (inhibitors)
  - No accumulation of MCL-1 protein
  - No cardiotoxicity observations in MTD, DRF in NHPs by any means
  - Very high degradation potency in mouse models, in NHP and in human cells *ex vivo*
  - **Candidate drug in place**
- **Initial indications**
  - Hematological cancers
  - Solid tumors
- **Expected milestones**
  - IND-enabling studies completion in H2 2025

CT-02: First-in-Class NEK7 Degraders for Autoimmune (CT-02S), Neuroinflammation & Obesity (CT-02B)

Captor Therapeutics®

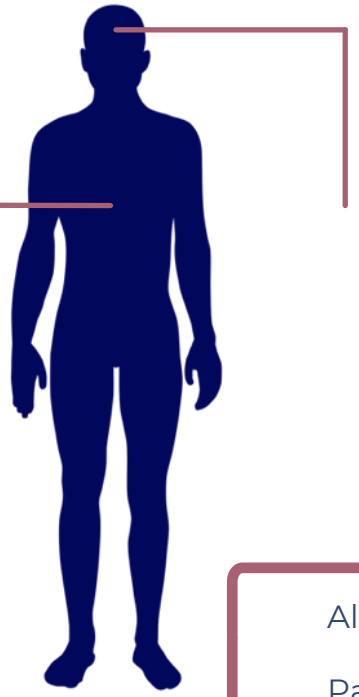
Significant market opportunities for Captor's NEK7 degraders

CT-02S
CPT-635(r)

Peripheral autoimmunity

NEK7 degraders could be used in combination with available therapeutics to manage comorbidities

Three significant therapeutic areas:



CT-02B
CPT-732(r)

Neurodegenerative diseases

Growing evidence for role of pathological activation of innate immunity in the pathogenesis of NDDs

Limited treatment strategies available: opportunity to target neuroinflammation via NEK7 degradation & inhibit disease progression

Obesity/ Metabolic	Autoimmune	Cardiovascular
16% living with obesity worldwide[5]	5-10% of global population[6]	19.8M deaths in 2022 due to CVD[7]
Global market size (2030):		
$100B[1]	$10.9B[2]	$152.6B[3]

- Alzheimer's: 35.8M patients worldwide[10]
- Parkinson's: 8.5M patients worldwide (2019)[11]
- Multiple Sclerosis: 2.8M patients worldwide[12]
- Huntington's: 400,000 patients worldwide[8]
- ALS: 362,000 patients worldwide[9]

NDD market size is estimated to reach $75B[4] by 2030

1. https://www.goldmansachs.com/intelligence/pages/anti-obesity-drug-market.html
2. https://www.databridgemarketresearch.com/reports/global-autoimmune-disease-treatment-market
3. https://www.researchandmarkets.com/report/cardiovascular
4. https://www.researchandmarkets.com/report/neurodegenerative-disease-drug
5. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
6. J Autoimmun. 2010 May;34(3):J168-77.
7. J Am Coll Cardiol. 2023 Dec 19;82(25):2350-2473
8. https://pubmed.ncbi.nlm.nih.gov/36161673/
9. https://pubmed.ncbi.nlm.nih.gov/31797084/
10. https://www.who.int/news-room/fact-sheets/detail/dementia
11. . https://www.who.int/news-room/fact-sheets/detail/parkinson-disease
12. Mult Scler. 2020 Dec;26(14):1816-1821

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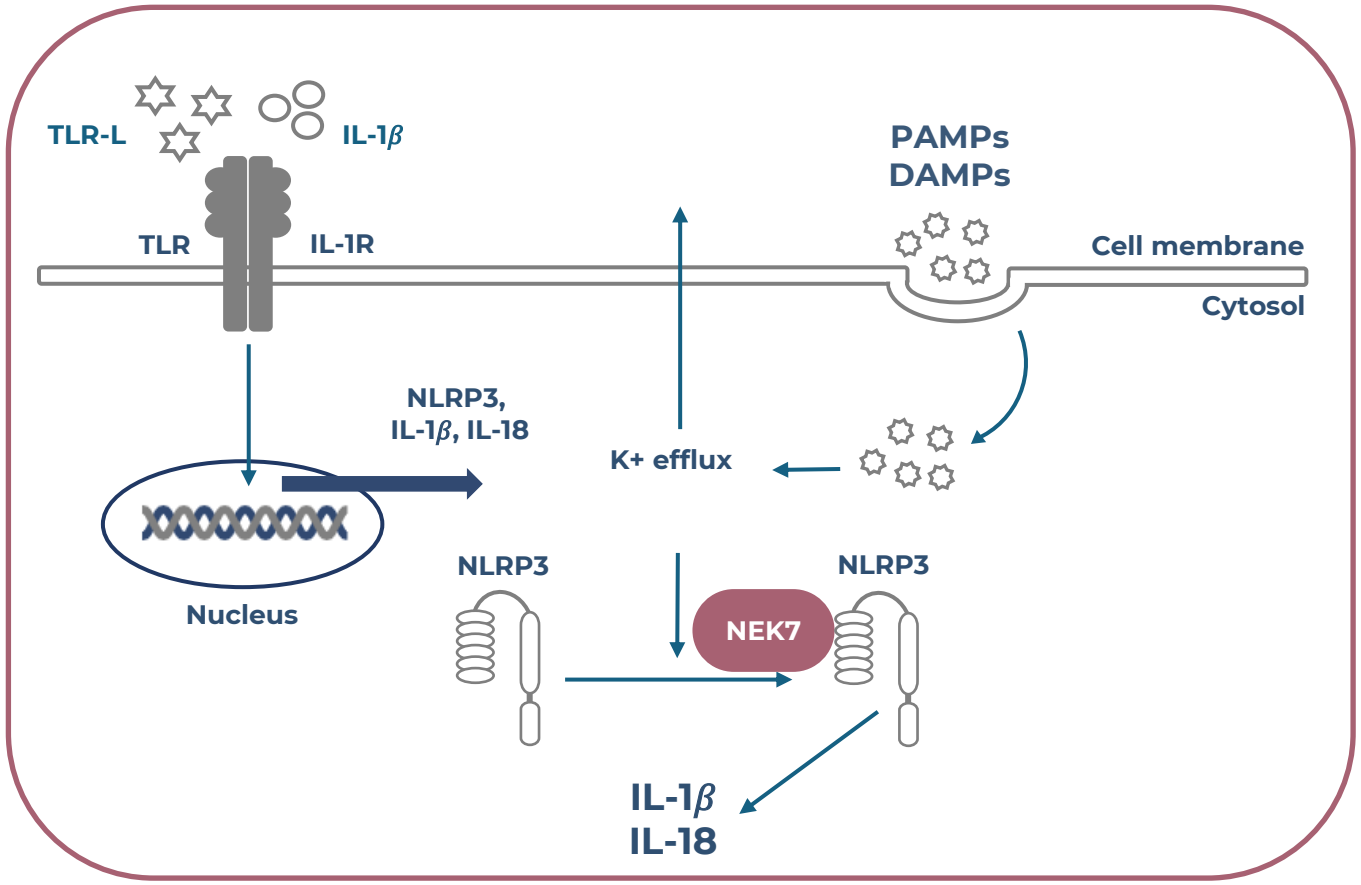
NEK7 as a new target of the NLRP3 inflammasome pathway



NEK7 overview

NEK7 is master regulator of the NLRP3 inflammasome complex through its scaffolding function

NEK7 KO/KD in mouse abrogates production of IL-1 beta in response to stimulating factors.

Haploinsufficient, NEK7$^{+/-}$, mice show no internal anatomical or growth abnormalities.

Antagonists of IL-1β or IL-1R are approved in:

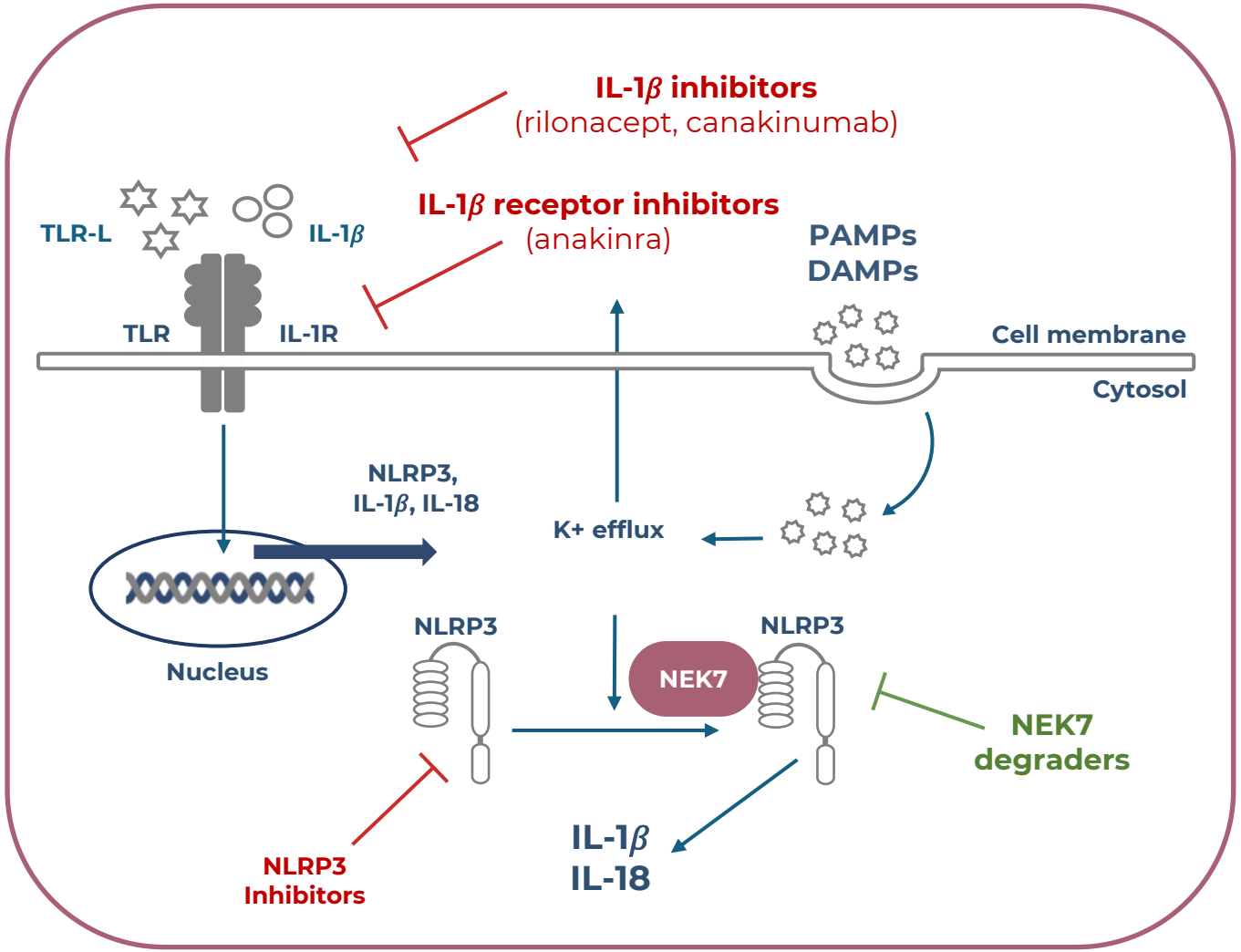
- CAPS syndromes (FCAS, MWS, NOMID)
- inflammatory disorders, e.g. familial mediterranean fever (FMF), tumor necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS) / mevalonate kinase deficiency (MKD), Still's disease, and gouty arthritis.

