Captor Therapeutics®

Corporate Overview
Q3 2023

September 2023

All images by Piotr Piatek

Legal notice

This document and the information contained herein (unless otherwise indicated) have been prepared by Captor Therapeutics S.A. (the “Issuer”) solely for informational purposes. For this notice, the presentation that follows shall mean and include the slides that follow, the oral presentation of the slides by the Issuer or any person on behalf of the Issuer, any question-and-answer session that follows the oral presentation, hard copies of this document, and any materials distributed at, or in connection with the presentation (collectively, the “Presentation”). By attending the meeting at which the Presentation is made, or by reading the Presentation, you will be deemed to have (i) agreed to all of the following restrictions and made the following undertakings and (ii) acknowledged that you understand the legal and regulatory sanctions attached to the misuse, disclosure or improper circulation of the Presentation.

The information contained in this Presentation may not be reproduced or redistributed in any way, in whole or in part, to any other person without the prior written consent of the Issuer. This Presentation does not purport to contain all the information that may be required by the recipient to assess the Issuer or its securities. The Issuer prepared this Presentation based on the information which it has and from sources believed to be reliable. To the extent available, the industry, market, and competitive position data contained in this Presentation come from official or third-party sources. There is no guarantee of the accuracy or completeness of such data.

This Presentation contains neither a complete nor a comprehensive financial or commercial analysis of the Issuer, nor does it present its position or prospects in a complete or comprehensive manner. The Issuer has prepared the Presentation with due care, however certain inconsistencies or omissions might have appeared in it. Therefore, it is recommended that any person who intends to undertake any investment decision regarding any security issued by the Issuer shall only rely on information released as an official communication (i.e., current/periodic reports) in accordance with the legal and regulatory provisions.

This Presentation may contain certain forward-looking statements, forecasts, estimates, projections, and opinions ("Forward-looking Statements"). By their nature, Forward-looking Statements involve known and unknown risks, uncertainties, assumptions, and other factors because they relate to events and depend on circumstances that will occur in the future whether or not outside the control of the Issuer. No representation is made or will be made that any Forward-looking Statements will be achieved or will prove to be correct. Actual future results and operations could vary materially from the Forward-looking Statements. Similarly, no representation is given that the assumptions disclosed in this Presentation upon which Forward-looking Statements may be based are reasonable. The recipient acknowledges that circumstances may change, and the contents of this Presentation may become outdated as a result. The assumptions included herein do not constitute profit forecasts or profit estimates.

No warranties or representations can be made as to the comprehensiveness or reliability of the information contained in this Presentation. Neither the Issuer nor its directors, managers, advisers or representatives of such persons shall bear any liability that might arise in connection with any use of this Presentation. Furthermore, no information contained herein constitutes an obligation or representation of the Issuer, its managers or directors, its shareholders, subsidiary undertakings, advisers or representatives of such persons.
Data contained in this Presentation is valid as of the day of its preparation. Consequently, this Presentation will not be subject to changes, updates or modifications to account for events which might occur after this day.

This Presentation does not constitute or form part of, and should not be construed as, an offer to sell or issue, or the solicitation of an offer to purchase, subscribe to, or acquire the Issuer or the Issuer´s securities, or an inducement to enter into investment activity in any jurisdiction in which such offer, solicitation, inducement or sale would be unlawful before registration, exemption from registration or qualification under the securities laws of such jurisdiction. No part of this Presentation, nor the fact of its distribution, should form the basis of, or be relied on in connection with, any contract or commitment or investment decision whatsoever. This presentation is not for publication, release, or distribution in any jurisdiction where to do so would constitute a violation of the relevant laws of such jurisdiction nor should it be taken or transmitted into such jurisdiction.

Captor Therapeutics®

Advanced therapies from targeted protein degradation

Captor Therapeutics: Warsaw Exchange listed biotech (WSE: CTX): ~110 FTEs dedicated to targeted protein degradation (TPD) with facilities in Poland and Switzerland

$2 billion innovation support program in Poland allows a capital sparing R&D model: secured >$40m EU non-dilutive funds to date: new additional grant in June '23 of ~$12.8m

In financial year 2022, 65% of overall R&D costs were covered by non-dilutive funding

Fully-owned, differentiated, oncology and inflammation pipeline:

- Tissue-activated degrader of GSPT1, NEK7 and SALL4 for liver cancer: potential best in class profile, CTA 2023
- Kinetics-optimized degrader of MCL1 for heme & solid tumours, potential best in class profile; CTA/IND H2 2024
- 2 series of selective molecular glue NEK7 degraders - systemic series for chronic inflammation and metabolism indications; and brain penetrant series for neuroinflammation, *in vivo* POC planned 2023
- Potential first-in-class selective degrader of PKCϴ for autoimmune indications in *in-vivo* studies

Discovery platform: Optigrade™

- Empowers both molecular glue and bifunctional degrader discovery
- Industry-leading protein engineering, structural biology and biophysics team >30 internal FTEs
- Novel E3 ligases for TPD (targeted protein degradation demonstrated with the E3 Ligase KLHDC2)
- Strategic partnership with Ono Pharmaceutical to develop degraders of a neurodegeneration target

Captor Therapeutics®

Fully owned pipeline

Programme	Target	Indications	Modality	Discovery	Preclinical*	IND Filing	Phase IA / IB	Phase II
CT-01	GSPT1, NEK7, SALL4	Hepatocellular carcinoma, Lung cancer, NET tumours	MG					
CT-02	NEK7	Autoimmunity, CNS, Metabolism, Oncology	MG					
CT-03	MCL1	Liquid & solid tumours	BIFD					
CT-05	PKCϴ	Autoimmunity, Oncology, Transplantation, Metabolism	BIFD					
CT-09	IDP** target	CRC, Hemato-oncology, immuno-oncology	MG BIFD					
	New E3 ligase degraders	Autoimmunity, Cancer	MG BIFD					

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

Assumed stage at the end of 2025

** Intrinsically disordered protein

Captor Therapeutics®

An experienced leadership team

Tom Shepherd, Ph.D.
Chief Executive Officer

Michal Walczak, Ph.D.
Chief Scientific Officer

Radoslaw Krawczyk
Chief Financial Officer

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

Andrew Saunders
Chief Medical Officer

Paweł Dobrzański, Ph.D.
Head of Biology

Michał Biśta, Ph.D.
Head of Structure, Fragments and Biophysics

Robert Dyjas
Head of Medical Affairs and Clinical Development

Donald Coppen, Ph.D.
Business Development Director

Anna Pawluk, Ph.D.
Head of Operations

Tomas Drmota, Ph.D.
VP Early Discovery

Marta Tomaszewska
Head of HR

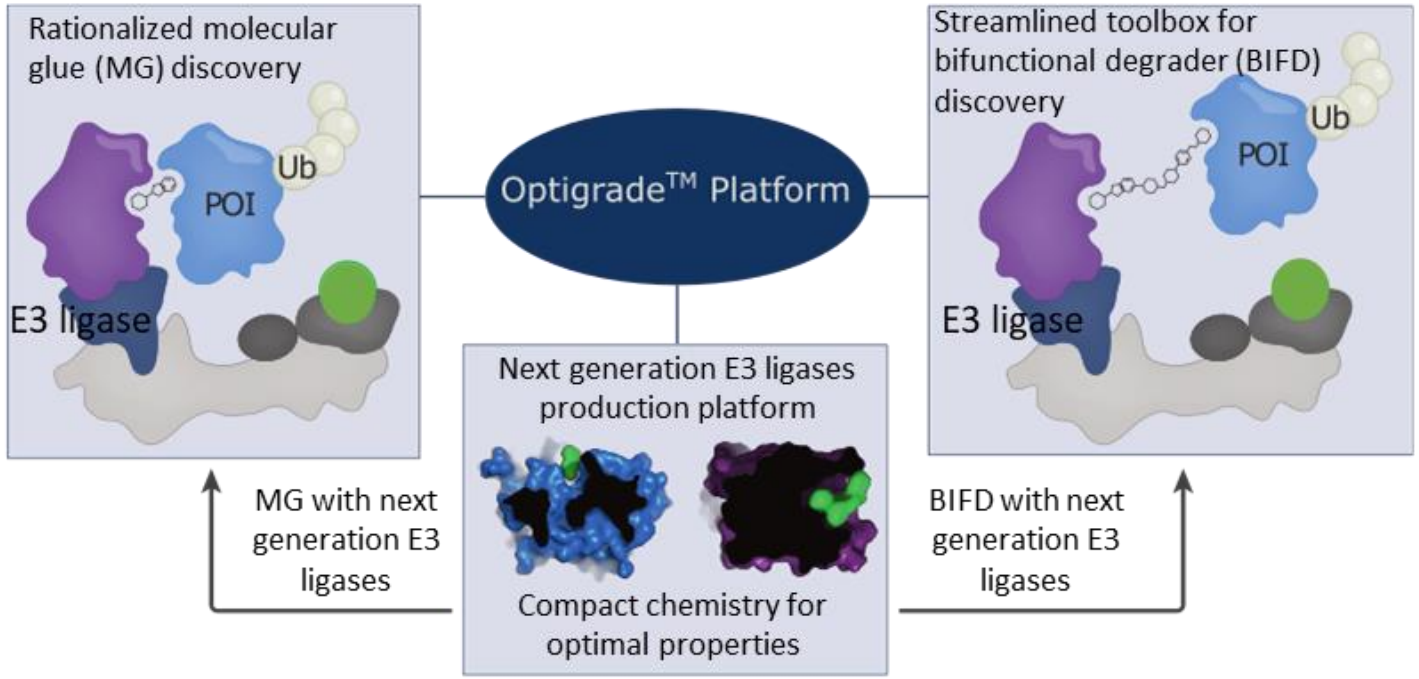
Optigrade™ Targeted Protein Degradation Platform
Molecular glues/ Bifunctional Degraders/ Novel E3 ligases

Targeted Protein Degradation (TPD) – a revolutionary approach

- TPD involves attaching ubiquitin to the target protein, marking it for degradation in the proteasome, the cell's waste disposal system
  - Ubiquitin serves as a molecular tag in this process and its attachment is facilitated by a cascade of enzymes known as ubiquitin ligases
- TPD encompasses two main strategies, molecular glues and bifunctional degraders:
  - **Molecular glues** bind exclusively to ubiquitin ligase, altering its surface and facilitating novel interactions that result in ubiquitination and degradation of previously untargeted substrates
  - **Bifunctional degraders** simultaneously bind to the target protein and ubiquitin ligase, promoting their proximity and leading to ubiquitination and subsequent degradation of the target protein

Captor Therapeutics®

Optigrade™ discovery platform – importance of structure



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

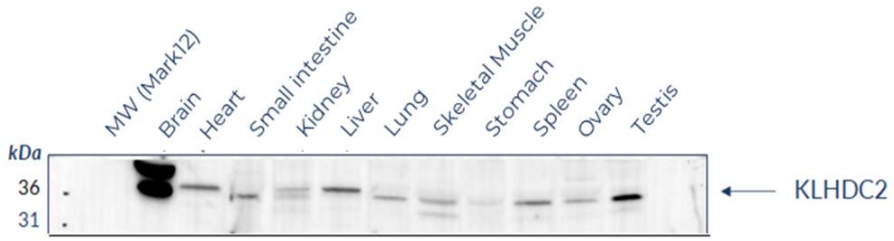
- Industry leading capability in protein engineering and structural biology
- Unique structure-guided lead optimization paradigm gives high potency & selectivity with good pharmaceutical properties
- Proprietary, focused library of molecular glue compounds with improved chemical stability
- “Silent” ligase ligands for enhanced selectivity of bifunctional degraders (no intrinsic degradation capacity)
- Library of ~100 novel E3 Ubiquitin Ligase proteins

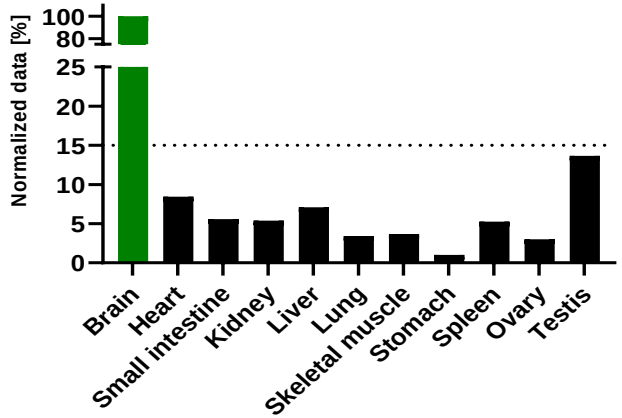
Captor Therapeutics®

Attractive features of KLHDC2 E3 ligase

Cullin 2-type E3 ligase	CRL2 are validated with highly effective VHL-based degraders
engaged in protein quality control via DesCEND pathway	versatility by targeting a wide range of proteins for degradation
localized in nucleus and cytoplasm	allows degradation in both cell compartments
ubiquitously expressed	potential to have an organism-wide impact
non-essential although embryonic lethal. Dickinson et al., Nature 2016	opportunity for reduced side effects due to redundant activity
10 members of KLHDC family	potential for targeting other family members

Human tissue expression



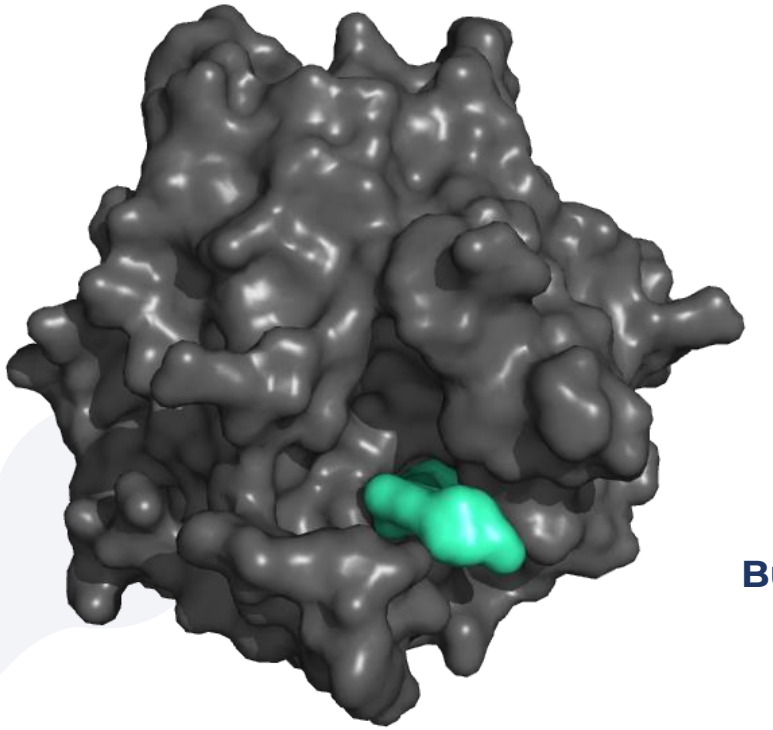


Captor Therapeutics®

Captor ligands for KLHDC2

Hit-to-lead process

- 3 chemotypes identified
- over 30 X-ray structures solved
- low nanomolar affinity



Known exit vectors

- 5 different EVs identified
- potential for modulation of TCF with different proteins
- regulation of selectivity and efficiency of degradation

In cellulo activity

- cell penetrant
- target engagement

Optimized ligand:

LE = 0.37, MW = 430Da, logP= 1.6, TPSA= 101 Å^2

KD = 12nM

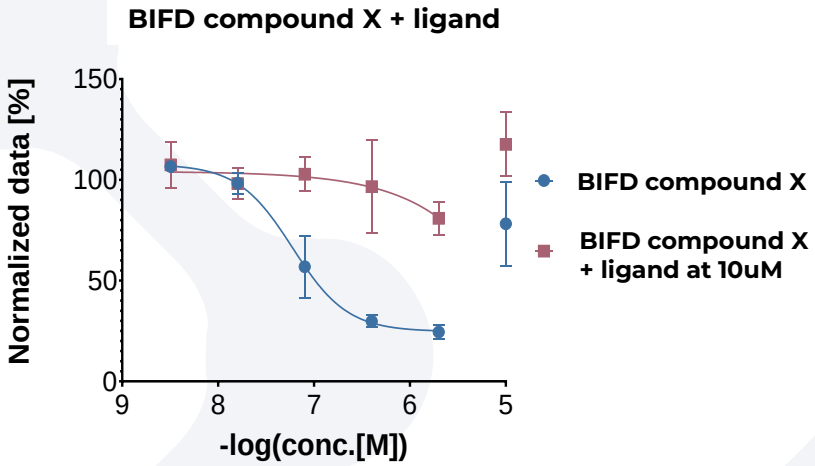
Building block for bifunctional degraders

- advantage over the degron-based PROTACs due to small size and better bioavailability
- **ternary complex and degradation confirmed for first bifunctional degraders**

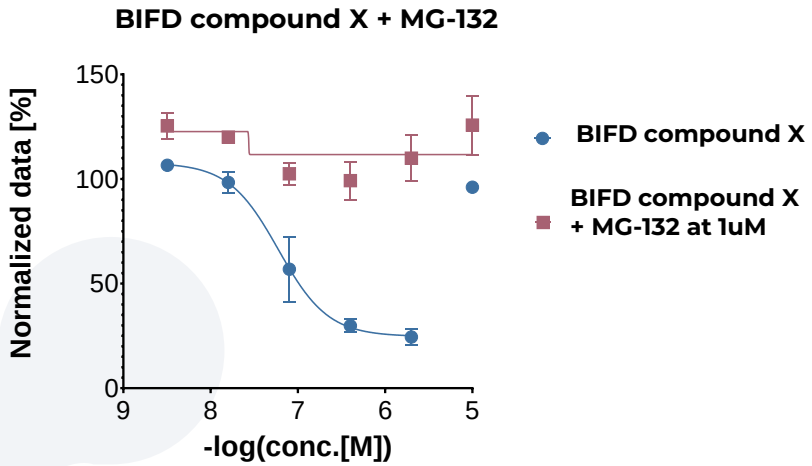
Captor Therapeutics®

Bifunctional compound X degrades BRD4 via KLHDC2

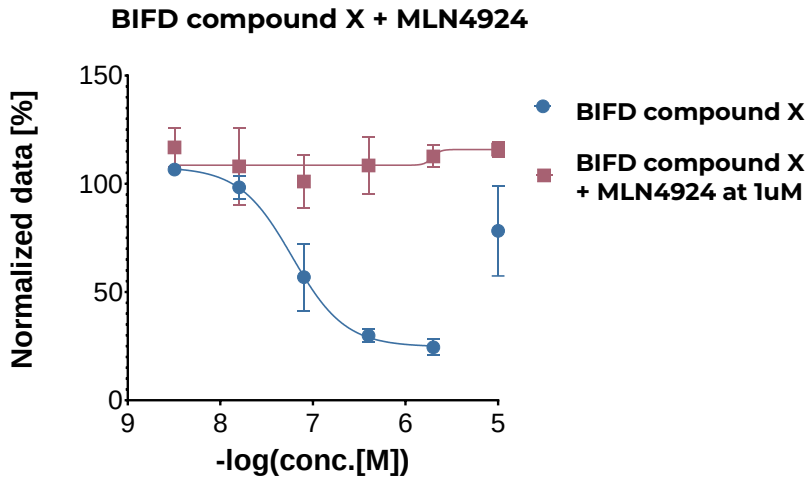
± KLHDC2 competitive ligand



± Proteasome inhibitor



± Neddylation inhibitor



All measurements at 4h

Conclusions:

- **BIFD compound X** degrades BRD4 protein
- Degradation is abrogated when a competing **KLHDC2 ligand** (blocking interaction with the protein) is added
- **MG-132** and **MLN4924** inhibitors completely block degradation – indicating dependence of the degradation process on the Proteasome and Cullins (CUL2)
- Two additional kinase proteins have also been degraded in this model system using KLHDC2

Captor Therapeutics®

Collaborative opportunities using Optigrade™

- Captor is interested in leveraging its TPD platform against new targets of interest to potential partners through collaboration

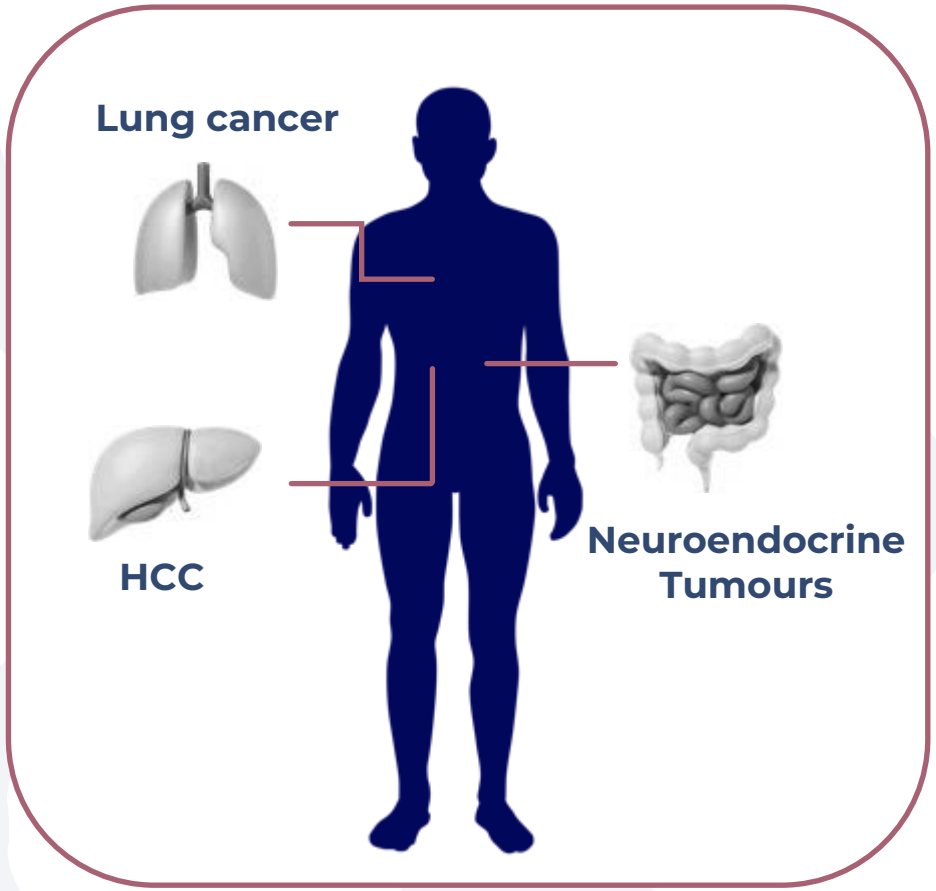
- All three pillars of the Optigrade™ platform can be usefully applied to find high quality degrader drugs against new targets:
  - **Molecular glues:** Captor has a proven track record of finding molecular glues against novel targets (e.g. NEK7) using its unique structure-guided lead optimisation platform and proprietary molecular glue library
  - **Bifunctional degraders:** Captor has proven its capacity to drug new targets with the development of our first-in-class, highly selective degrader of the target MCL-1
  - Captor is at the leading edge of research on **New E3 ubiquitin ligases**: for next generation degraders that avoid some of the disadvantages of the Cereblon E3 ligase

- Captor is one of the few companies who can bring all these modalities to a collaborative research project

Captor Therapeutics®

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

CPT-6281 – first-in-class MG degrader of GSPT1, NEK7 & SALL4



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

SALL4 is expressed in fetal liver, silenced in adults, but often re-expressed in HCC and correlates with poor prognosis

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

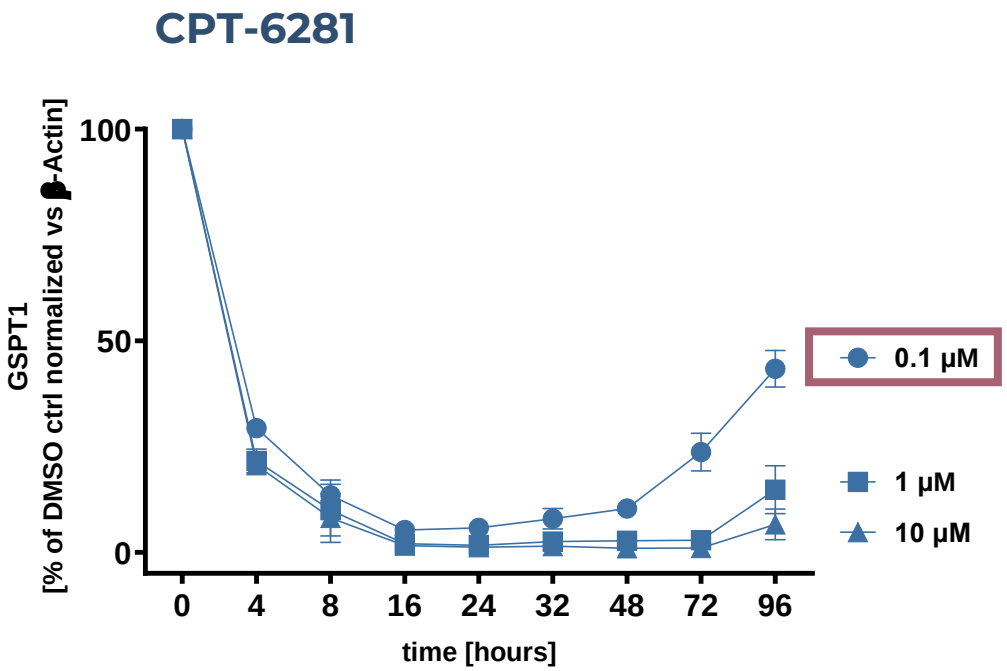
CPT-6281 is a pro-drug activated by an enzyme present at high levels in the liver, lungs and certain gastrointestinal tumours

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

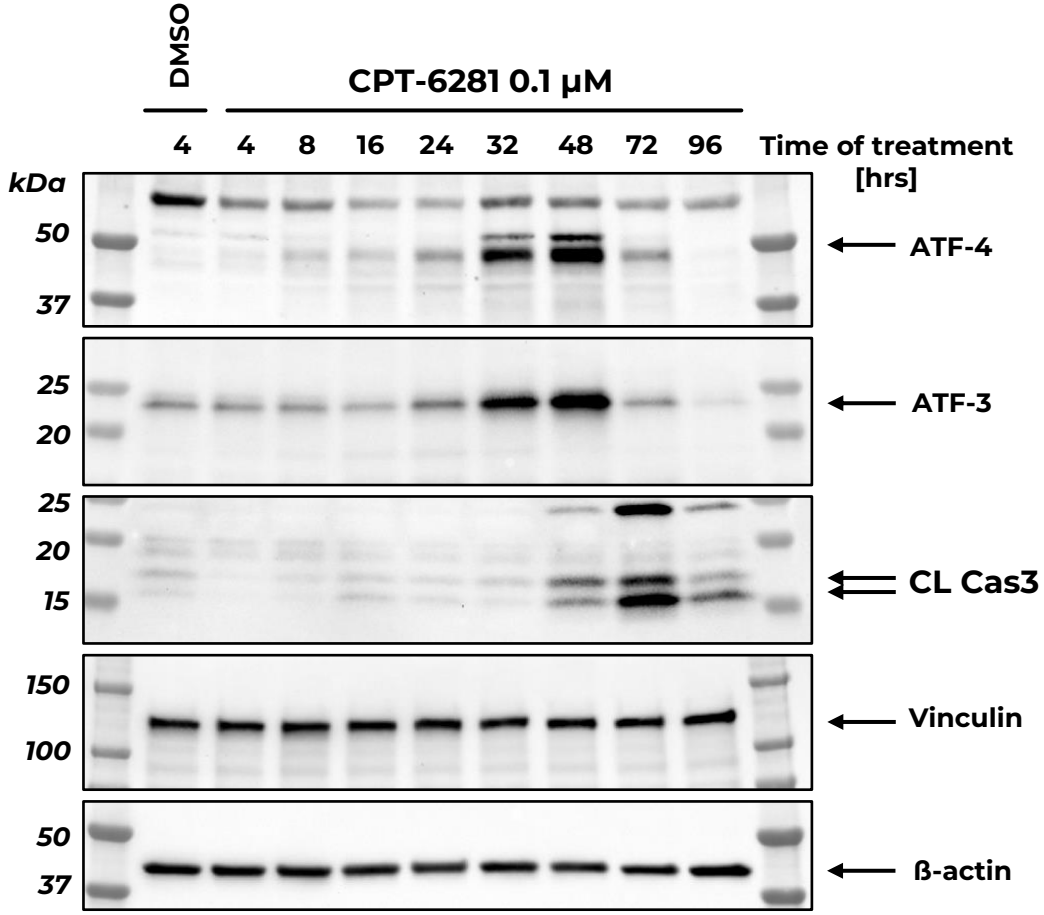
Captor Therapeutics®

CPT-6281 triggers ISR-dependent cell death in Hep3B cells

Densitometry results of WB analysis of GSPT1 degradation



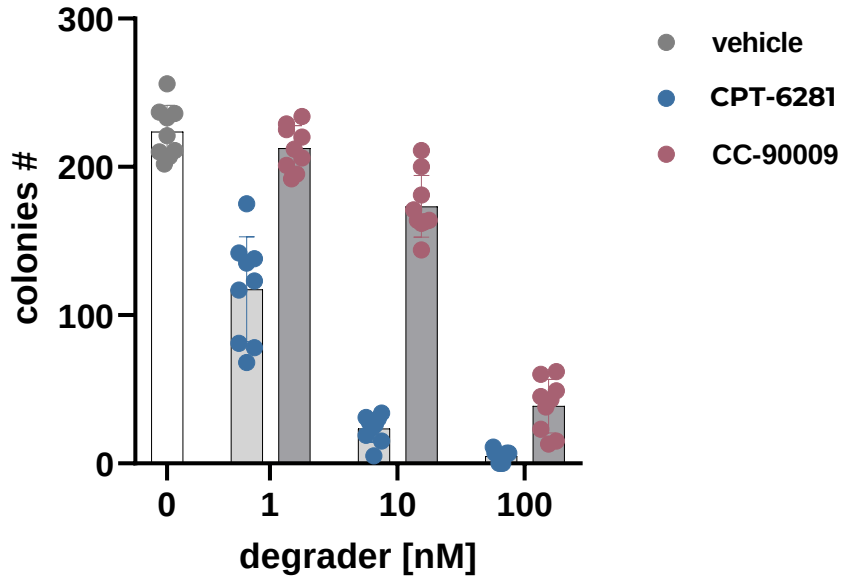
WB analysis of ISR markers during ABS-752 treatment