Degradation of NEK7 inhibits the production of pro-inflammatory cytokines in *in vitro* models and halts disease progression in pre-clinical mouse models of chronic NLRP3-related diseases*.

1. Shi et al; Nature Immunology, vol 17 (2016);
2. Sharif et al.; Nature, vol 570, (2019);
3. He et al.; Nature, vol 530, (2016);
4. Walle and Lamkanafi; Nature Reviews Drug Discovery vol 23
*own results conducted by Captor Therapeutics

Captor Therapeutics®

NEK7 as a new target of the NLRP3 inflammasome pathway



Differentiation

From anti-IL-1β antagonists:

Once daily oral administration instead of injection

Uncoupling pharmacokinetics from pharmacodynamics potentially offers a better safety profile

From NLRP3 inhibitors:

Uncoupling pharmacokinetics from pharmacodynamics potentially offers a better safety profile and prolonged efficacy

High safety profile: due to multiple functions of NLRP3 outside of the inflammasome, there are serious safety concerns about NLRP3 inhibitors

Complete IL-1β shutdown potentially manifests in recurring infections

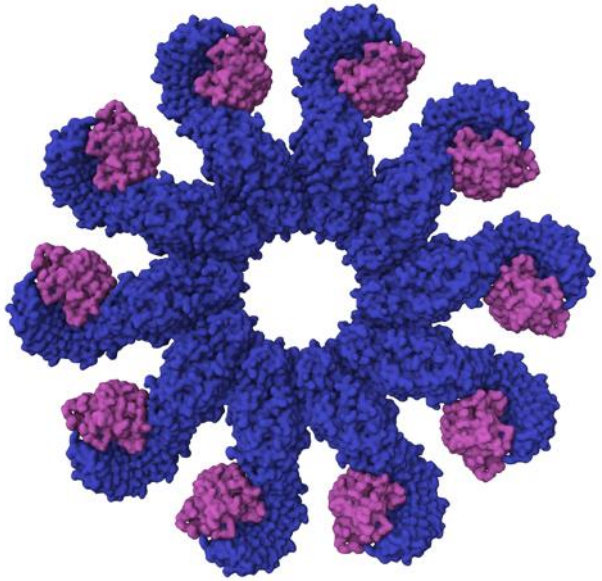
NLRP3 requires high coverage by inhibitors, which is recapitulated in increased frequency of dosing (BID) of some of the clinical compounds, e.g. DFV890 (Novartis)

1. Molina-Lopez et al; Nature Communications, vol 15, (2024); https://www.ema.europa.eu/en/medicines/human/EPAR/ilaris
2. https://www.ema.europa.eu/en/medicines/human/EPAR/kineret
*own results conducted by Captor Therapeutics

Captor Therapeutics®

Intervention in NLRP3 pathway *via* NEK7 degradation

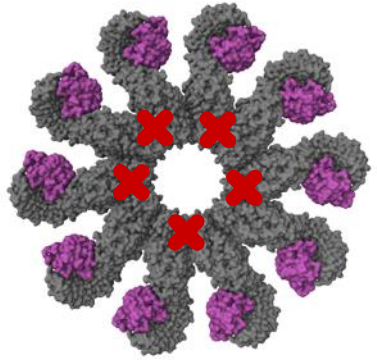
Aberrant activation of NLRP3



NLRP3 inflammasome

NEK7

NLRP3 inhibition

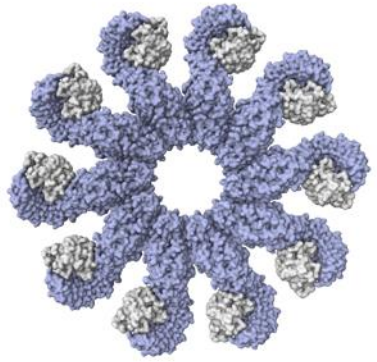


COMPLETE INACTIVATION OF NLRP3

INCREASED INFECTIONS, TOXICITY FROM NON-INFLAMMASOME FUNCTIONS OF NLRP3

NEK7 degradation

PARTIAL INACTIVATION OF NLRP3



MAINTAINED IMMUNITY

CT-02 (NEK7)

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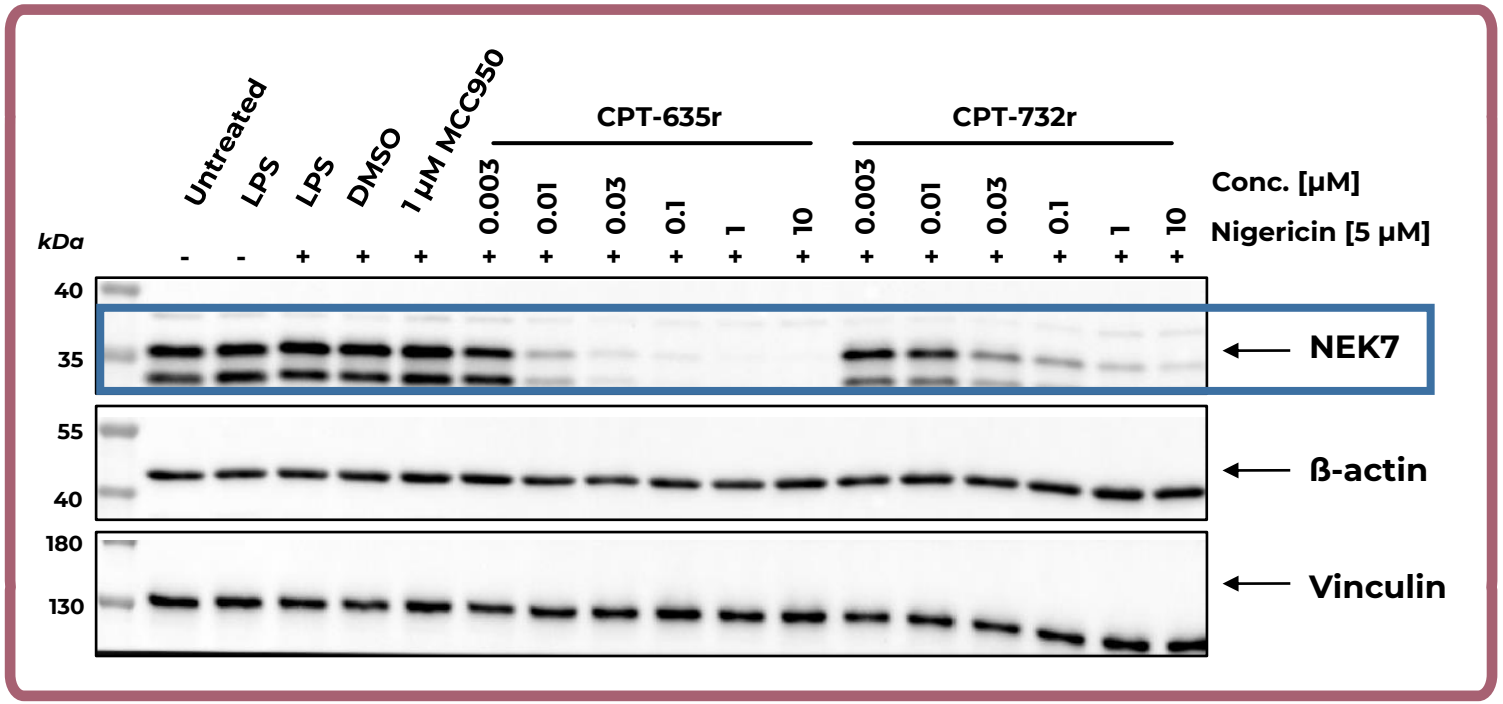
Potent degradation of NEK7 in human macrophages *in vitro*



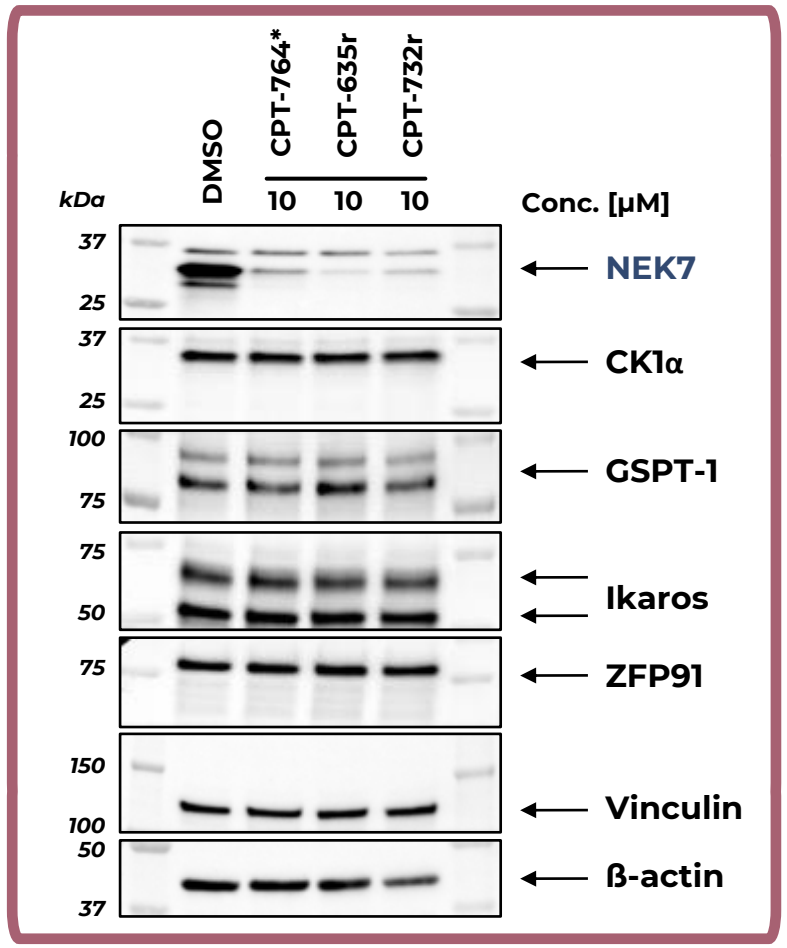
CPT-635r and CPT-732r degrade NEK7 protein dose-dependently in human PBMC-derived macrophages with LPS+Nigericin activated inflammasome

Human PBMC differentiated into macrophages with M-CSF; treatment with compounds – 24h; inflammasome activation: LPS – 3h, Nigericin – 1h
MCC950 – NLRP3 inhibitor (Roche/ Inflazome); CPT-635r – racemate of CPT-635, CPT-732r – racemate of CPT-732

CT-02 (NEK7)

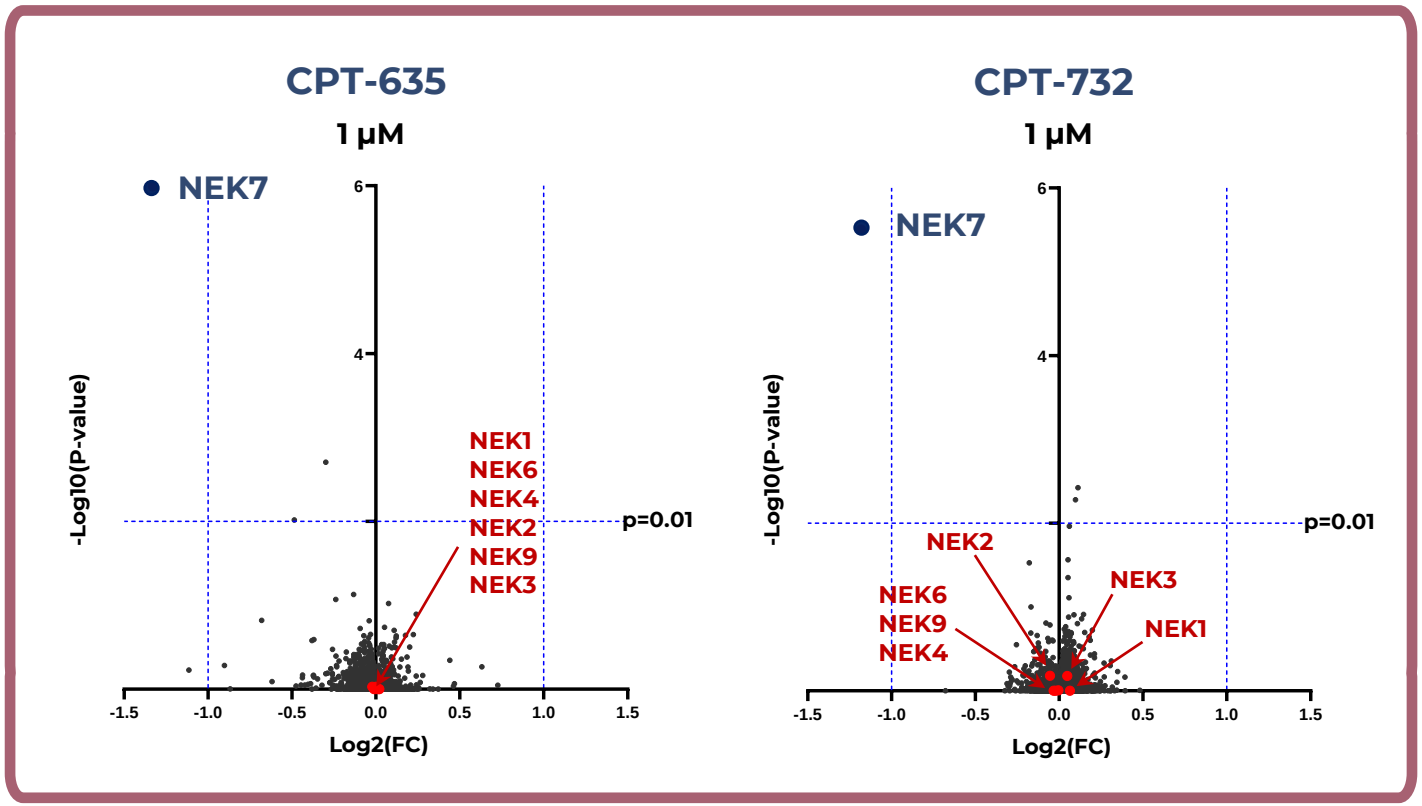
Captor Therapeutics®

High selectivity of NEK7 molecular glue degraders



*Early lead compound

CPT-635r – racemate of CPT-635, CPT-732r – racemate of CPT-732



Confirmed degradation of NEK7 in hPBMCs

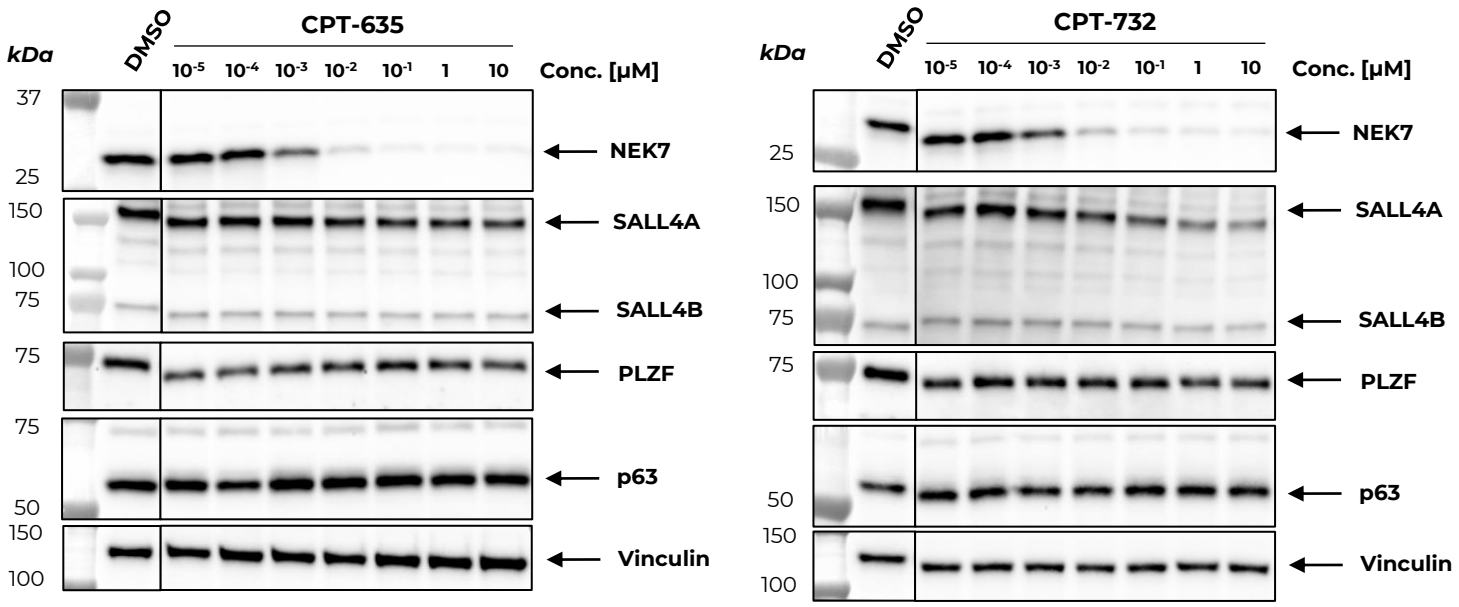
No off-targets, even at high doses

CT-02 (NEK7)

Captor Therapeutics®

High selectivity of diastereoisomers against teratogenic targets

Kelly neuroblastoma cell line



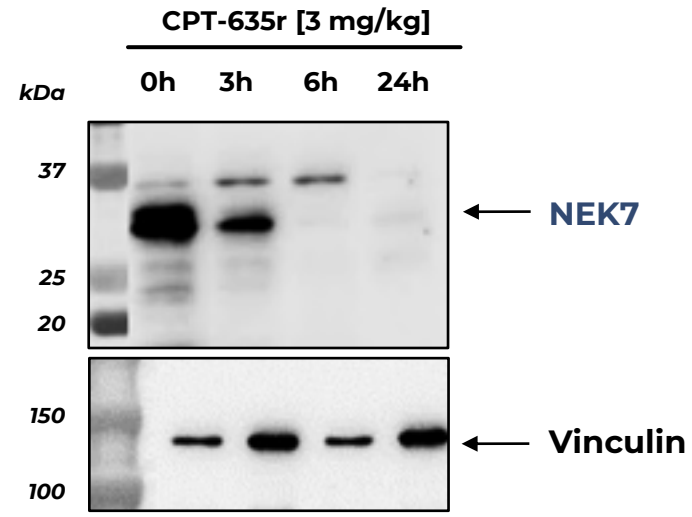
Cells were treated with the compounds for 24 hours.