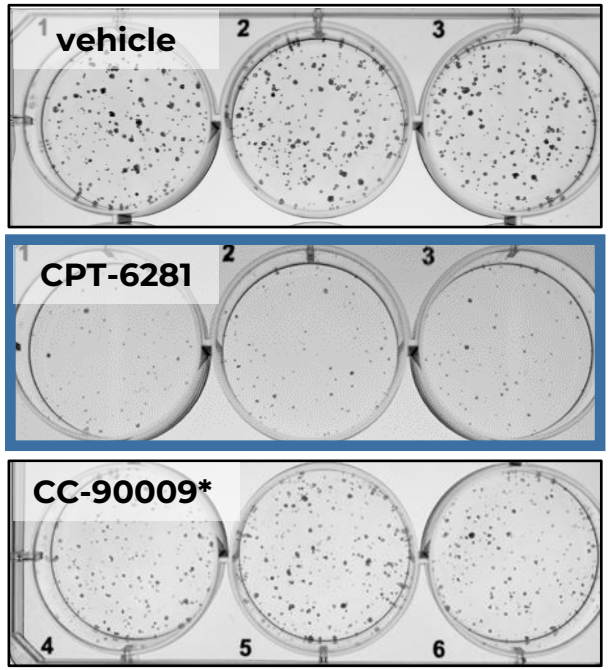
Hep3B cells, 96h treatment with 0.1 , 1 and 10 µM compound

CPT-6281 impaired the ability of single HCC cells to form colonies

Colony count
(colony = ca. 50 cells)



Colony formation at 1 nM compounds

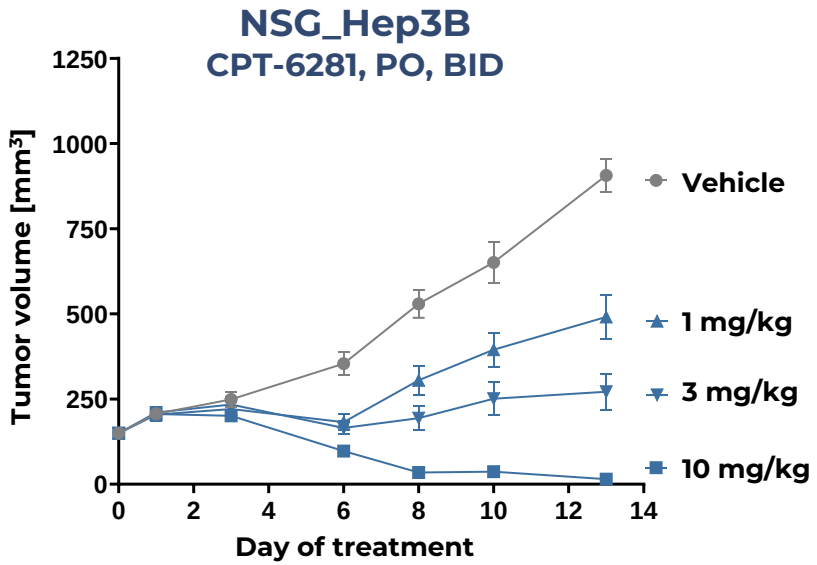


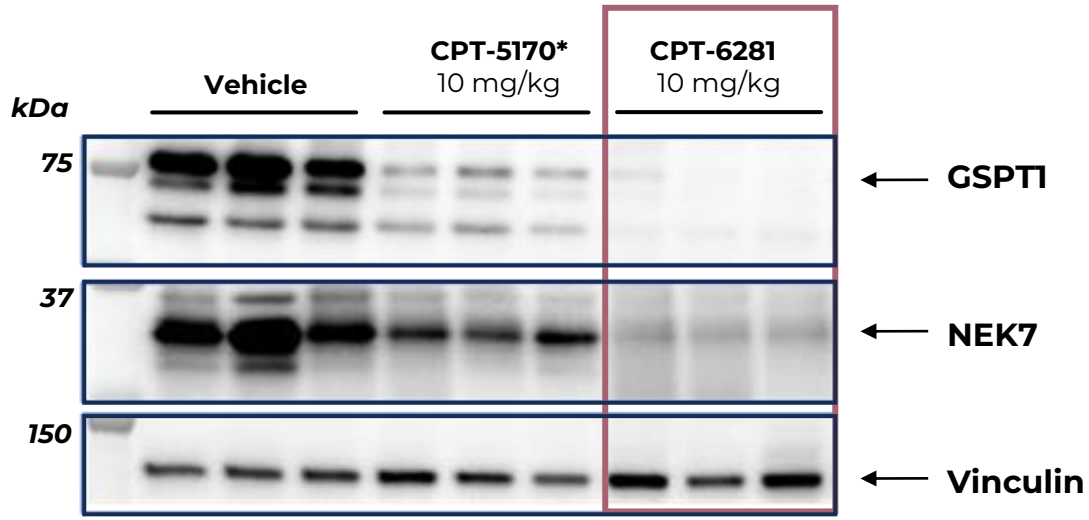
HCC clonogenic assay – 8 days treatment with 1, 10 and 100 nM compounds plate

*CC-90009 = BMS/ Celgene GSPT1 degrader in clinical development for AML

Captor Therapeutics®

Highly potent CPT-6281 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 CT-01

CPT-6281 strongly inhibits liver cancer growth in Hep3B model at all tested doses in keeping with potent degradation of the target

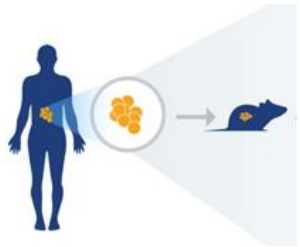
*Earlier iteration from CT-01 programme

Captor Therapeutics®

Convincing tumor growth inhibition in HCC PDX models

CrownBio
CONNECTING SCIENCE TO PATIENTS

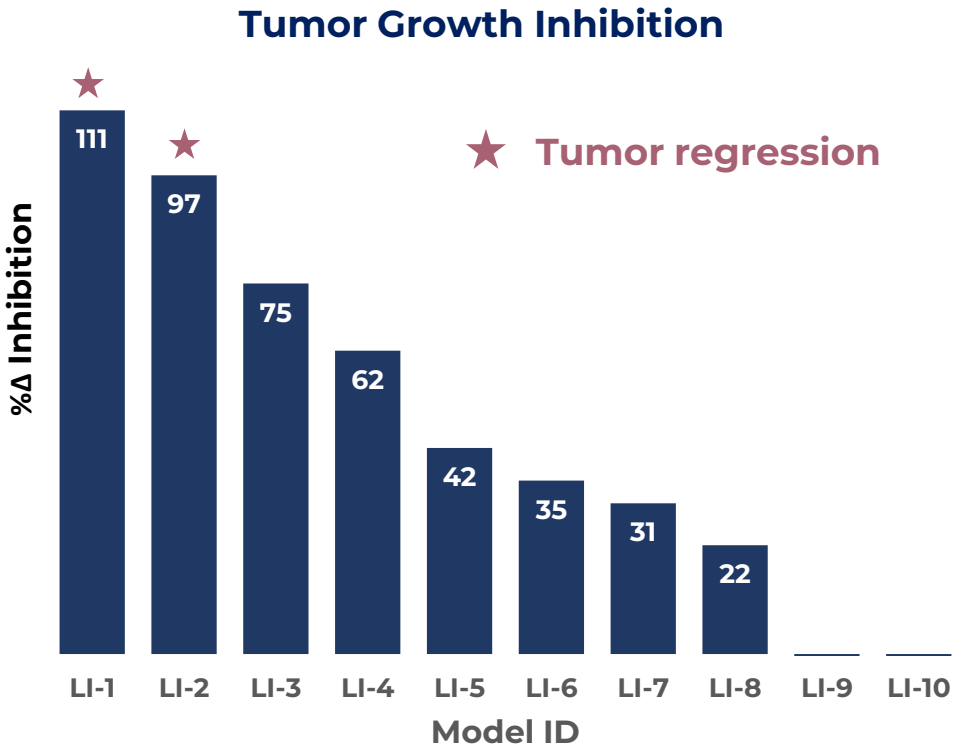
PDX Models/



10 randomly selected HCC models

CPT-6281, 100mg/kg, BID

3 animals per vehicle & treatment groups



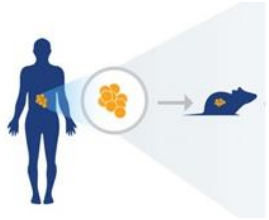
Efficacy demonstrated in 8/10 PDX models; TGI>50% in 4 models, 2 models with regression

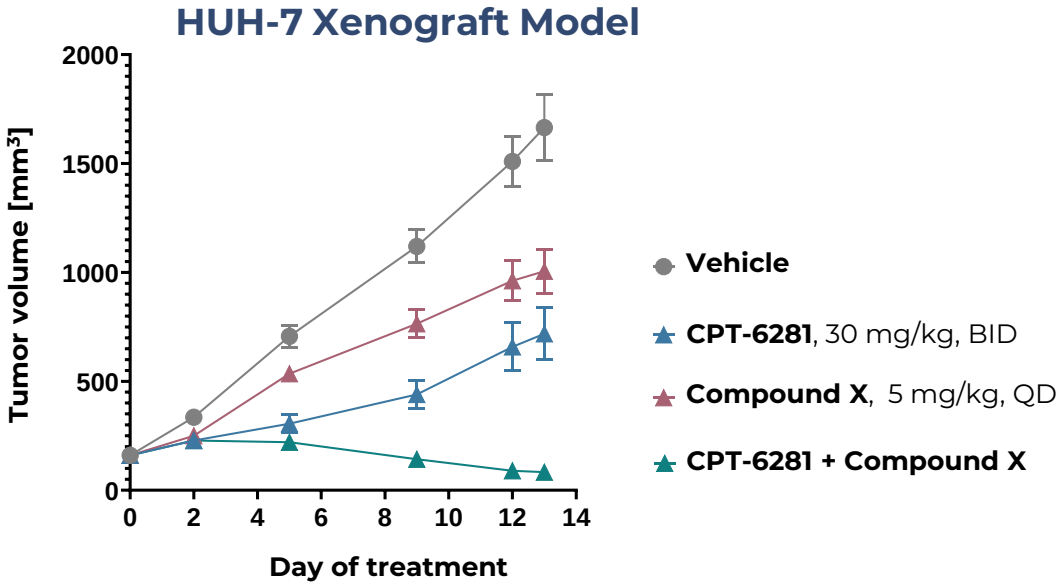
Captor Therapeutics®

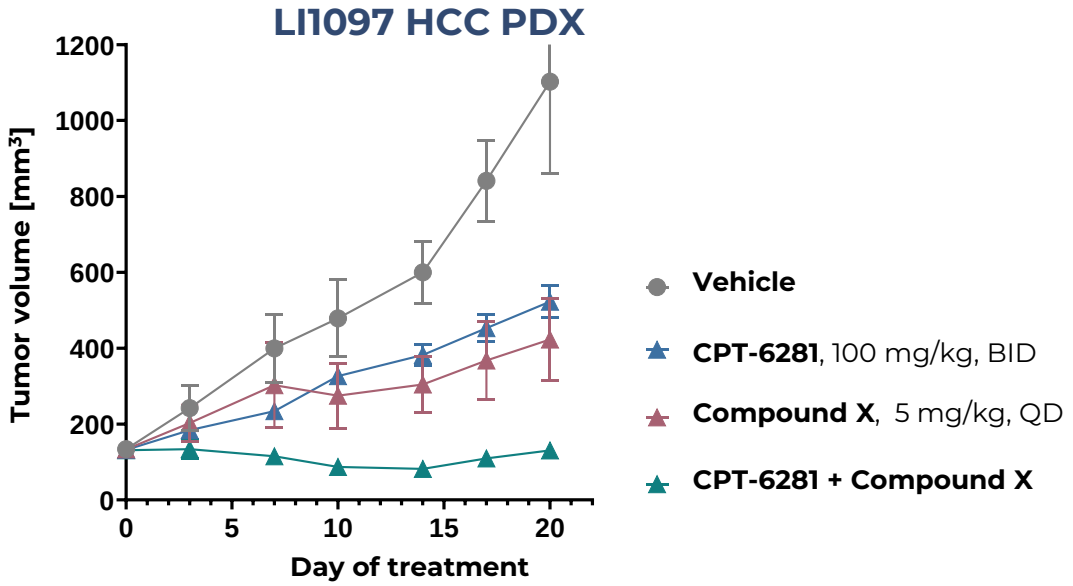
Combination with an approved drug is synergistic in less sensitive tumors

CrownBio
CONNECTING SCIENCE TO PATIENTS

PDX Models/







Combination with compound X sensitizes poorly or non-responding cancer cells due to the complimentary modes of action of degrader and Compound X

Captor Therapeutics®

Status of preclinical development of CPT-6281

In vitro and *in vivo* pharmacology studies	✓
Drug Substance synthesis optimization and manufacture for tox	✓
MTD/DRF tox studies in rats and NHP	✓
DMPK studies	✓
GLP tox studies In-life phase complete	✓
GLP tox studies Histopathology, TK, safety pharmacology analysis	**Ongoing**
Drug Substance GMP manufacture	**Ongoing**
Drug Product development and GMP manufacture	**Ongoing**
PK & PD assays development for the clinic	**Ongoing**

Captor Therapeutics®

Development timeline – CPT-6281

Molecular Glue

Initial indication:

Hepatocellular carcinoma

Degradation profile

GSPT1, SALL4, NEK7

Target tissue activated pro-drug

DRF studies complete

GLP toxicology underway

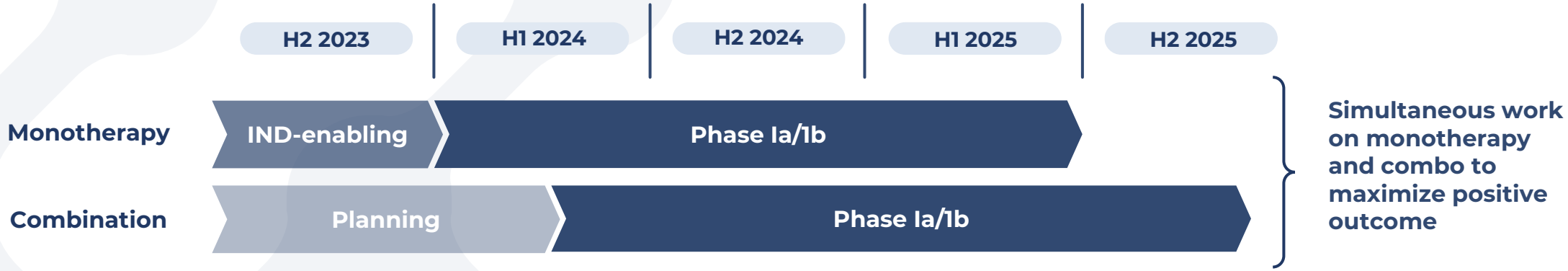
Manufacturing scale-up complete

Expected milestones:

CTA submission for initiation of clinical trials in Q4 2023

Initial phase I top-line data to be reported by the end of 2024

Combination study data in 2025



Captor Therapeutics®

Summary

CPT-6281 first-in-class MG degrader of GSPT1, NEK7 & SALL4 with target tissue pro-drug activation for liver, lung and neuroendocrine cancers

- CPT-6281 degrades GSPT-1, NEK7 and SALL4 and is cytotoxic in cancer cell lines *in vitro* & *in vivo*
- CPT-6281 potently inhibits tumor growth in Hep3B xenograft models and in HCC PDX models
- CPT-6281 is a pro-drug converted to the active degrader intracellularly by an enzyme highly expressed in the liver
- CPT-6281 is non-toxic to human primary hepatocytes *in-vitro*, well in excess of doses that are toxic to cancer cells
- In-life phase of GLP toxicology studies is complete with no gross findings
- Large scale non-GMP batches have been produced
- GMP manufacturing for clinical supplies underway

Captor Therapeutics®

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

MCL-1 as a target in numerous cancers

MCL-1 is a key mechanism of drug resistance in cancer cells

Highly attractive target serving as a major survival signal in numerous cancers

Haematological malignancies

Multiple Myeloma (MM) | Acute Myeloid Leukaemia (AML) | Non-Hodgkin Lymphoma (NHL)

Selected solid tumours

Small cell lung cancer (SCLC) | Non-small cell lung cancer (NSCLC) | Triple-negative breast cancer (TNBC)

Despite years of effort no MCL-1 targeting drug has been approved

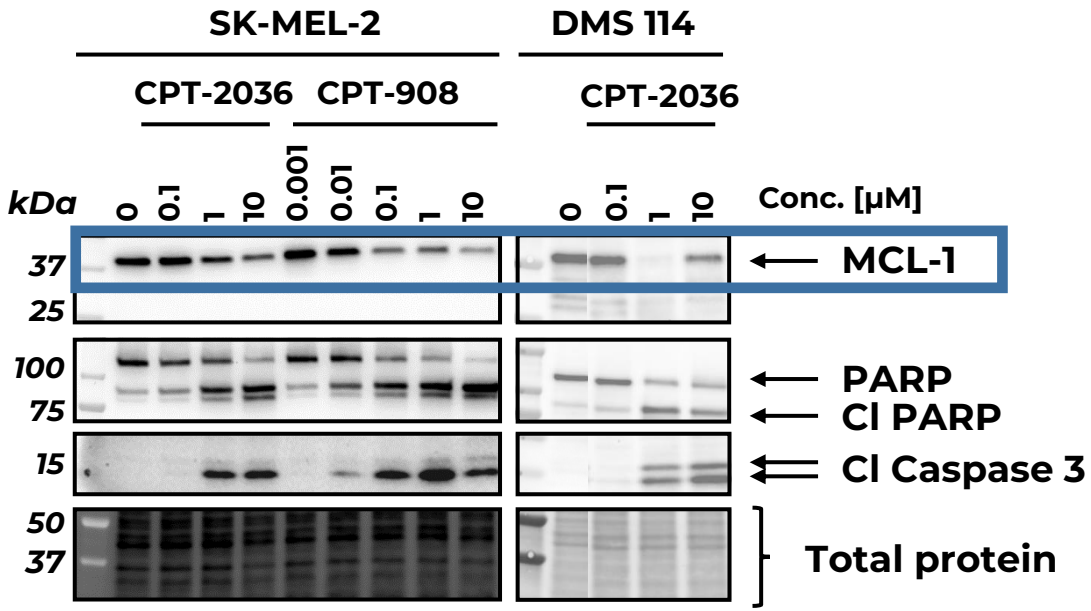
Captor Therapeutics®

MCL-1 degraders offer pharmacology distinct from inhibitors

- MCL-1 degraders reduce MCL-1 protein levels, **unlike inhibitors that accumulate MCL-1**
- Reduction of MCL-1 by ca. 70% results in apoptosis induction in cancer cells
  - Monoallelic KO of MCL-1 in mice is viable and without phenotype
- CPT-908 is a pro-drug of CPT-2036 optimised for potency in NHP and human
- CPT-2036 and CPT-908 are synergistic with different drugs
- CPT-908 is more potent than the clinical inhibitor, MIK665 (Servier/Novartis), in patient-derived AML cells
- Both Captor degraders, when administered above the effective dose, do not affect Troponin-I levels in NHPs – an indicator of cardiac safety

Captor Therapeutics®

Potent degradation of MCL-1 across different *in vitro* models



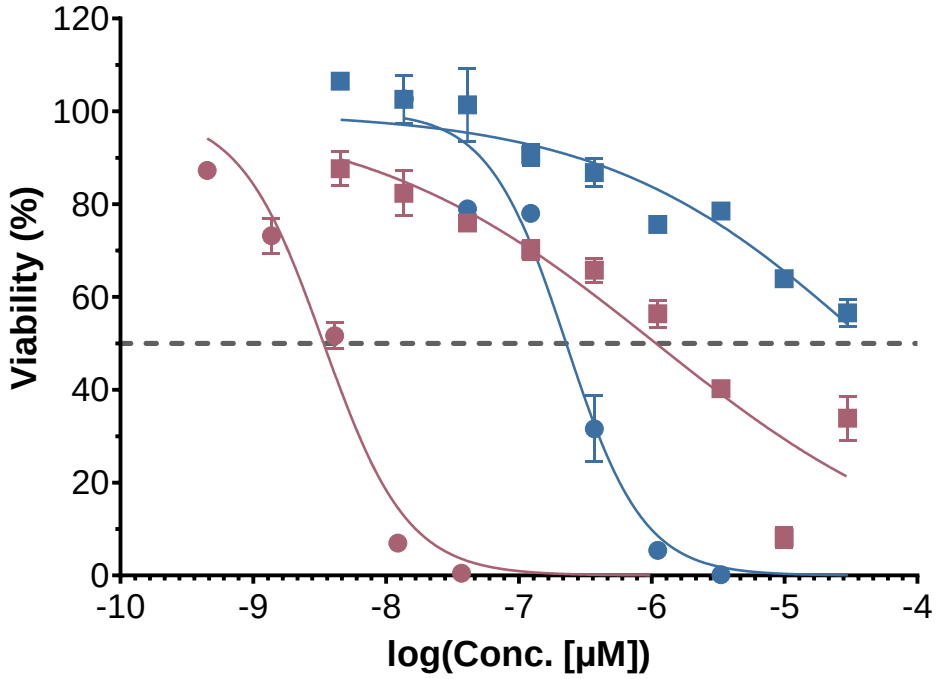
SK-MEL-2 - 24h treatment with compounds; **DMS 114** – 6h treatment

	DC_{50}/D_{max}	
Cell line	**CPT-2036**	**CPT-908**
MV4-11	79 nM / 96%	1 nM / 99%
hsPBMC	26 nM / 87%	1 nM / 88%
SK-MEL-2	1 uM/ 50%	56 nM/ 75%
HCC1187	Not tested	<100 nM/ 91%
DMS 114	144 nM/ 95%	Not tested

CPT-908 & CPT-2036 degrade MCL-1 in pM to nM range and are active in different cancer cell lines

Captor Therapeutics®

Cell line and PBMCs sensitivity to CPT-2036 & CPT-908



Cell line	pIC_{50} CPT-2036	pIC_{50} CPT-908
MV-4-11	6.5 ± 0.1	8.5 ± 0.2
MV-4-11 Ven-resistant	-	11.5 (N=1)
MV-4-11 Ven-resistant + Venetoclax	-	12.0 (N=1)
WSU-DLCL-2	5.4 ± 0.2	7.6 ± 0.1
DMS 114	6.2 ± 0.3	7.8 ± 0.1
OPM-2	6.6 ± 0.2	>8.3 ± 0.1
hsPBMC	4.9 ± 0.7	6.3 ± 0.5
hiPSC-CM	4.8 ± 0.8	5.8 (N=1)

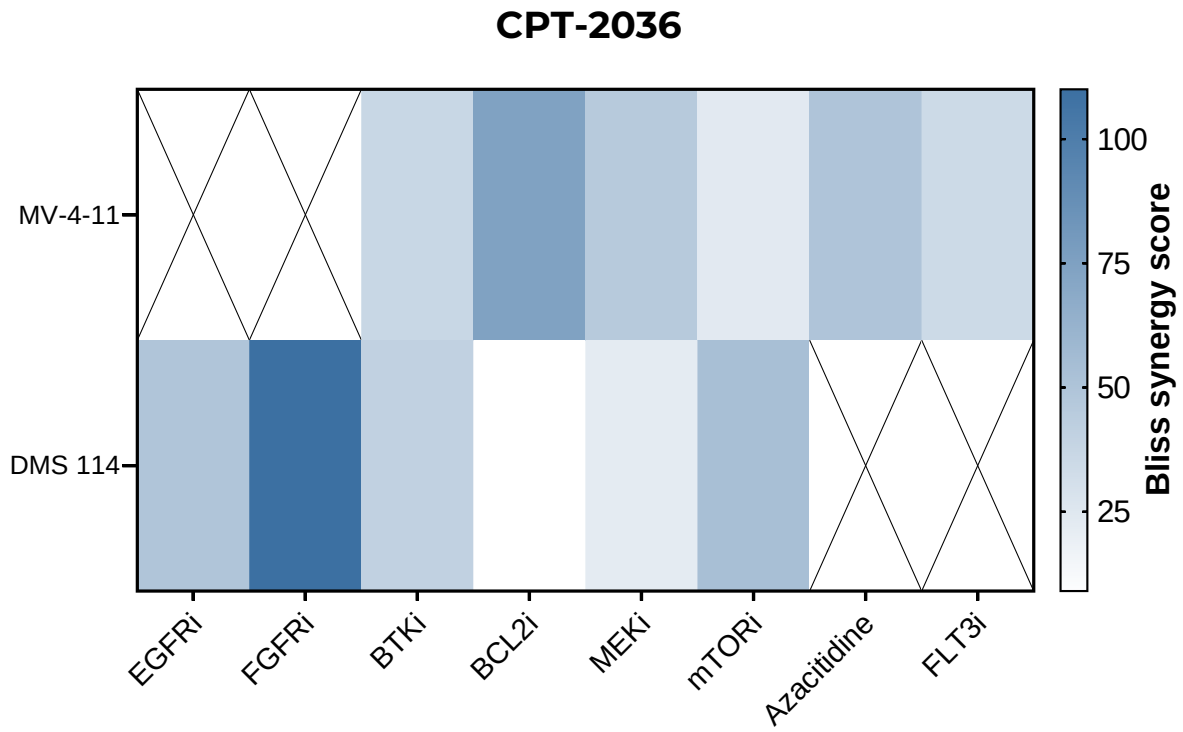
PBMCs and hiPSC-cardiomyocytes are much less sensitive than cancer cell lines to degradation

CT-03 – MCL-1

Captor Therapeutics®

CPT-2036 in combination with chemotherapeutic agents

Co-treatment with **CPT-2036** and different chemotherapeutic agents in **MV4-11** and **DMS 114** for 72 h. Viability assessed by CTG assay.

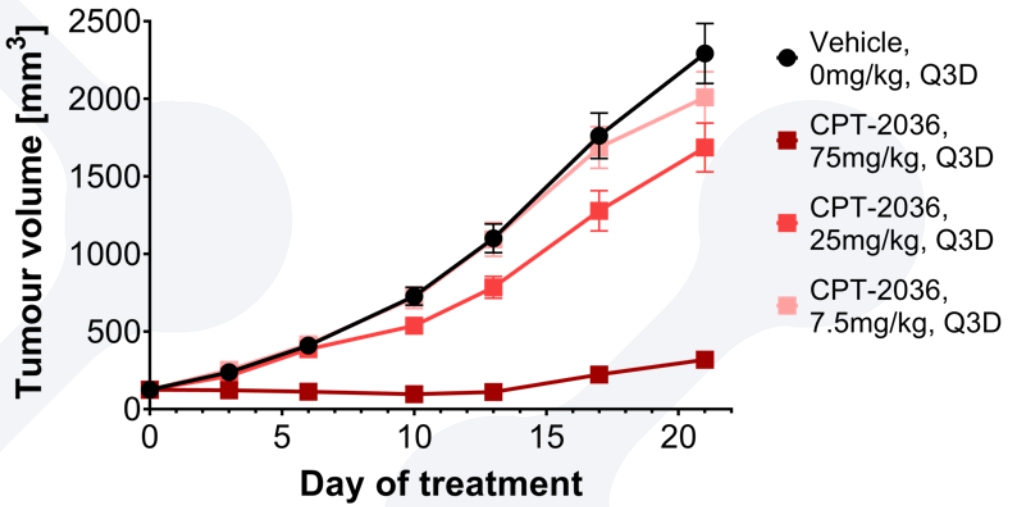


CPT-2036 shows synergy with different approved drugs including venetoclax (BCL2 inhibitor) and FGFR2 inhibitors

Captor Therapeutics®

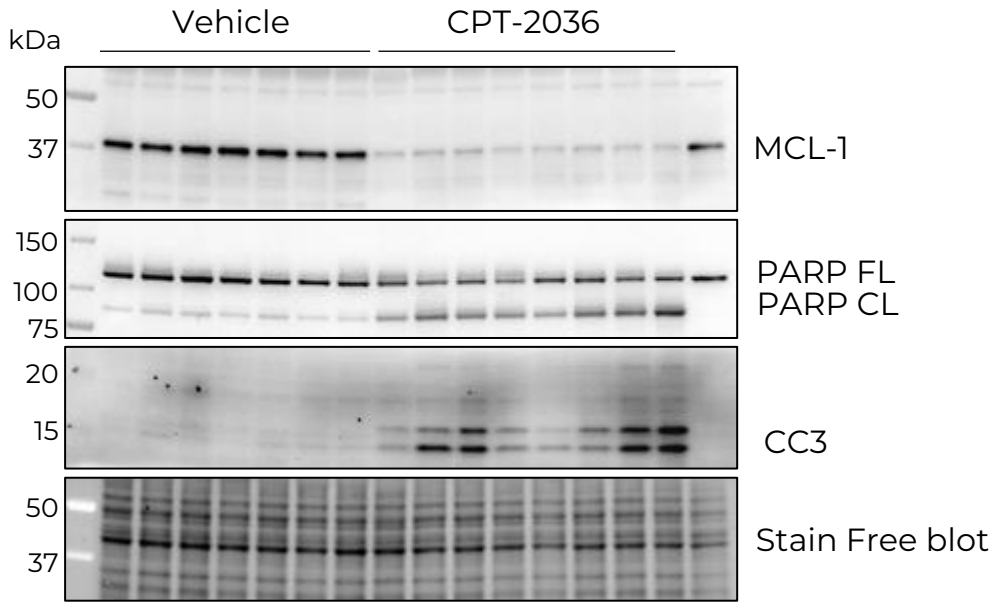
CPT-2036 effective *in-vivo* in AML and lung cancer models

Strong tumor growth inhibition in intermittent dosing (every 3 days)