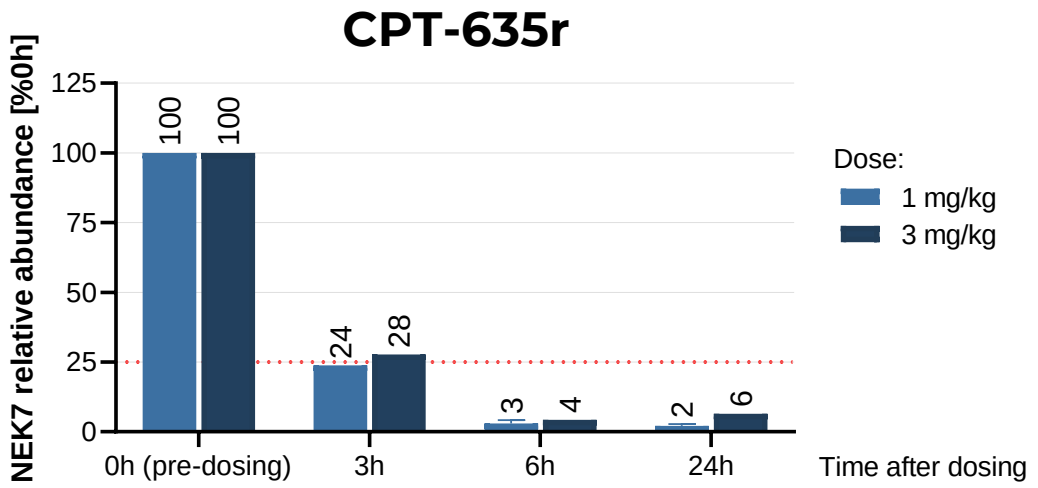
High selectivity against off-targets suspected of teratogenicity: SALL4, PLZF and p63

Target	CPT-635		CPT-732	
	DC_{50}	D_{max}	DC_{50}	D_{max}
NEK7	0.809 nM	99.2%	2.77 nM	95.6%
SALL4A	>10 µM	39.2%	>10 µM	48.7%
PLZF	>10 µM	27.3%	>10 µM	30.1%
p63	>10 µM	29.4%	>10 µM	0%

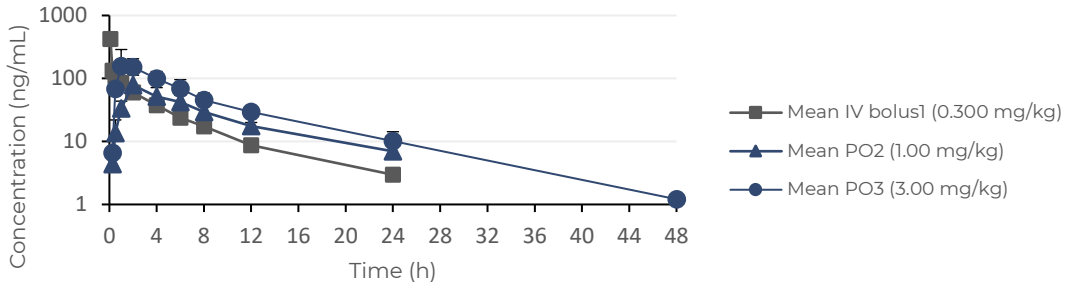
Captor Therapeutics®

CPT-635r efficiently covers & degrades NEK7 in NHPs after a single dose





Mean Plasma Concentration of CPT-635r after IV bolus & PO dosing

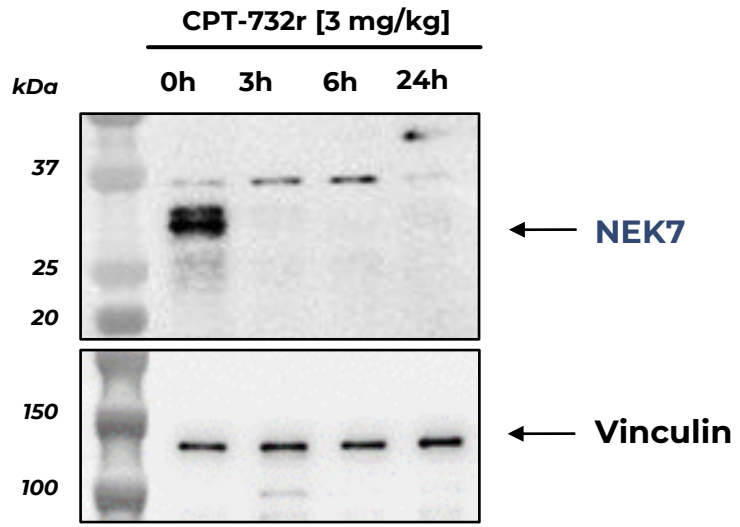


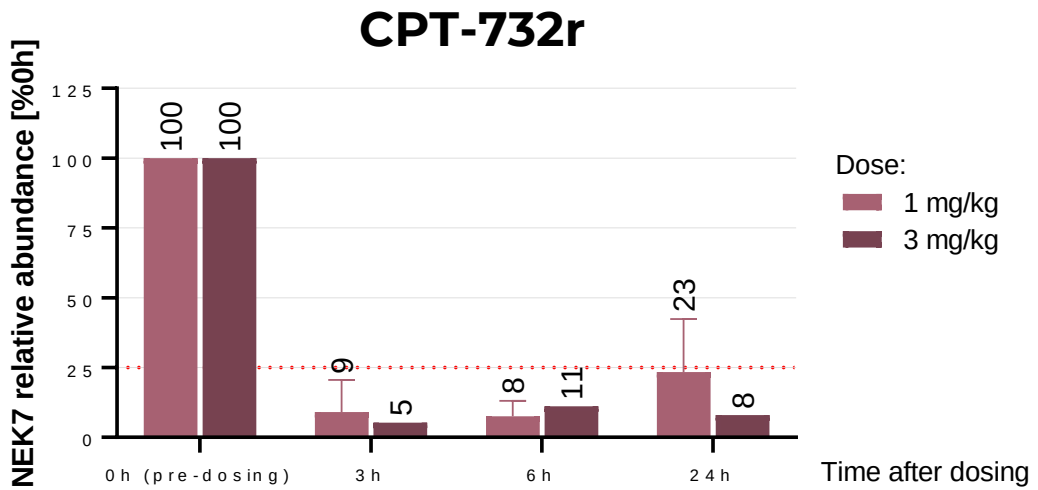
NEK7 degradation observed in monkey PBMCs isolated at 3, 6, and 24 h after PO administration of CPT-635r [1 & 3 mg/kg]

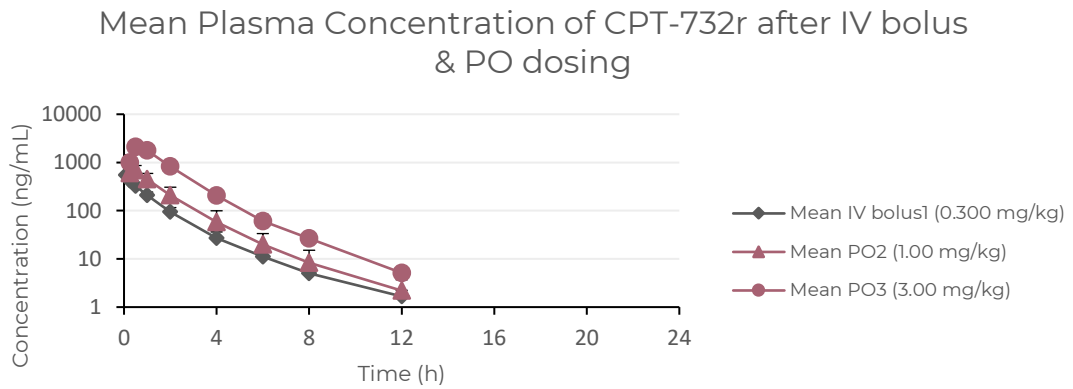
CT-02 (NEK7)

Captor Therapeutics®

CPT-732r efficiently covers & degrades NEK7 in NHPs after a single dose





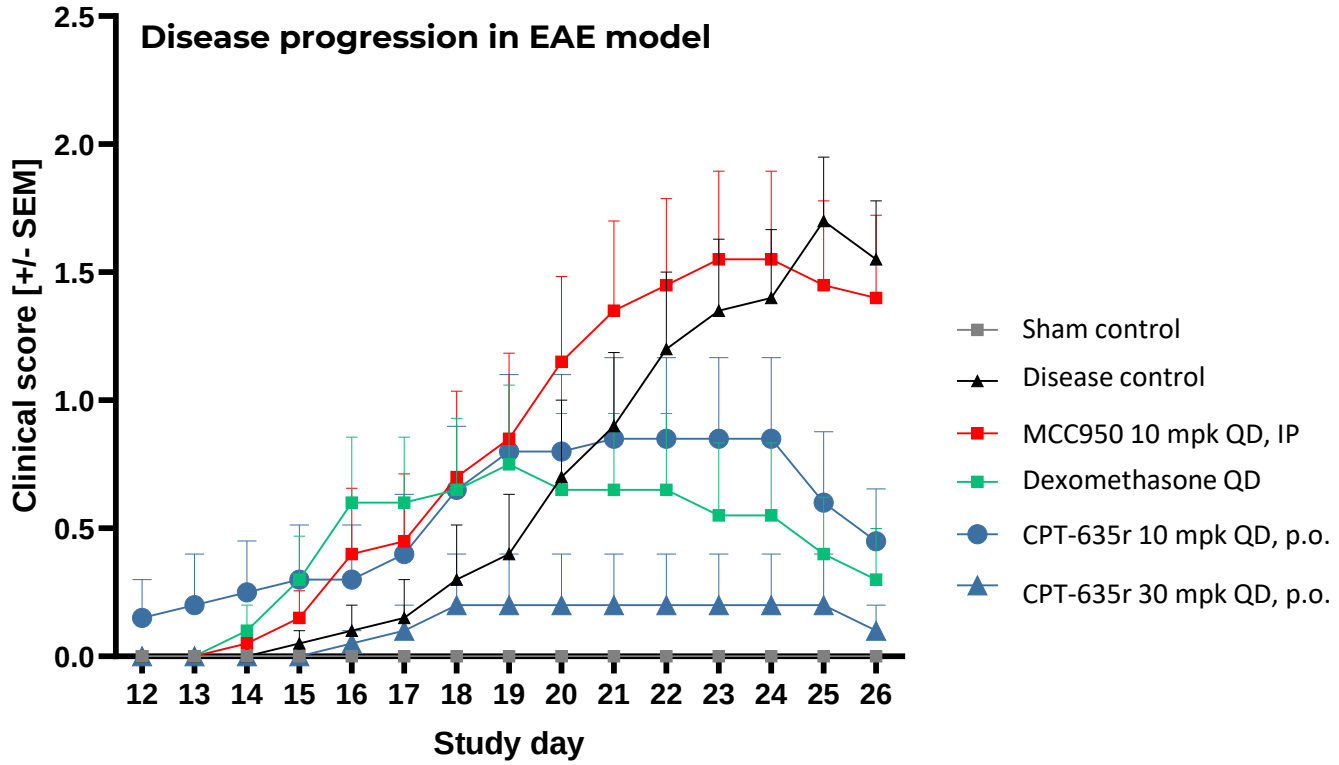


NEK7 degradation observed in monkey PBMCs isolated at 3, 6, and 24 h after PO administration of CPT-732r [1 & 3 mg/kg]

CT-02 (NEK7)

Captor Therapeutics®

High efficacy of CPT-635r with oral dosing in EAE mouse model *in vivo*



Clinical Score	Clinical Sign
0	Normal mouse; no overt signs of disease
0.5	Tail weakness/partial tail weakness (50% of length)
1	Loss of tail tonicity (complete tail paralysis)/ Limp tail
1.5	Limp tail and weakness in one hind limb
2	Partial hind limb paralysis/ Limp tail and weakness in both hind limbs
2.5	Both hind limbs have some movement, but both are dragging at the feet

Dosing: QD (once a day)
Route of administration:
CPT-513, dexamethasone - PO
MCC950 - IP

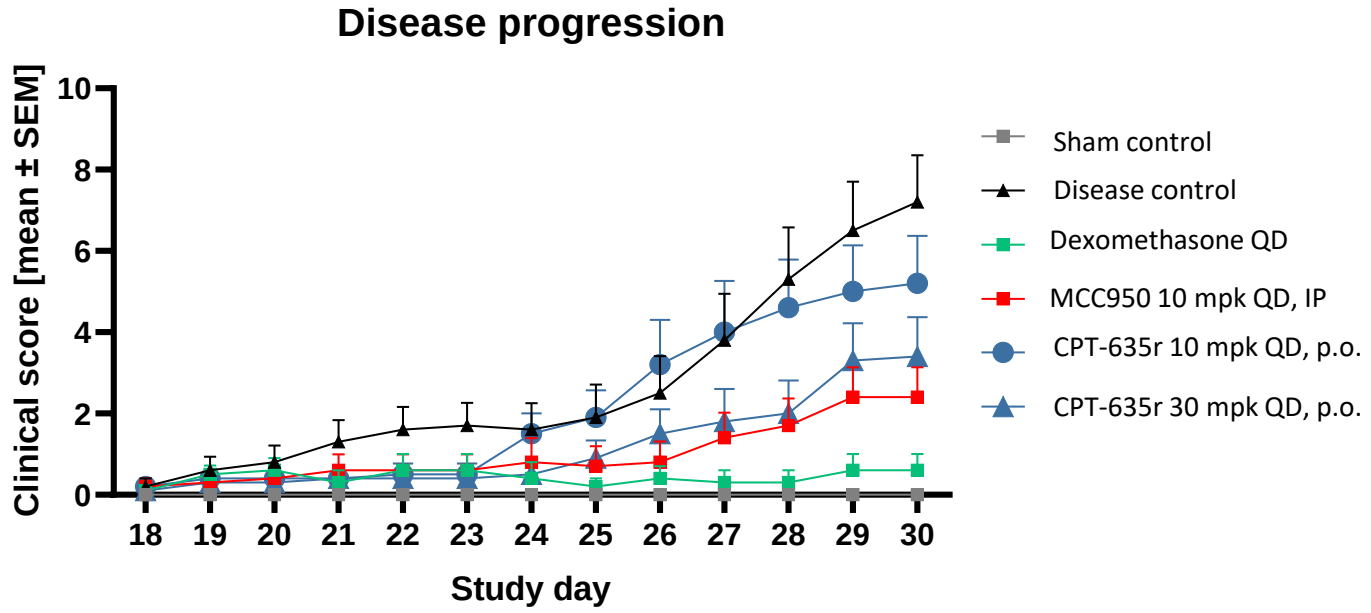
C57BL/6 female mice (10 mice per group)
Clinical score/ disease index monitored based on a predefined scale including motor skills and tail / limb weakness

Treatment for 16 days did not induce any side effects
Body weight in the groups treated with NEK7 degraders was higher than in the group treated with Dexamethasone

Note: CPT-635r is approximately 40% less potent (DC50) in murine systems compared to human / primate

MOG_{35-55} Induced Experimental Autoimmune Encephalomyelitis (EAE) In Mice

Therapeutic potential of NEK7 degraders in Collagen-Induced Arthritis model



Clinical Score	Clinical Sign
0	No redness or swelling
1	Slight swelling in ankle and or redness in one toe
2	Progressive swelling from ankle to midfoot and or involvement of more than two toes
3	Swelling and inflammation in entire foot
4	Swelling and inflammation in entire foot including toes

Dosing: QD (once a day)
Route of administration:
CPT-513, dexamethasone - PO (oral)
MCC950 - IP (intraperitoneally)

Male DBA1/J Mice (10 mice per group)

Clinical score/ disease index was assessed by trained, blinded personnel for swelling of digits/paws and erythema

Treatment over 32 days did not induce any side effects

Treatment with CPT-635r at a dose of 30 mg/kg reduced the clinical score by approximately 50% compared to the control group, to a degree comparable to MCC950. Dose-dependent therapeutic effect is observed (30 mpk vs.10 mpk)

T/B-cell driven; Collagen-Induced Arthritis

CT-02 (NEK7)

Captor Therapeutics®

Differentiated safety profile of NEK7 degraders vs. NLRP3 inhibitors

	CPT-635	CPT-732	NLRP3 inhibitors
Structural features	Classical scaffold	Classical scaffold	Most inhibitors based on sulfonamides; Anhydrases as off-targets[5]
Inhibition of IL-1ß	Max. 80-90%	Max. 80-90%	100%

	NEK7	NLRP3
Alternative functions (unrelated to inflammasome)	Suspected role in mitotic spindle formation, but not seen with CTX degraders	• Sterile necroinflammation, fibrosis, tissue repair[1] • Apoptosis regulation in tubular cells in kidneys (mice showed renal problems upon MCC950 administration)[2] • Innate immune homeostasis in the airway[3] • Regulation of IL-33 production[4]

1. https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2023.1214289/full
2. https://portlandpress.com/clinsci/article/136/2/167/230637/Adverse-renal-effects-of-NLRP3-inflammasome
3. https://www.mucosalimmunology.org/article/S1933-0219(22)00433-0/fulltext
4. https://www.nature.com/articles/s41419-021-04159-9
5. https://pubs.acs.org/doi/10.1021/acschembio.1c00218

Captor Therapeutics®

CT-02: Excellent degraders from two different strategies

Two series of potent NEK7 degraders:
autoimmune diseases (CPT-635) and **neurodegenerative disorders** (CPT-732, brain-penetrant)

Activity confirmed *in vitro i*n mouse, monkey and human cells and *in vivo* in mice and monkeys

Specificity-driven safety demonstrated in *in vitro* analysis, *in vivo* tolerability studies and confirmed in the clean CEREP panel

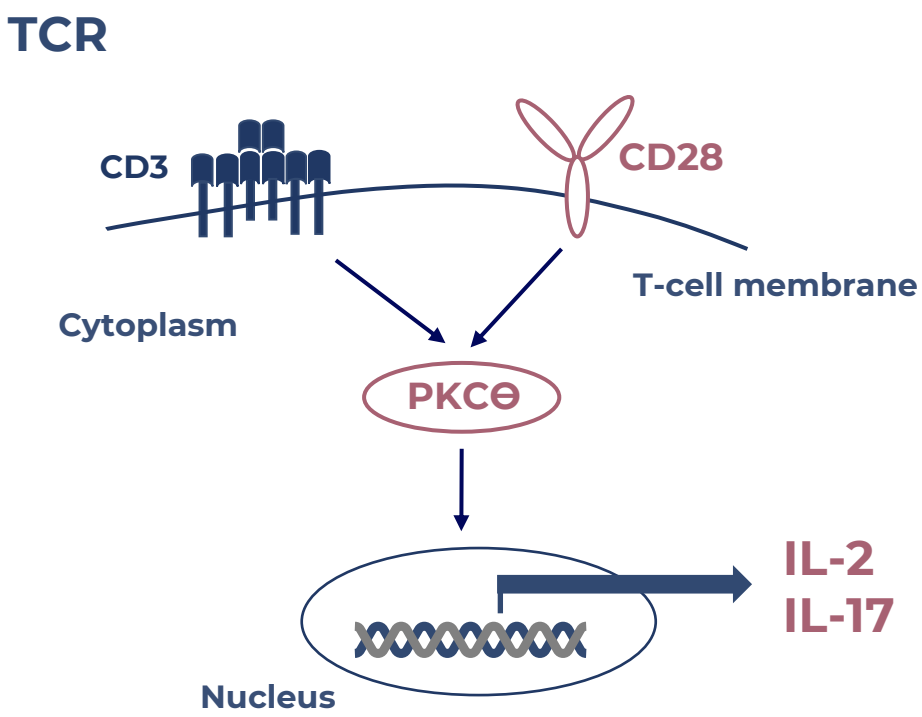
PK/PD results in monkeys illustrate the attractive features of drug candidates

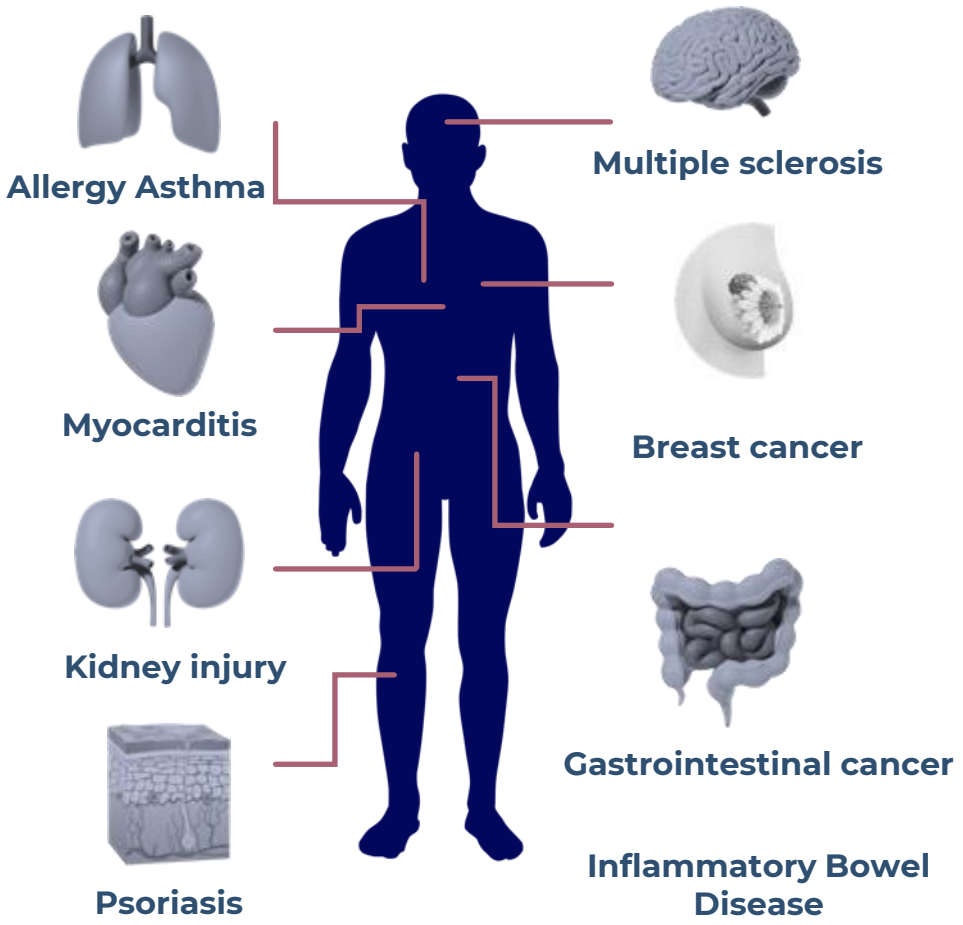
In vivo proof of efficacy in disease models with no signs of toxicity