Mice with 150 mm^3 leukaemia cell line MV4-11, IV

Potent MCL-1 degradation and apoptosis activation in SCLC xenograft model

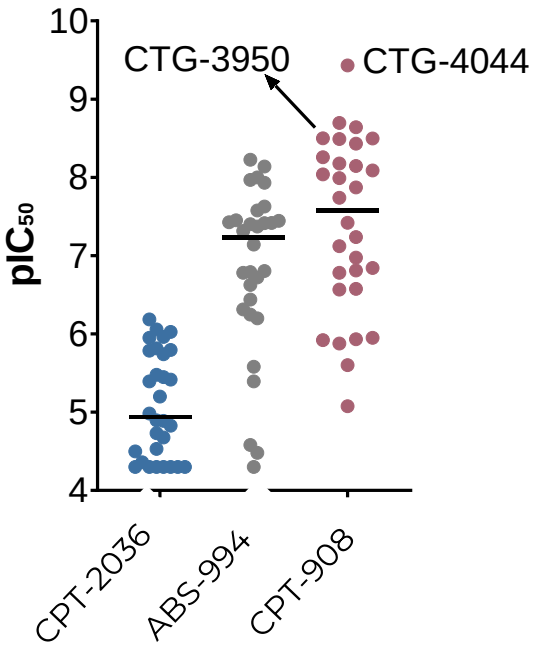


DMS-114, 75 mpk, IV, single injection

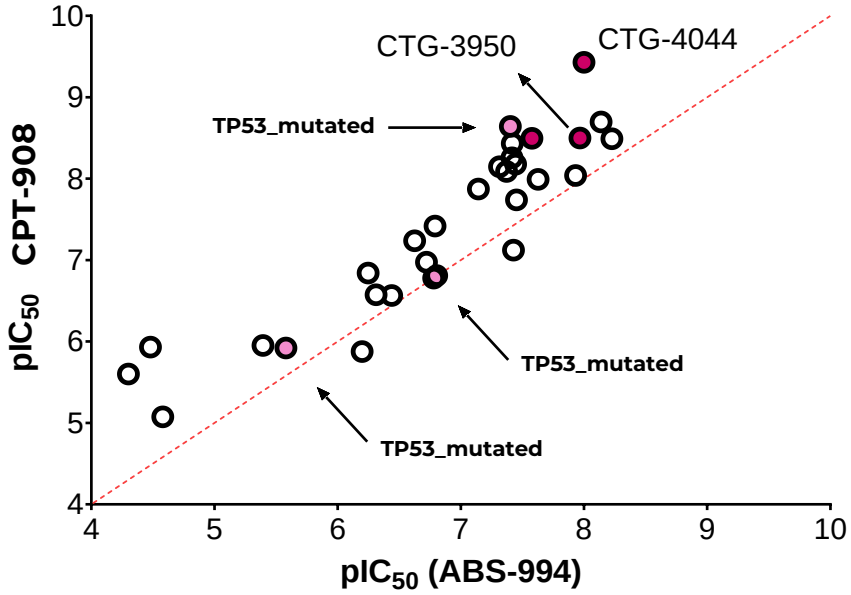
Captor Therapeutics®

High potency of CPT-908 in AML *ex vivo* models

pIC_{50} values of tested compounds in each of the 30 AML *ex vivo* models



CPT-908 is more potent than ABS-994 in most of the tested models



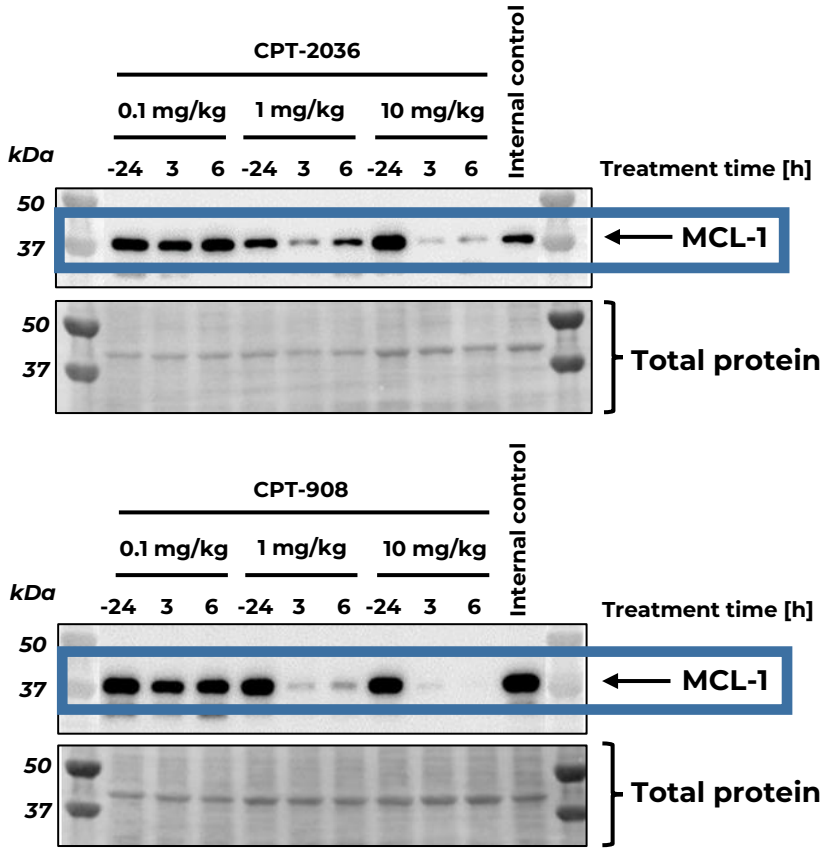
ABS-994 - MIK665, MCL-1 inhibitor in Ph I/II (Servier/Novartis)
VitroScreen, Champions Oncology
CTG-4044 and CTG-3950 – patients resistant to Gilteritinib or Venetoclax, respectively

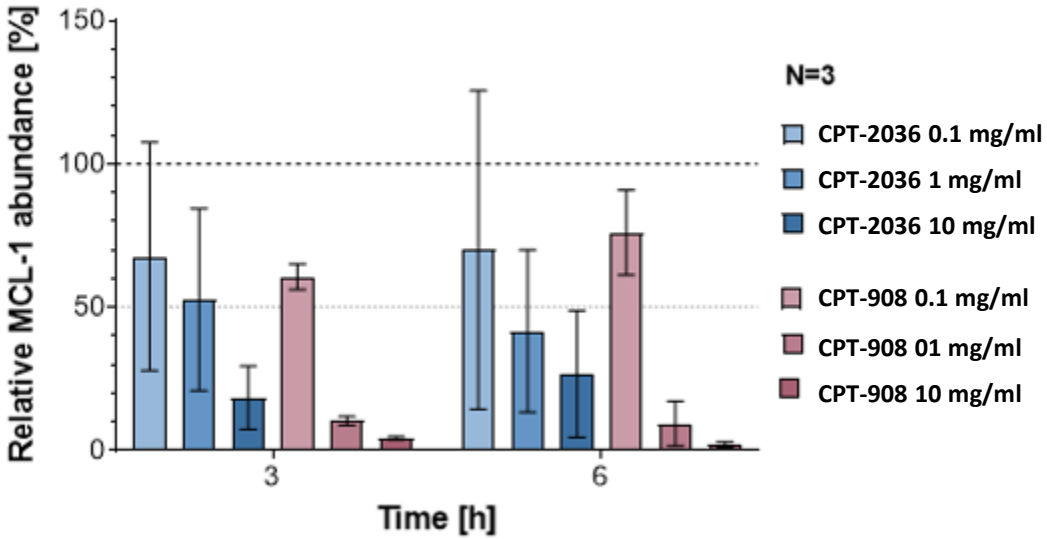
CT-03 – MCL-1

CPT-908 is more potent than MIK665 in a panel of 30 PDX cell lines and shows nM activity in cells refractory to gilteritinib and venetoclax

Captor Therapeutics®

Strong PD effect of both CPT-908 & CPT-2036 *in vivo* (NHP PBMCs)





Male Cynomolgus Monkey, IV injection

CPT-908 is >10x more potent in NHP than CPT-2036

Captor Therapeutics®

Development timeline – CT-03

Partnering:

Open to partnering now

Bifunctional Degrader

Initial indications:

Blood cancers, subsequently solid tumours

Degrader profile

Selective first-in-class MCL1 degraders,

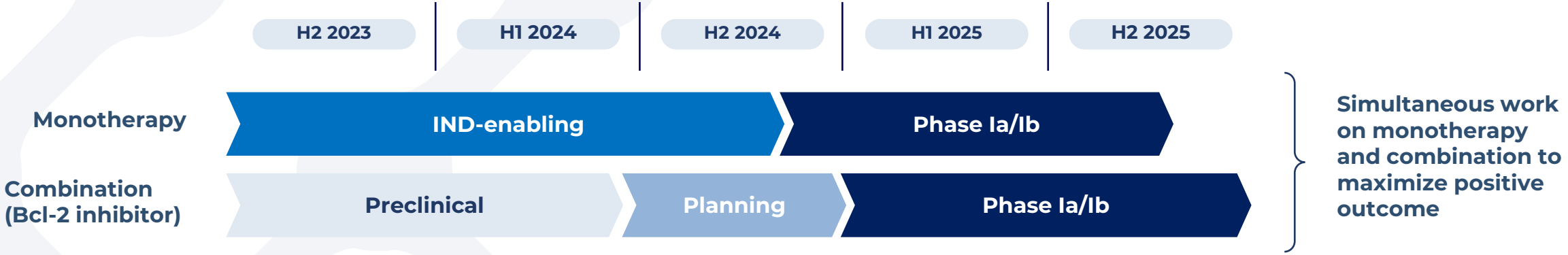
Activity proven in *in vivo* models

Candidate selection studies underway

No indicators of cardiac safety issues

Expected milestones:

- Candidate selection planned for Oct 2023
- GLP tox start Nov 2023 (Comp 1) or Mar/Apr 2024 (Comp 2)
- IND/CTA approval in Q3/4 2024
- Initiation of Phase I clinical trial Q4 2024
- Phase Ia/Ib top-line data reported 2025



Captor Therapeutics®

Summary

Two MCL-1 bifunctional degraders have been developed with *in vitro* potency (DC_{50}) of <1 nM & 100 nM

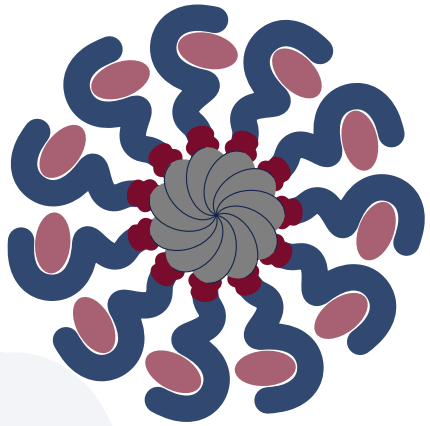
- CPT-2036 & CPT-908 selectively degrade MCL-1 and are cytotoxic in cancer cell lines *in vitro* & *in vivo*
- Both CPT-908 & CPT-2036 potently inhibit tumor growth in MV4-11 xenograft models
- CPT-908 & CPT-2036 degrade MCL-1 in NHP PBMCs *in vitro* & *in vivo*
- PBMCs and hiPSC derived-cardiomyocytes are much less sensitive than cancer cell lines in viability assays
- CPT-2036 & CPT-908 do not affect NHP troponin-I levels *in-vivo* at doses higher than the effective dose
- ~1 kg of CPT-2036 non-GMP was produced and is a single synthesis step from CPT-908

Candidate selection planned for Q4 2023

Captor Therapeutics®

CT-02: First-in-Class NEK7 degraders for autoimmune & neurodegenerative diseases

CT-02: Vast market potential for inflammasome modulators



Inflammasome: NEK7 complex

Caspase 1

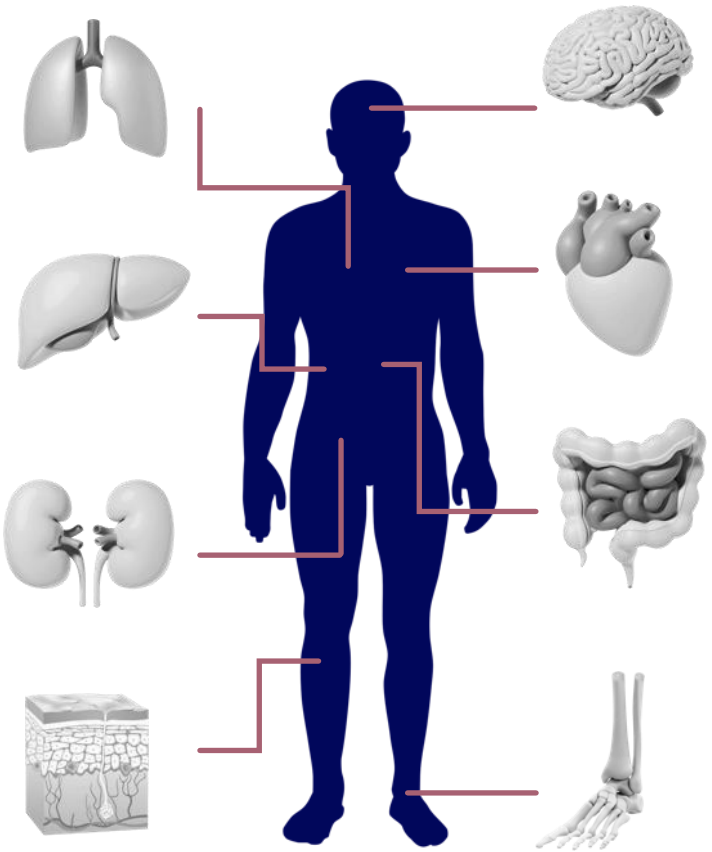
IL-1β | **IL-18** | **Gasdermin D**

Allergy
Asthma

Fibrotic diseases

Lupus nephritis

Psoriasis



Neuroinflammation
(AD, PD, MS, ALS)

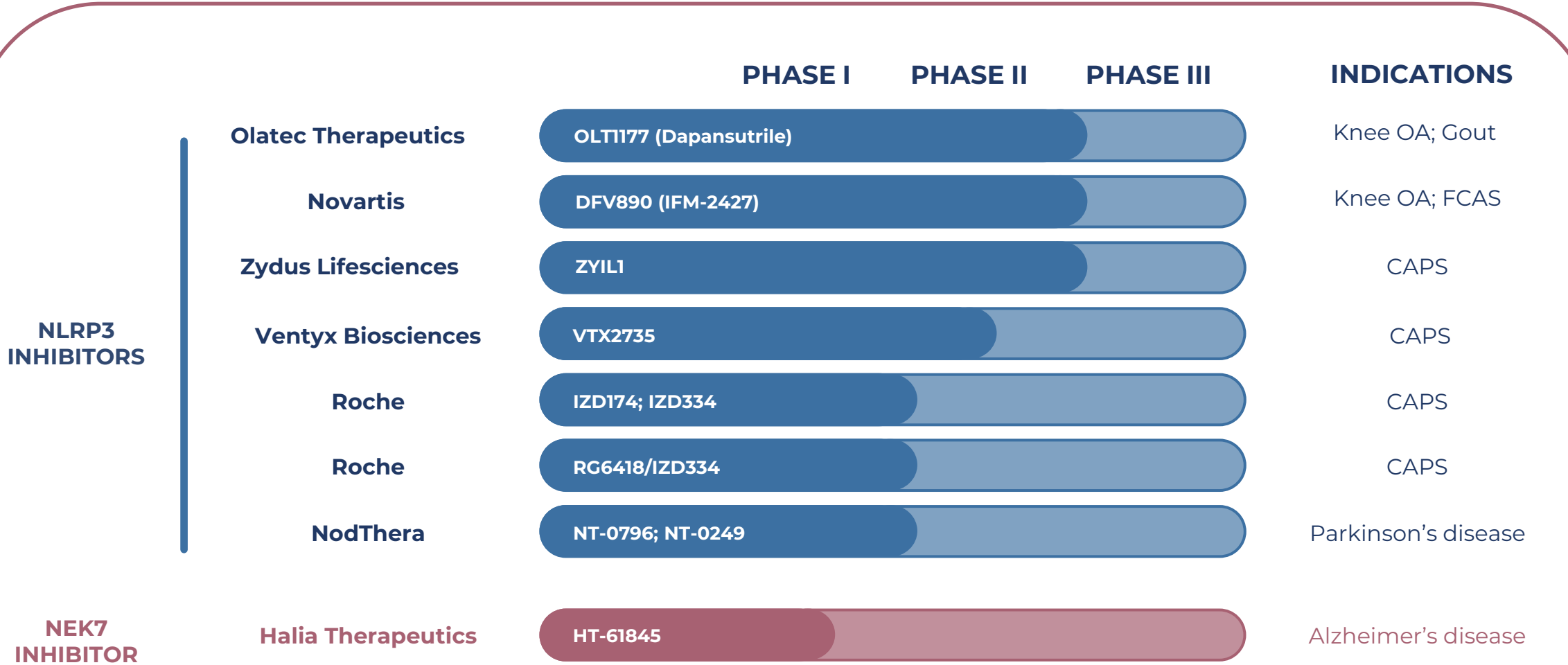
Myocardial infarction
Diabetic cardiomyopathy

Inflammatory Bowel Disease

Gout
Rheumatoid Arthritis

Captor Therapeutics®

Development of NLRP3/NEK7 inhibitors is growing rapidly

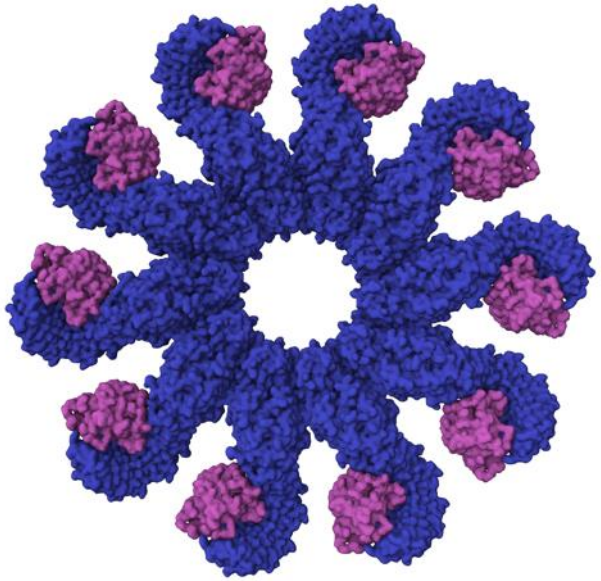


Two NEK7 molecular glue degraders (Novartis, Monte Rosa) in preclinical

Captor Therapeutics®

Intervention in NLRP3 pathway *via* NEK7 degradation

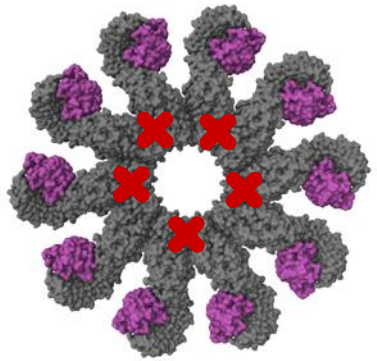
Aberrant activation of NLRP3



NLRP3 inflammasome

NEK7

NLRP3 inhibition

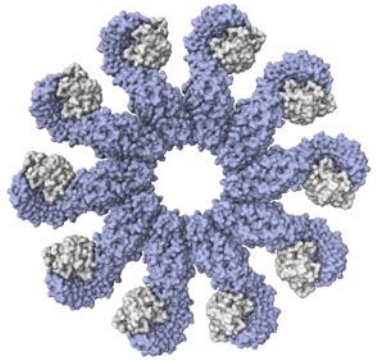


COMPLETE INACTIVATION OF NLRP3

INCREASED INFECTIONS *via* REDUCED IMMUNITY

NEK7 degradation

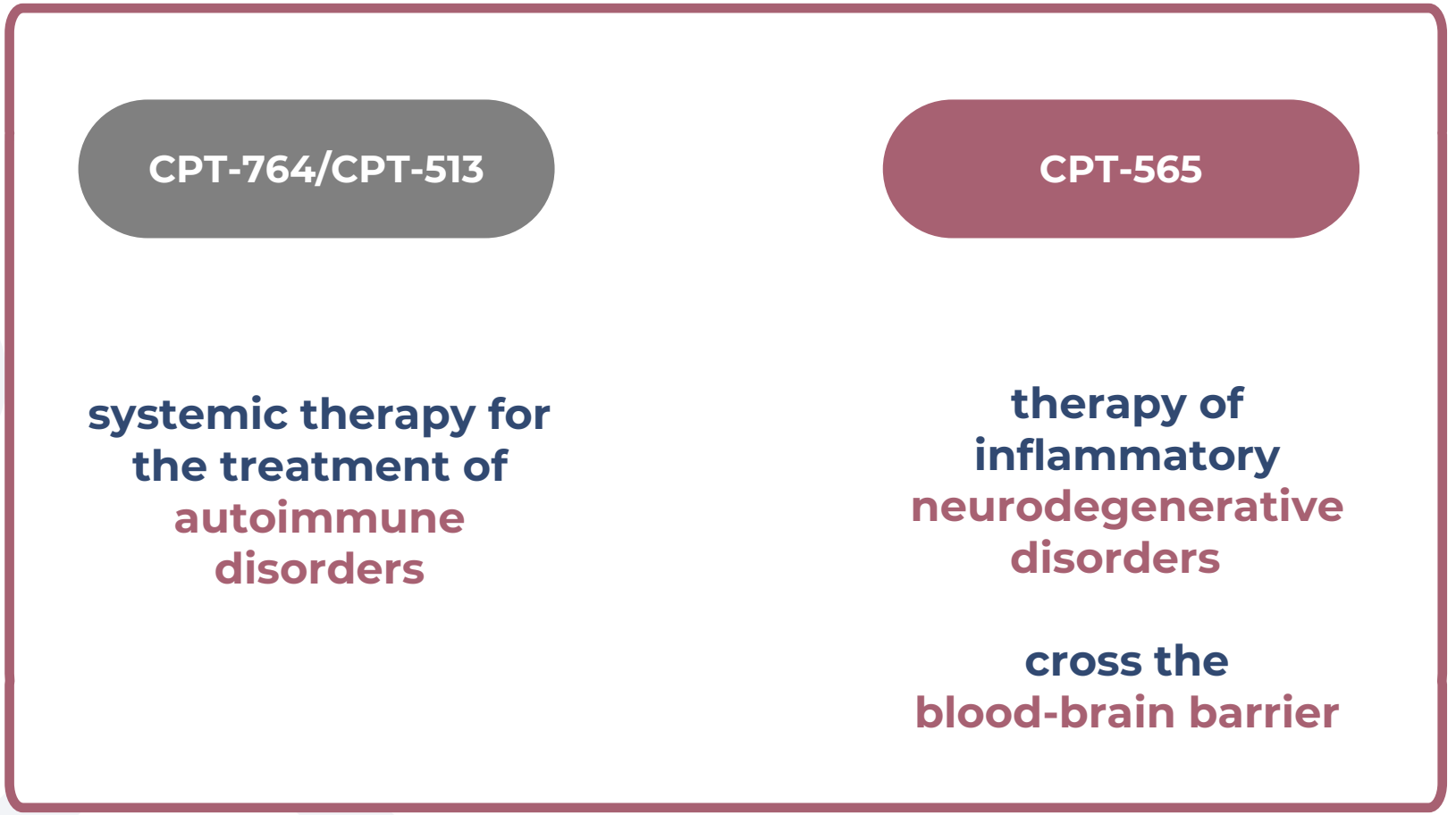
PARTIAL INACTIVATION OF NLRP3



MAINTAINED IMMUNITY

Captor Therapeutics®

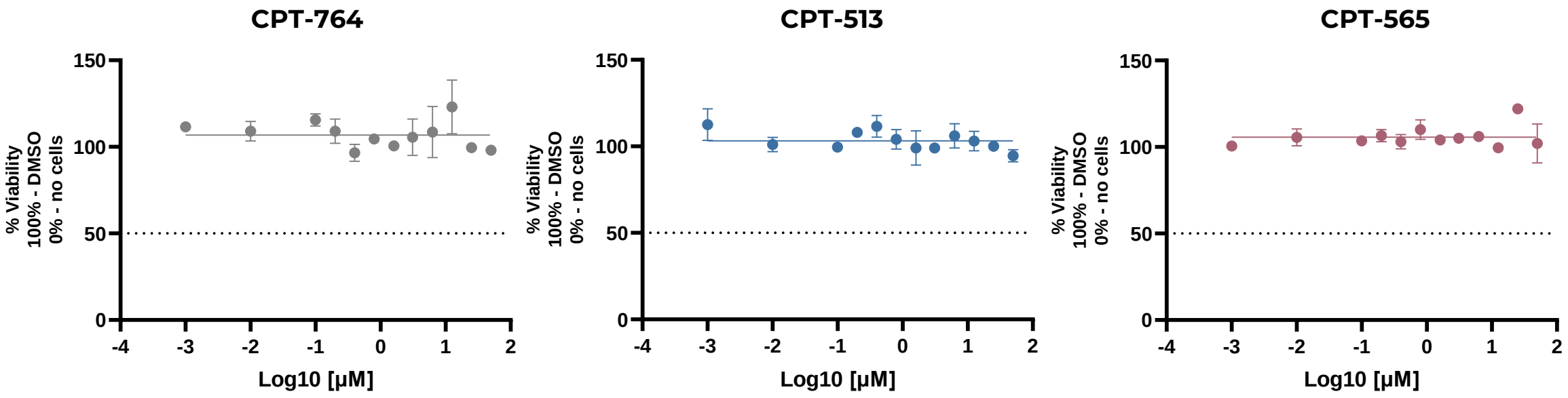
Captor Therapeutics has developed two series of NEK7 degraders



CPT-513 is an optimized lead compound of CPT-764 with improved NEK7 degradation and DMPK parameters

Captor Therapeutics®

CPT-764, CPT-513 & CPT-565 do not affect viability of human PBMC *in vitro*



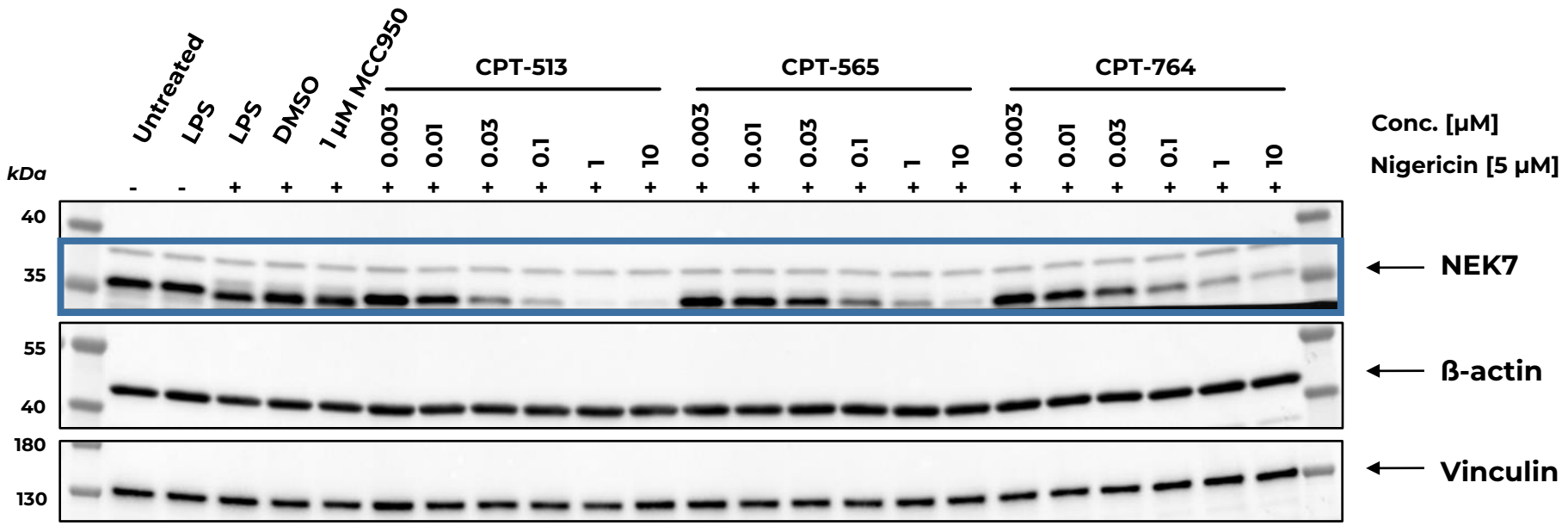
Effect of CPT-764, CPT-513 & CPT-565 compounds on human PBMC viability (CTG analysis, 72h treatment)

representative graph; (N=5)

CPT-764, CPT-513 & CPT-565 post 72h treatment are non-cytotoxic in human PBMC

Captor Therapeutics®

Potent degradation of NEK7 in human macrophages *in vitro*



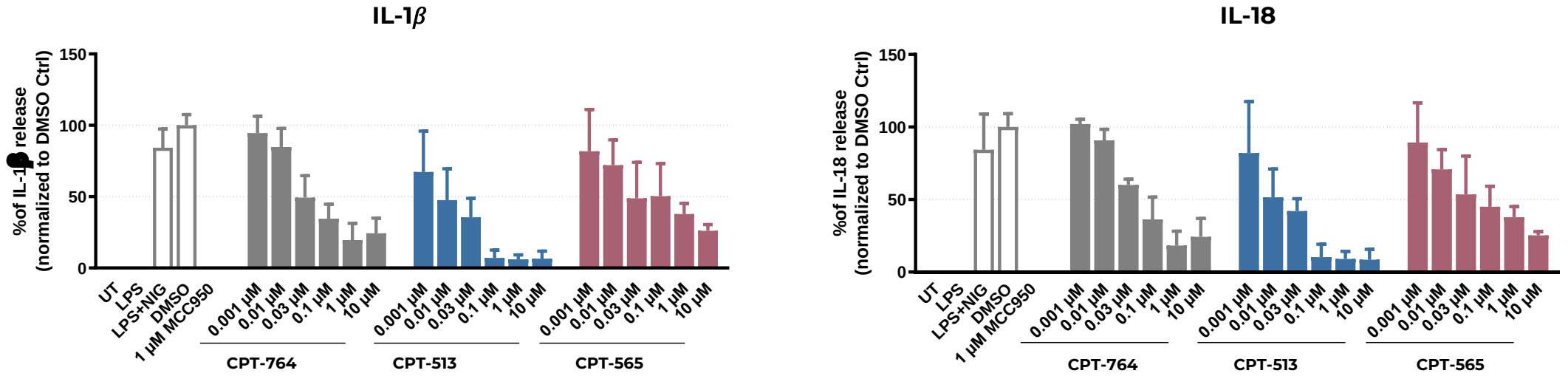
CPT-513, CPT-764 and CPT-565 degrade NEK7 protein dose-dependently in human PBMC-derived macrophages with LPS+Nig activated inflammasome

Human PBMC differentiated into macrophages with M-CSF; treatment with compounds – 24h; inflammasome activation: LPS – 3h, Nig. – 1h

Captor Therapeutics®

Lead compounds decrease levels of IL-1β and IL-18 *in vitro*

ELISA analysis of cytokines IL-1ß and IL-18 produced by human macrophages treated with CPT-764, CPT-513 & CPT-565 (24h treatment)

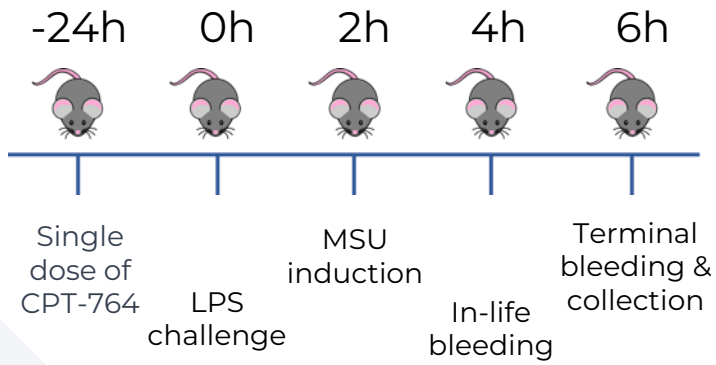


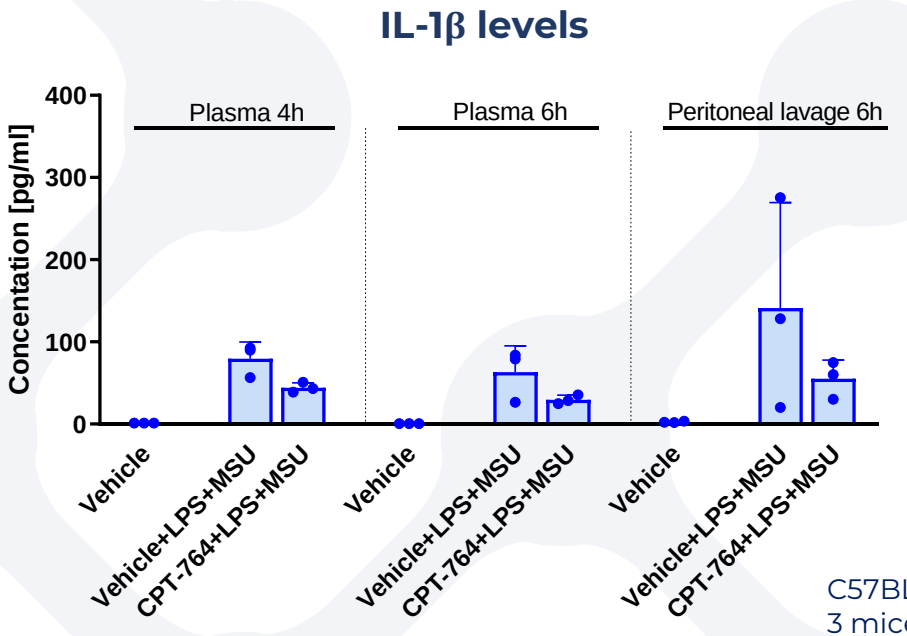
Human PBMC differentiated into macrophages with M-CSF; treatment with compounds – 24h; inflammasome activation: LPS – 3h, Nig. – 1h