CT-05: First-in-Class PKCΘ Degraders for Autoimmune Disorders

Captor Therapeutics®

PKCϴ: an undrugged high value target

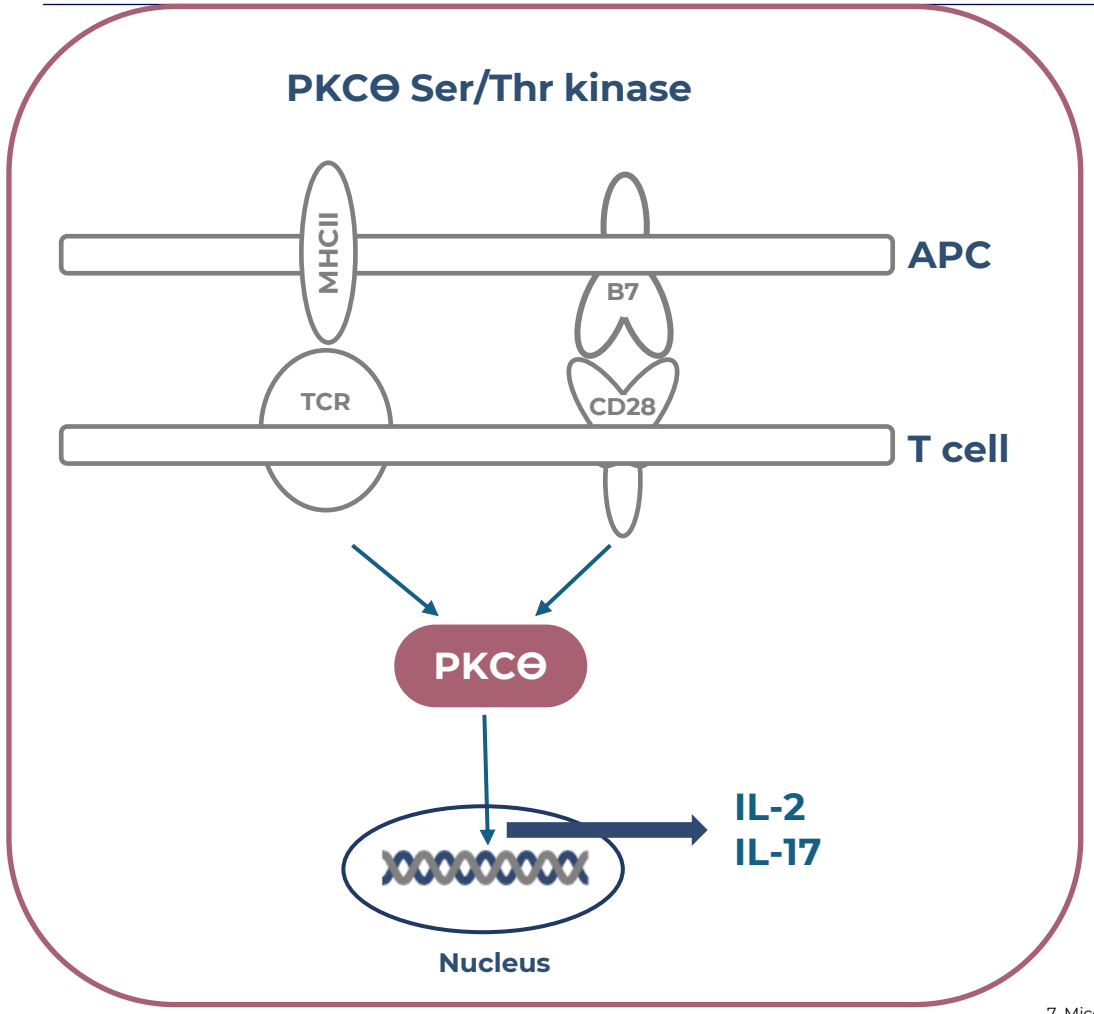




CT-05 (PKCϴ)

Captor Therapeutics®

PKCϴ Biology and target rationale



Target Biology and rationale

PKCϴ has a thoroughly established role in regulatory and effector T cell functions[1,2]

PRCKQ locus was shown associated with several immune-related diseases in multiple GWAS studies (type I diabetes, rheumatoid arthritis, celiac disease)[3-6]

Human and mouse genetics

PKCϴ KO mice show impaired *in vivo* T cell activation, decreased IL-17 production and are protected from T cell-mediated inflammatory diseses (EAE, colitis)[7,8]

Clinical pathway validation

PKCϴ inhibitor – Sotrastaurin (AEB071) – has been shown effective in preventing IL-17 production and to have a potential for therapeutic option in psoriasis[9-11]

Currently, undergoing clinical evaluation is a novel inhibitor from Exscientia / BMS

1. PKC-theta in regulatory and effector T cell functions, Brezar V., 2015, Front. Immunol. 6
2. Intervention of PKC-θ as an immunosuppressive regimen, Sun Z., 2012, Front Immunol. 3: 225
3. Meta-analysis of genome-wide association study data identifies additional type 1 diabetes risk loci, Cooper J.D. , 2008, Nat. Genet. 40, 1399–1401
4. Common variants at CD40 and other loci confer risk of rheumatoid arthritis, Raychaudhuri S. , 2008, Nat. Genet. 40, 1216–1223
5. Genome-wide association study meta-analysis identifie seven new rheumatoid arthritis risk loci, Stahl E.A, 2010, Nat. Genet. 42, 508–514
6. Meta-analysis of genome-wide association studies in celiac disease and rheuma toid arthritis identifies fourteen non-HLA shared loci., Zhernakova A. , 2011, PLoS Genet. 7, e1002004
7. Mice deficient in PKC theta demonstrate impaired in vivo T cell activation and protection from T cell-mediated inflammatory diseases, Anderson K., 2006, Autoimmunity, 6: 469-487
8. Resistance to experimental autoimmune encephalomyelitis and impaired IL-17 production in protein kinase C θ-deficient mice, Tan S-L., 2006, J Immunol. 176(5): 2872-2879
9. The PKC inhibitor AEB071 may be a therapeutic option for psoriasis, Skvara H., 2008, J Clin Invest. 118(9): 3151-9
10. The protein kinase C inhibitor sotrastaurin allows regulatory T cell function, de Weerd A., 2013, Clin Exp. Immunol. 175(2): 296-304
11. Targeting PKC in Human T Cells Using Sotrastaurin (AEB071) Preserves Regulatory T Cells and Prevents IL-17 Production, He X., 2013, J Invest dermatol. 134(4): 975-983

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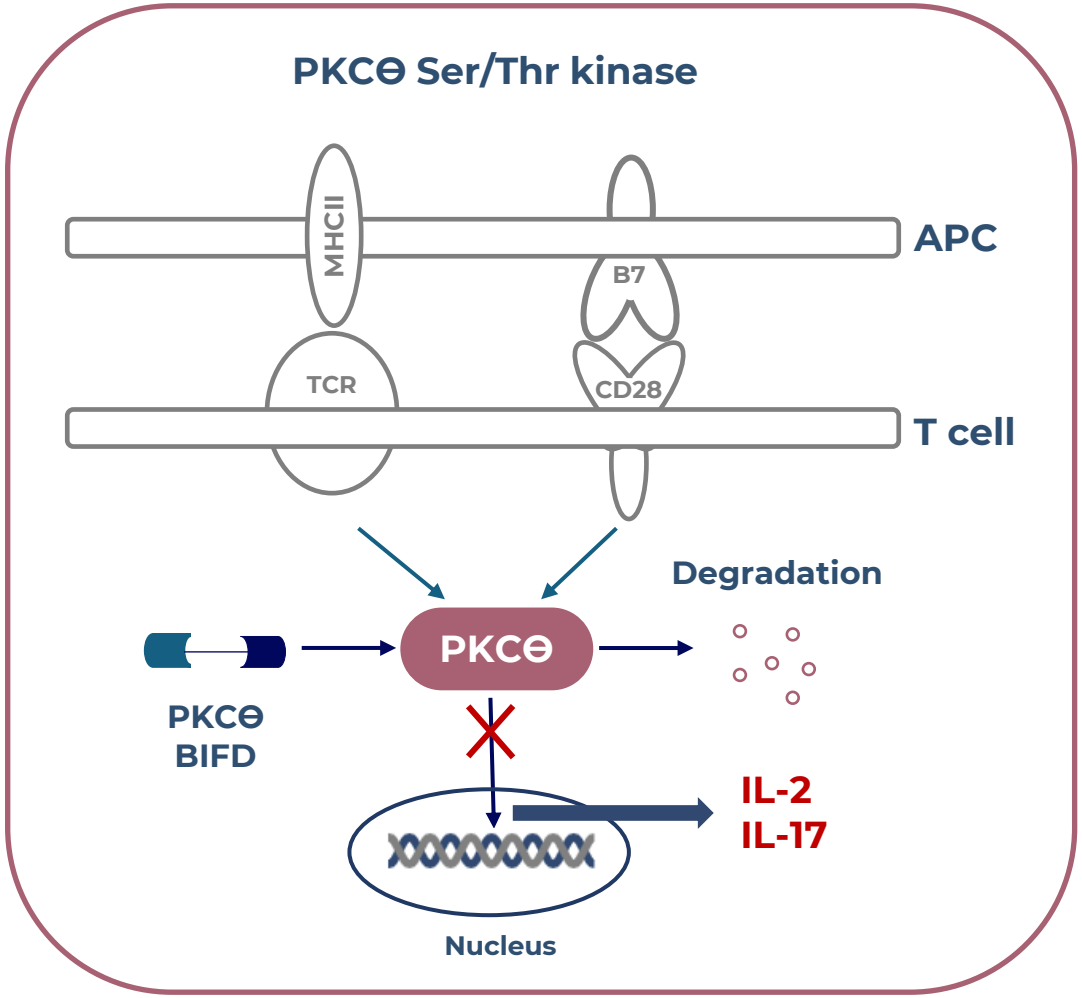
Rationale for targeted degradation of PKCϴ



PKCϴ is a master regulator of T cell differentiation, proliferation and functions.