The degradation of NEK7 by CPT-764, CPT-513 & CPT-565 results in a decrease in the production of pro-inflammatory cytokines IL-1β and IL-18 by activated human macrophages *in vitro*

Captor Therapeutics®

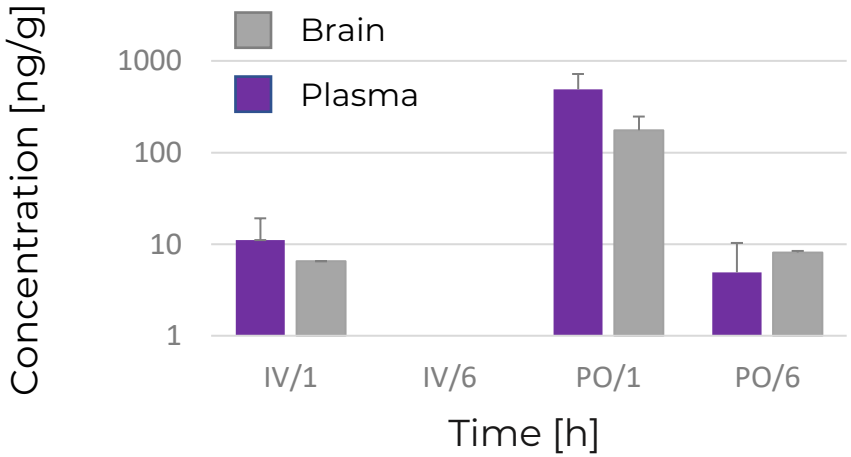
In vivo PoC in peritonitis model & brain penetration





C57BL/6-Crbntm1.1Ble/J;
3 mice per group

Plasma and brain concentration of CPT-565



Time point	Brain exposure (ng/g Tissue)	Plasma exposure (ng/ml)	Brain to Plasma ratio
1h (IV)	6.55	11.1	0.59
6 h (IV)	BLQ	BLQ	NC
1 h (PO)	175.2	494.9	0.35
6 h (PO)	8.1	4.9	1.65

Captor Therapeutics®

Summary

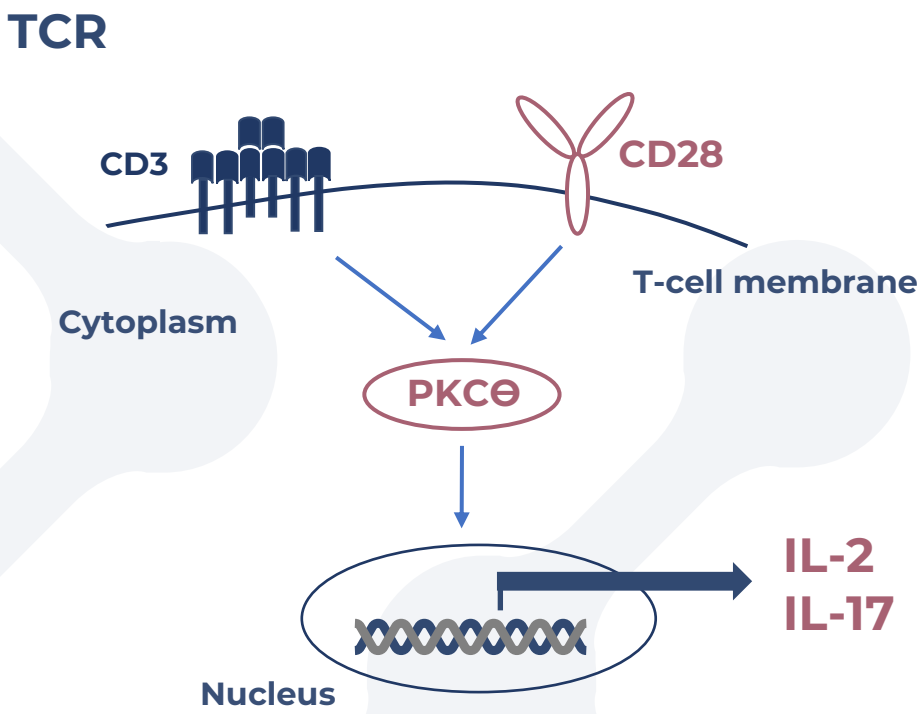
- Two NEK7 degrader series - potential in autoimmune diseases (CPT-513) and neurodegenerative disorders (CPT-565, brain-penetrant series)
- Dose-dependent nanomolar degradation of NEK7 in HiBiT assay and Western blot (human PBMCs)
- CPT-764, CPT-513 and CPT-565:
  - are non-cytotoxic to human, mouse and monkey PBMCs
  - degrade NEK7 in mouse and monkey PBMCs
  - degrade NEK7 in human macrophages & decrease pro-inflammatory cytokines IL-1β and IL-18
- *In vivo* tolerability study for CPT-764 conducted on C57BL/6-Crbntm1.1Ble/J mice with hsCRBN***** did not show signs of acute toxicity
- CPT-764 decreased IL-1ß and IL-18 in the murine peritonitis model induced by MSU crystals

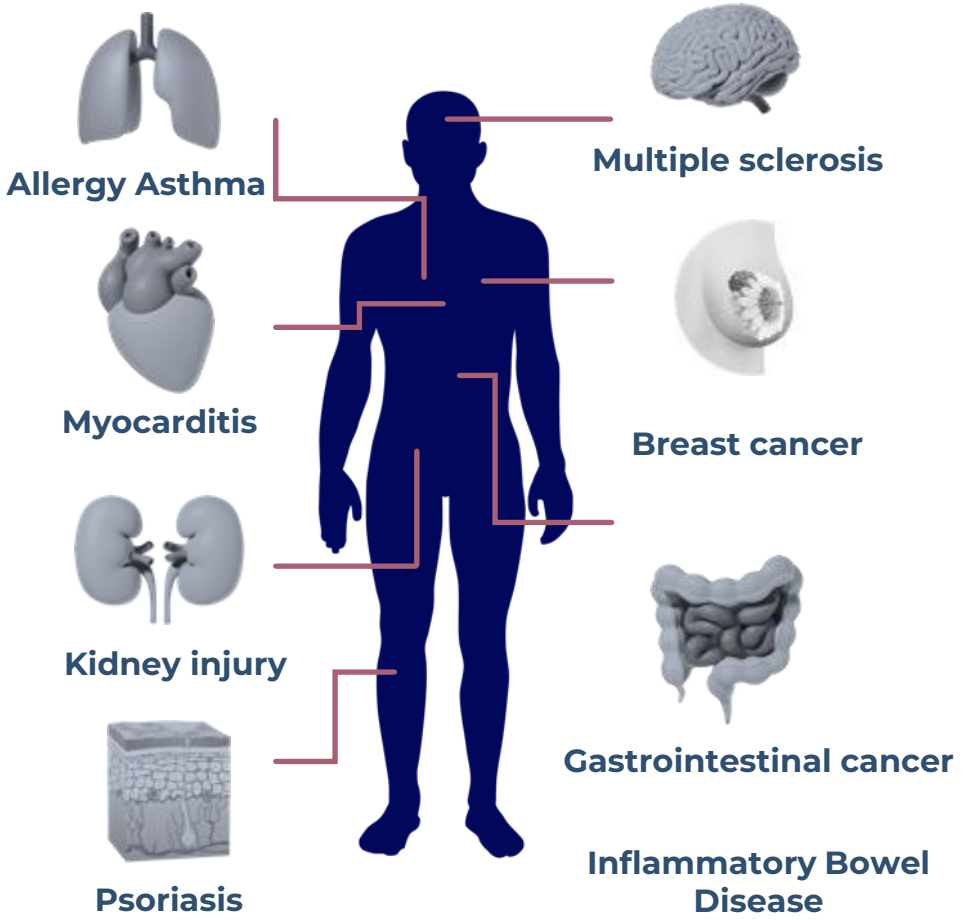
***** *transgenic mouse with humanised Cereblon*

Captor Therapeutics®

CT-05: First-in-Class PKCϴ degraders for autoimmune disorders

PKCΘ: an undrugged high value target





Captor Therapeutics®

Rationale for targeted degradation of PKCϴ

Multiple PKCϴ inhibitors evaluated in clinical trials:

1st generation (e.g. pan-PKC Sotrastaurin) – many side effects

2nd generation (e.g. Astellas, AbbVie, Celgene) - PKCϴ-selective but showed side effects due to unknown off-target(s) or poor target engagement

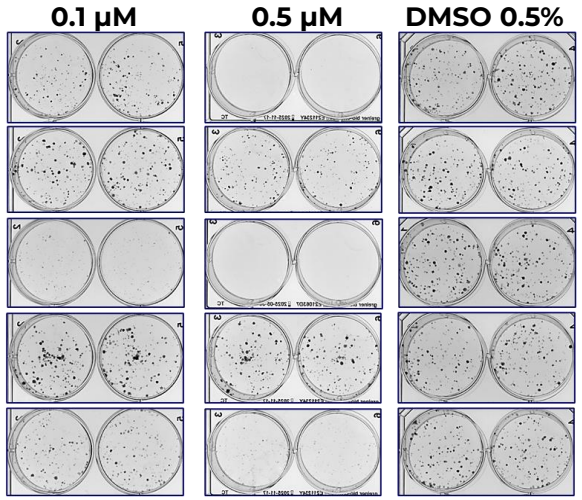
Recent revival, allosteric compound deal: Exscientia-BMS

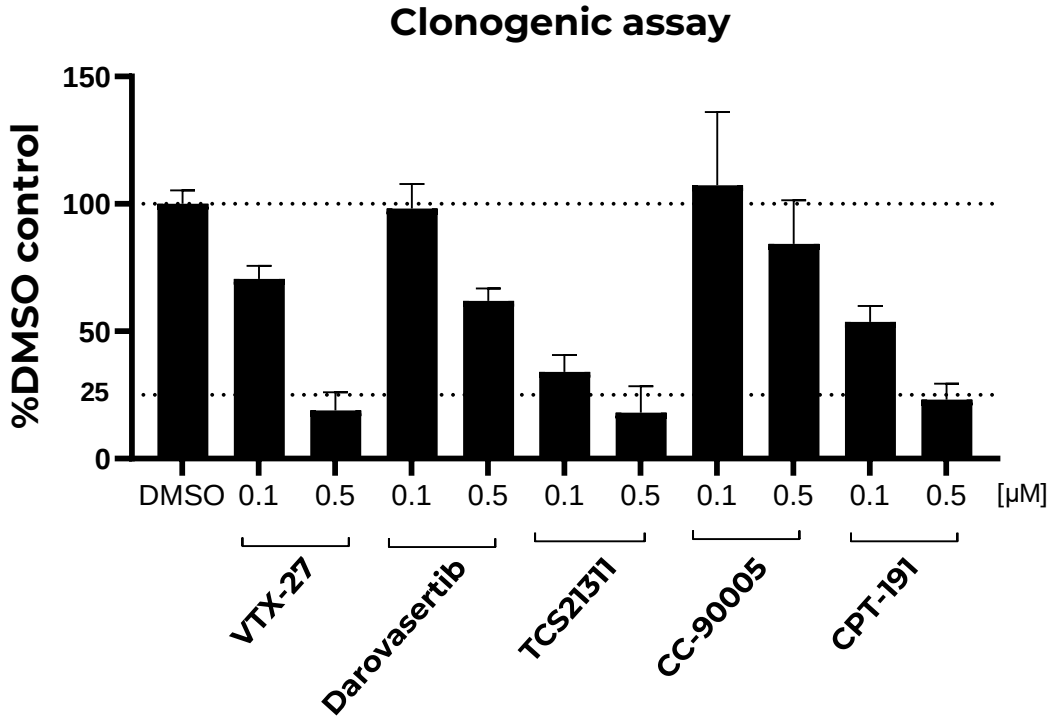
Bifunctional degraders offer selectivity superior to inhibitors *via* ternary complex formation

Captor Therapeutics®

Clonogenic assay – reported PKCϴ inhibitors in GIST-T1

Other PKCϴ non-selective inhibitors, developed in the past tested in Clonogenic assay