Drawbacks of the 1st and 2nd generation PKCϴ inhibitors were related to multiple side effects due to unspecificity and insufficient target coverage.

The degrader offers disabling not only kinase but also scaffolding functions of the protein.

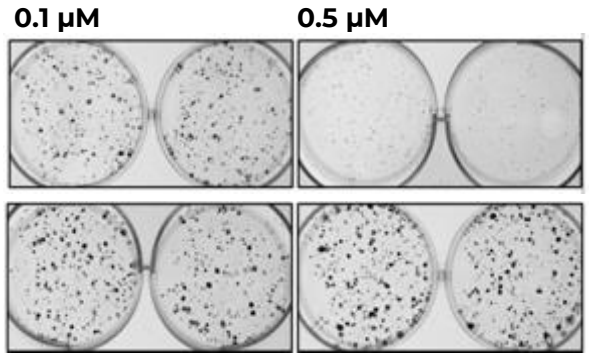
PKCϴ degradation has the potential to abolish T cell survival signal and promote the apoptosis of activated, self-reactive T cells in autoimmune diseases.

CPT-763 is highly selective in a panel of assays

Inhibitor shows significant effects on GIST-T1 non-immune cells
Degrader has no effect in same system

Big Pharma compound
CPT-191
Inadequate Selectivity

CPT-763
High Selectivity



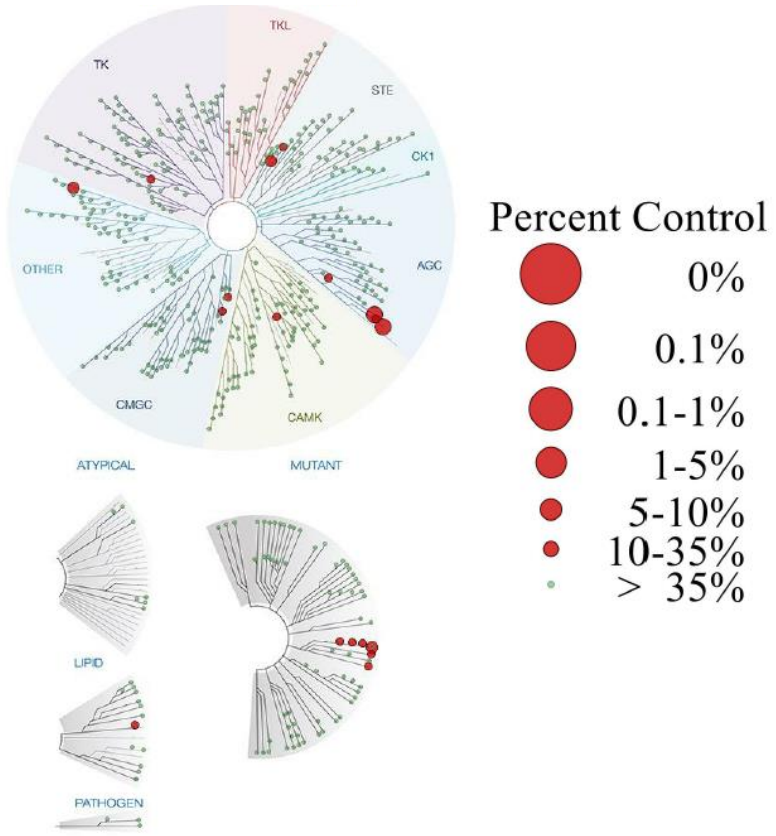
Compound	IC_{50}	I_{max}	DC_{50}
CPT-763	55 nM	82 %	29 nM
CPT-191	98 nM	99 %	N/A

IC_{50} and I_{max} values obtained in ELISA analysis

Excellent selectivity against a large number of kinases

KinomeScan results
TREE*spot*™ Interaction Map
panel of ca. 450 kinases

CPT-763 @ 10000nM



CT-05 (PKCϴ)

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Summary

- Established a screening workflow that allows for discovery of PKCθ degraders superior to existing inhibitors
  - Highly selective for PKCθ with no off-target toxicity
- Early stage of lead optimisation with 2 compounds has demonstrated:
  - *In vitro*: degradation of PKCθ in mouse & human T-cells & inhibition of IL-2 in human T-cells
  - *In vivo*: degradation of PKCθ in mouse splenocytes
- Next steps:
  - Partnering discussions

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Optigrade™ Targeted Protein Degradation Platform

Molecular glues

Bifunctional Degraders

Novel E3 ligases

LiLis™ program: developing novel E3 ligases beyond CRBN

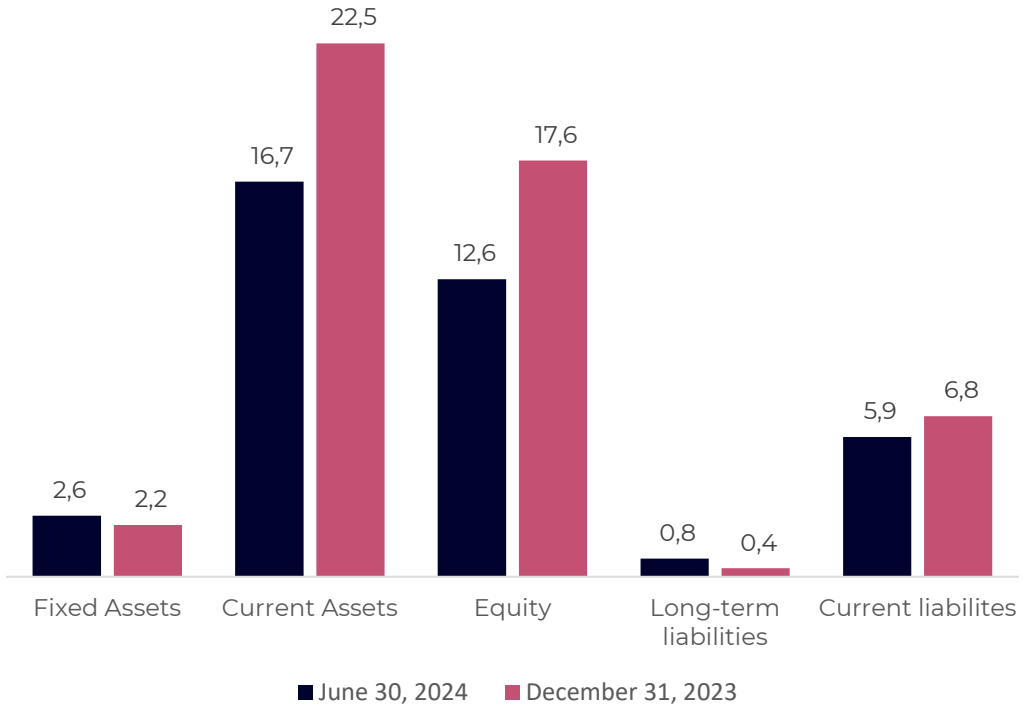
- Expanding the range of targets for effective degradation
- CRBN down regulation-driven resistance mechanisms in cancer
- Crowded IP space for CRBN binders
- Opportunity for cell type or cell compartment specificity

In-house developed E3 ligase production platform and is generating leads for novel E3s

Finance Highlights

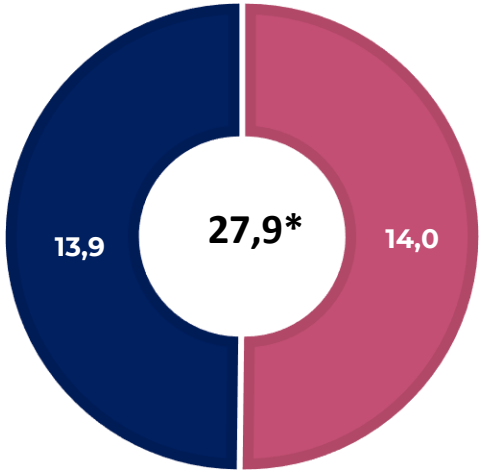
Balance sheet and cash position

Consolidated statement of financial position (US$, M)



Exchange rate USD/PLN as of June 28, 2024 – 4,0320

Cash position



Available funding secured (US$ M; as of June 30, 2024):

Total : US$ M 27,9*

- US$ M 14,0 cash
- US$ M 13,9 available grants (NCBR; ABM)