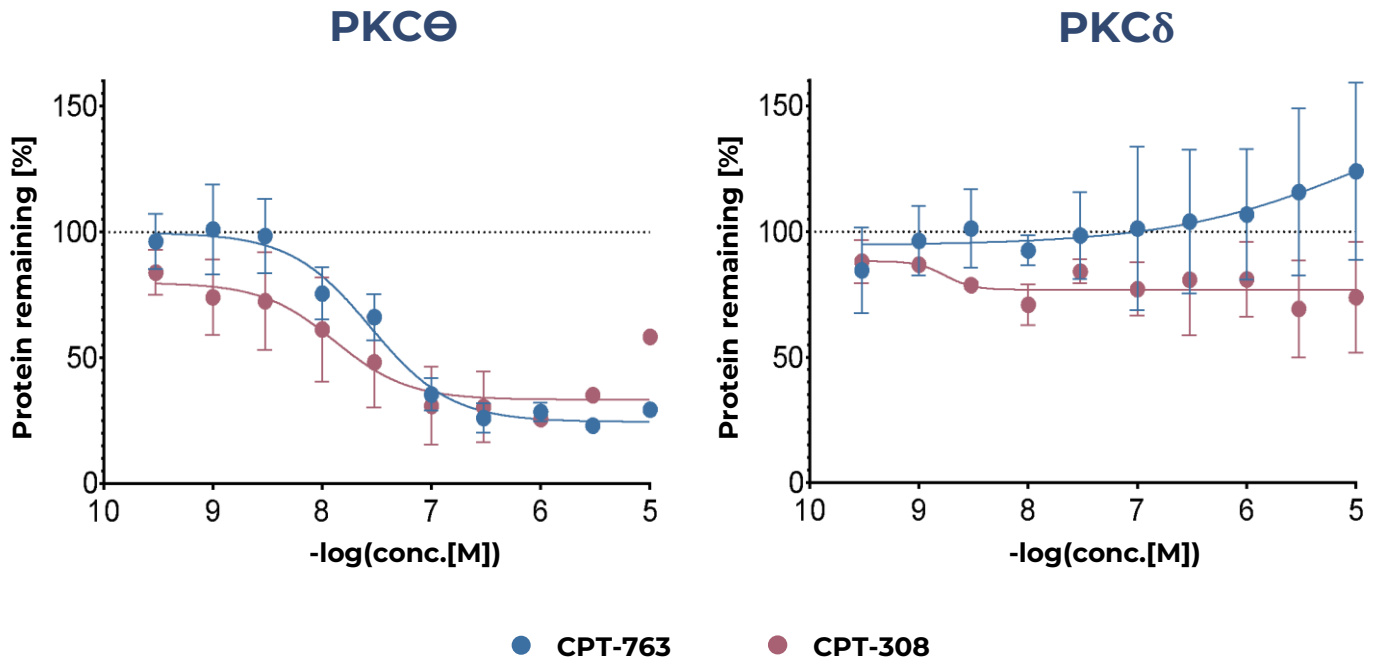


Reported PKCϴ inhibitors display a marked toxicity to GIST-TI cells

Captor Therapeutics®

CPT-763 & CPT-308 degrade PKCϴ in a human T cell line

stimulated Jurkat cells



Compound	DC_{50}	D_{max}
CPT-763	29 nM	75 %
CPT-308	18 nM	75 %

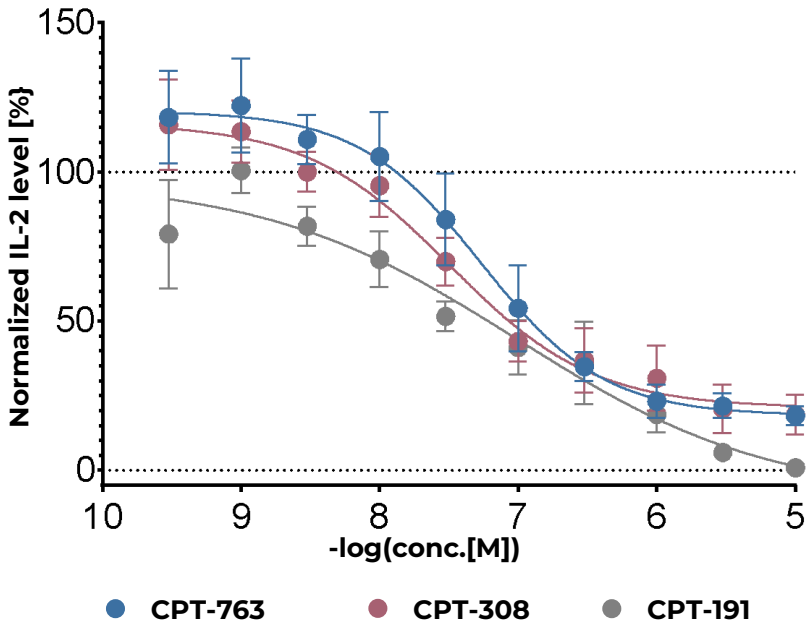
DC_{50} and D_{max} values from WB analysis; β-actin - loading control, N=3

CPT-763 & CPT-308 degrade PKCϴ efficiently, with no effect on PKCδ
(the isoform sharing highest level of amino acid homology)

Captor Therapeutics®

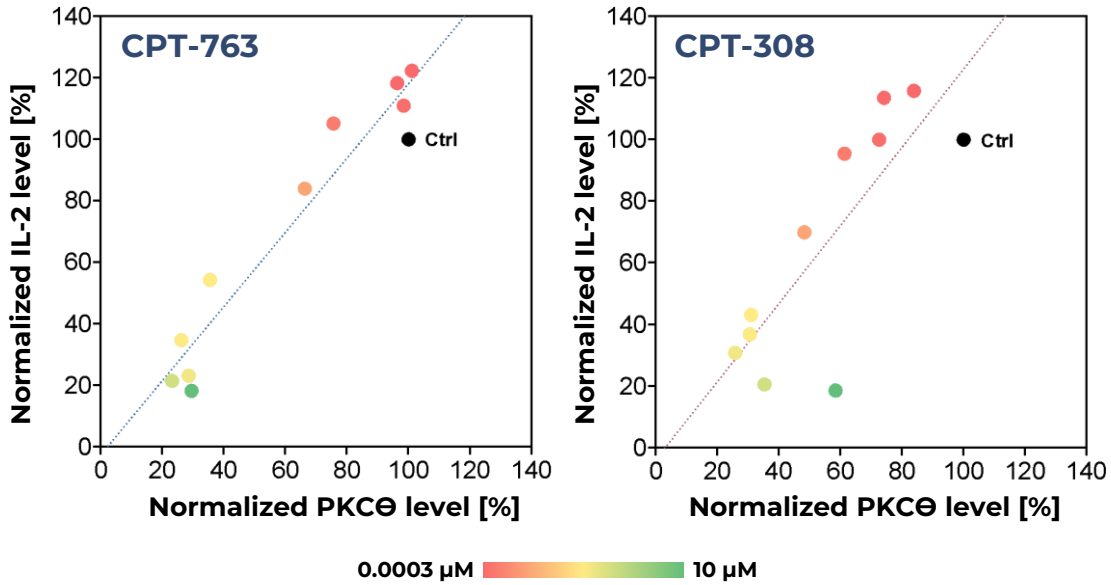
CPT-763 & CPT-308 inhibit IL-2 production in a human T cell line

ELISA analysis of IL-2 secretion upon PKCϴ degradation by CPT-763 & CPT-308, 7h



Compound	IC_{50}	I_{max}	DC_{50}
CPT-763	55 nM	82 %	29 nM
CPT-308	30 nM	81 %	18 nM
CPT-191	98 nM	99 %	N/A

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



Jurkat cells were pre-treated with CPT-763 & CPT-308 for 1h and stimulated with mix of anti-CD3/anti-CD28 tetramers
Cells and cell media were collected after 7h of incubation for downstream analysis (WB & ELISA)

Blocking of IL-2 cytokine secretion is correlated with selective degradation of PKCϴ

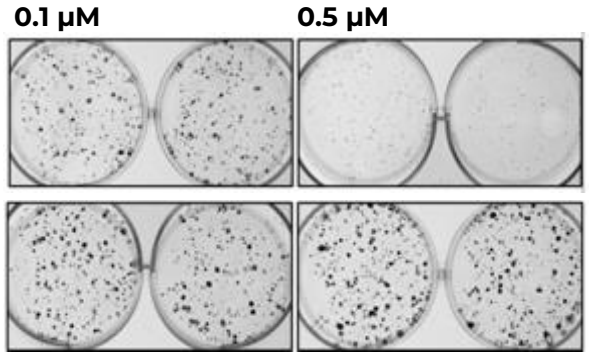
Captor Therapeutics®

CPT-763 is highly selective in a panel of assays

Inhibitor shows significant effects on non-immune cells
Degrader has no effect in non-immune cells

Astellas compound
CPT-191
Inadequate Selectivity

CPT-763
High Selectivity

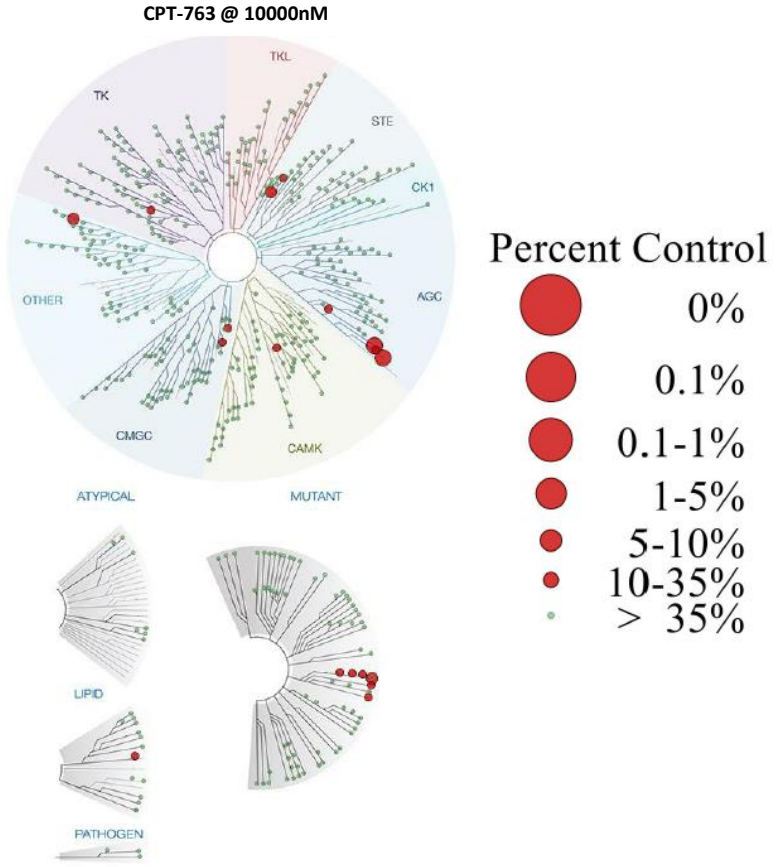


Compound	IC_{50}	I_{max}	DC_{50}
CPT-763	55 nM	82 %	29 nM
CPT-191	98 nM	99 %	N/A

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

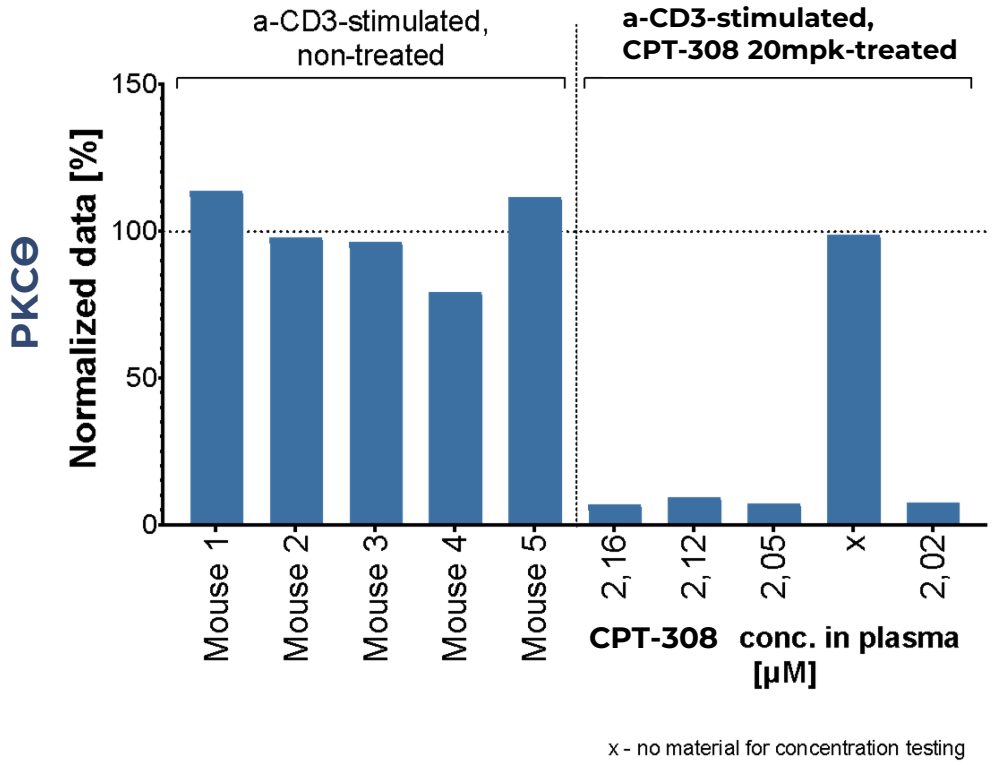
Excellent selectivity against a large number of kinases

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



Captor Therapeutics®

CPT-308 degrades PKCΘ *in vivo*



Efficient PKCθ degradation is observed in CPT-308-treated animals

Efficient degradation of PKCΘ in C57BL/6 mouse splenocytes is observed 6h after CPT-308 application

Captor Therapeutics®

Summary

- Established a screening workflow that allows for discovery of PKCθ degraders superior to existing inhibitors

- 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

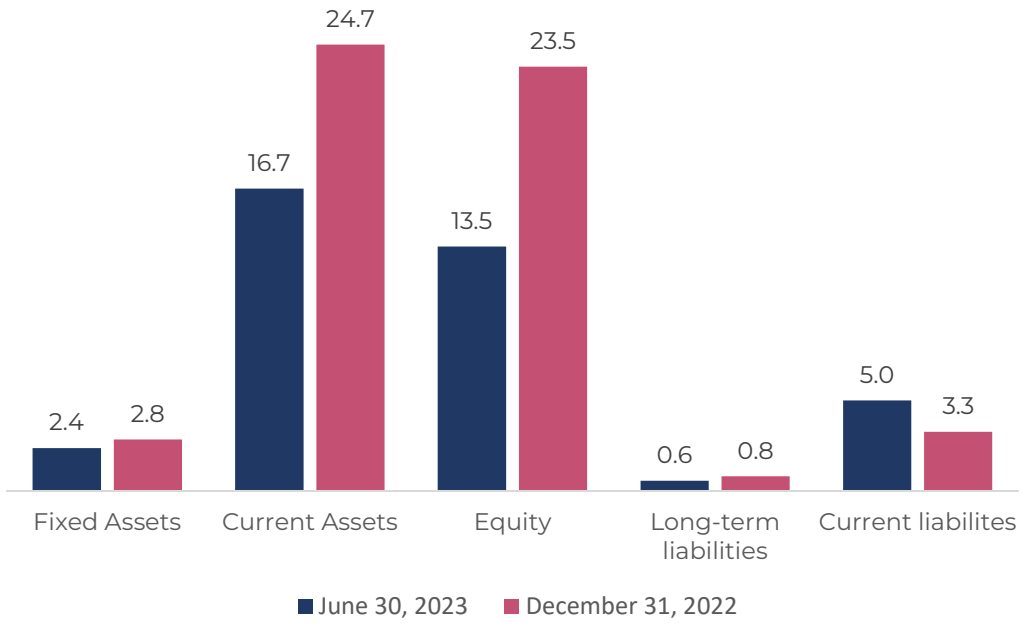
- Next steps:
  - Partnering discussions

Captor Therapeutics®

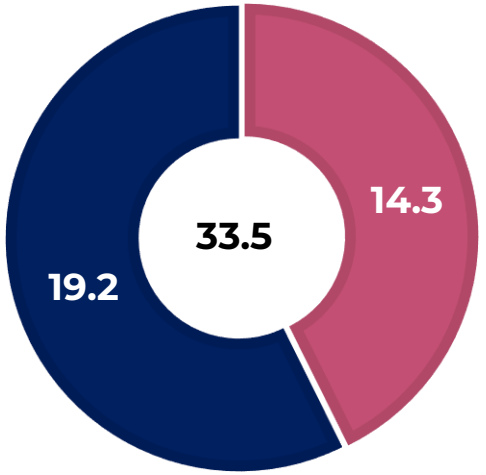
Finance highlights

Strong balance sheet and cash position

Consolidated statement of financial position (US$, M)



Cash position



Available funding secured (US$ M; as of June 30,2023):

Total : US$ 33.5 M

- US$ 14.3 cash, short-term bonds
- US$ 19.2 available grants (NCBR; ABM)

R&D costs in H1 2023:

Total : US$ 9.3 M

Cash outflow in H1 2023:

Total : US$ 7.6 M

Exchange rate USD/PLN as of June 30, 2023 - 4,10

Captor Therapeutics®

Captor Therapeutics®

Captor Therapeutics S.A
ul. Duńska 11
54-427 Wrocław, Poland

Captor Therapeutics GmbH
Hegenheimermattweg 167A
4123 Allschwil, Switzerland

Contact: investors.relations@captortherapeutics.com

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
(POIR.01.01.01-00-0740/19-00)

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)

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

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)

European Funds Smart Growth | Republic of Poland | The National Centre for Research and Development | European Union European Regional Development Fund

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)

MEDICAL RESEARCH AGENCY