*** Amount includes grant awarded for phasing in CT-03 and CT-01 project.**

R&D costs in H1 2024**:**

Total : US$ M 6,2

Cash outflow in H1 2024**:**

Total : US$ 4,3 M

Finance

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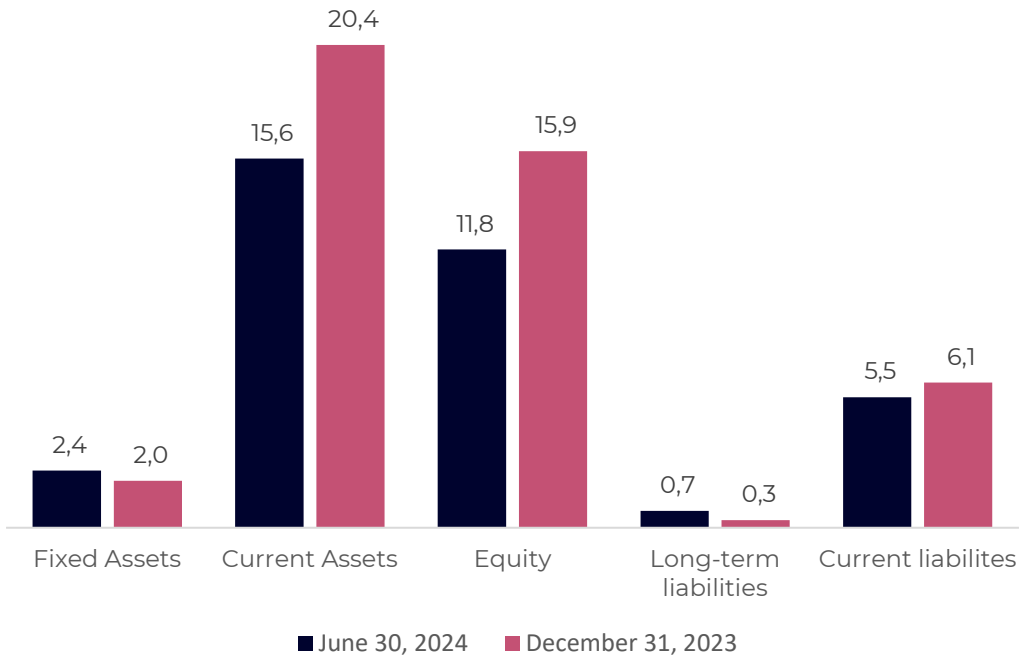
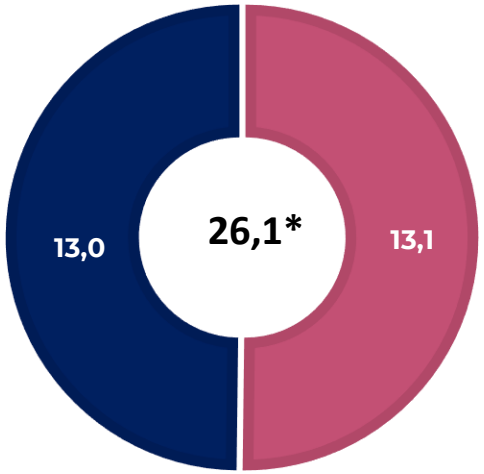
Balance sheet and cash position

Consolidated statement of financial position (EUR, M)



Exchange rate USD/PLN as of June 28, 2024 – 4,3130

Cash position



Available funding secured (EUR M; as of June 30, 2024):

Total : 26,1 M*

- EUR M 13,1 cash
- EUR M 13,0 available grants (NCBR; ABM)

*** Amount includes grant awarded for phasing in CT-03 and CT-01 project.**

R&D costs in H1 2024**:**

Total : EUR 5,8 M

Net Operational Cash Outflow in H1 2024

Total : EUR 4,1 M

Current (September 2024) guidance indicates cash runway until Q3 2025

Finance

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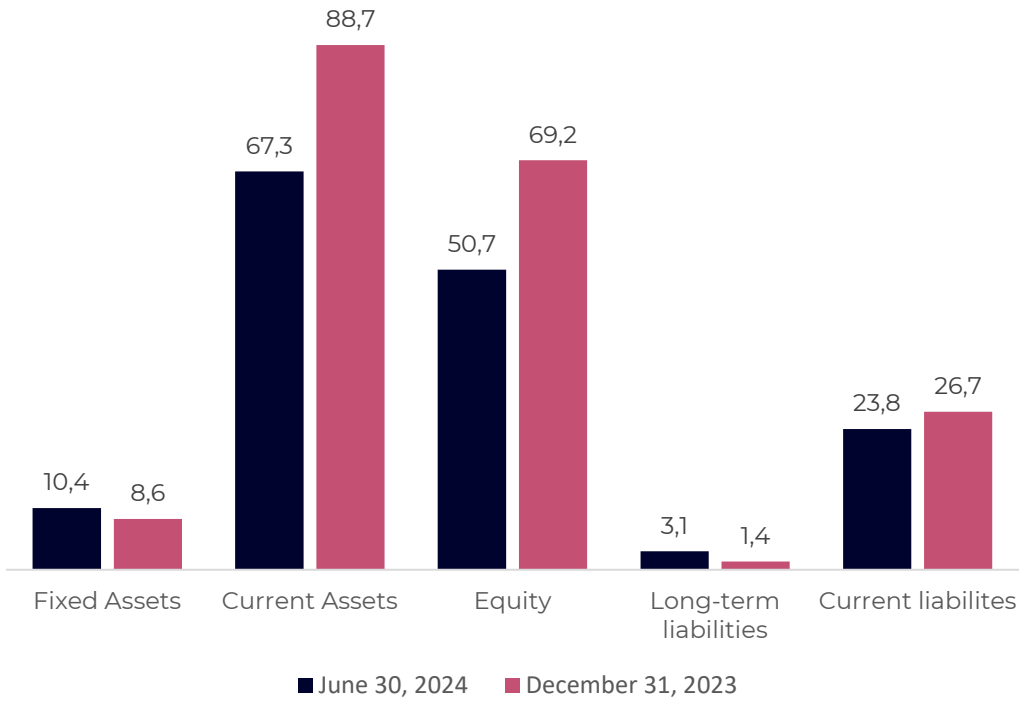
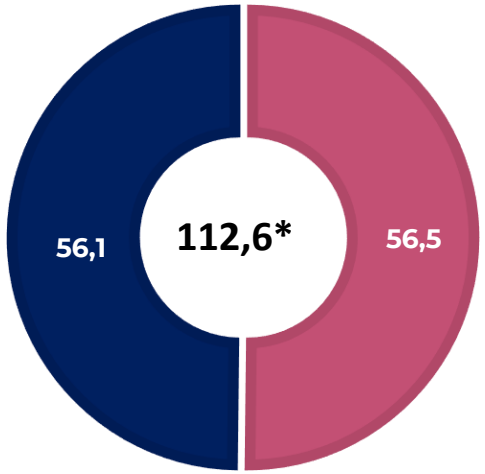
Balance sheet and cash position

Consolidated statement of financial position (PLN, M)



Cash position



Available funding secured (PLN M; as of June 30, 2024):

Total : **PLN 112,6***

- PLN M 56,5 cash
- PLN M 56,1 available grants (NCBR; ABM)

*** Amount includes grant awarded for phasing in CT-03 and CT-01 project.**

R&D costs in H1 2024**:**

Total : PLN 25,2 M

Net Operational Cash Outflow in H1 2024**:**

Total : PLN 17,5 M
(H1 2023 -PLN 31,5 M)

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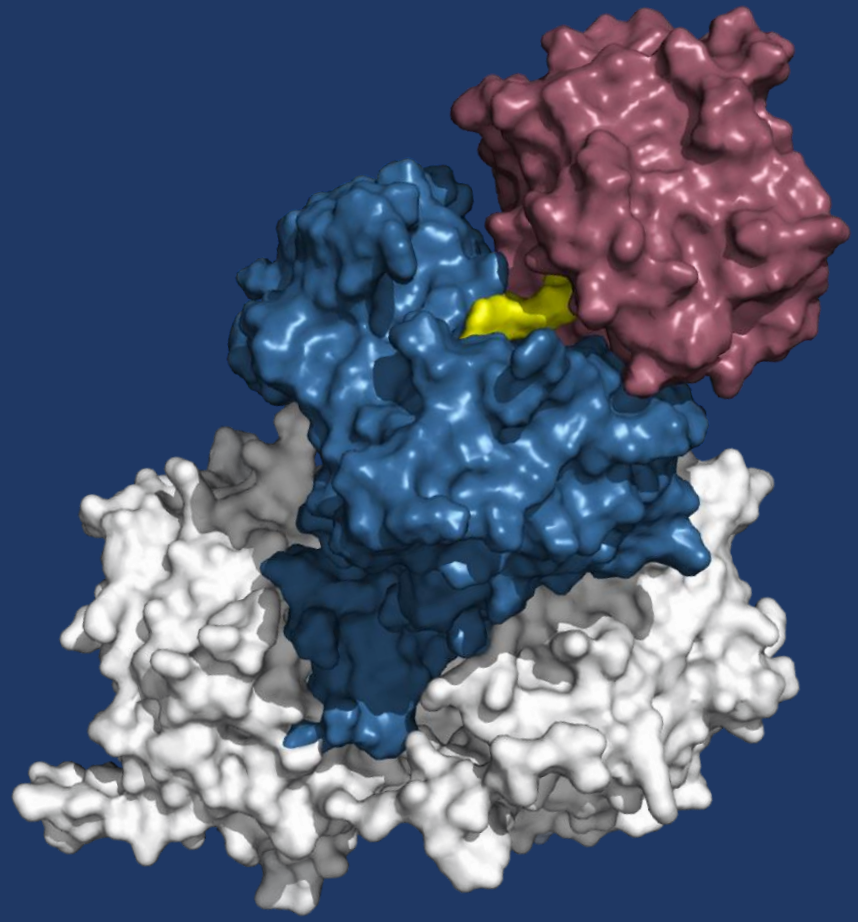

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Projects co-financed by the European Regional Development Fund:

Discovery and development of a new clinical drug candidate for the eradication of cancer stem cell in the treatment of hepatocellular carcinoma, through degradation of oncofetal transcription factor" (FENG.01.01.01-00-0740/19-00)

Discovery and development of a new clinical drug candidate for the eradication of cancer stem cell in the treatment of hepatocellular carcinoma, through degradation of oncofetal transcription factor - Stage II (POIR.01.01.IP.01-1001/23)

Inducing apoptosis with small molecules as therapeutic intervention in multiple severe malignancies (POIR.01.01.01-00-0956/17-01)

Inducing apoptosis with small molecules as therapeutic intervention in multiple severe malignancies – Stage II (FENG.01.01-IP.01-1002/23)

Application of targeted protein degradation technology in the treatment of psoriasis and rheumatoid arthritis (POIR.01.02.00-00-0079/18-00)

Development of an integrated technology platform in the field of targeted protein degradation and its implementation to the pharmaceutical market (POIR.01.01.01-00-0931/19-00)

Discovery and development of non-toxic ligase ligands and their application in the treatment of autoimmunological diseases (POIR.01.01.01-00-0741/19-00)

Project co-financed by the state budget from the Medical Research Agency:

Design and clinical development of a first-in-class small-molecule drug candidate for the treatment of colorectal cancer based on the stimulation of immune cells to increase anti-cancer activity through induced protein degradation (2022/ABM/06/00001 - 00)