Captor Therapeutics®

2023 Results and Update

All images by Piotr Piatek

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2023: a year of progress for Captor

- Secured resources for stable drug candidate development
  - PLN 40M equity raise; PLN 52M ABM grant; rephasing recommendation PLN 4.9M
  - Secure funding till Q3 2025
- CT-01: Growing market with inadequate treatment options; completed GLP regulatory studies, manufacture scale up of drug substance, and appointed global CRO partner to supervise first clinical trial
- CT-03: 2023 data from NHPs and mouse models shows excellent efficacy and selectivity, clean toxicity profile of our first-in-class MCL-1 degrader; IND-enabling studies in 2024
- CT-02; two parallel drug candidate projects:
  - Systemic program targeting autoimmune diseases
  - Brain penetrant program targeting neuroinflammation associated with neurodegenerative disease; growing importance of inflammation in CNS
  - Both programs are currently being tested in disease animal models
- Expanded Business Development collaborations in the USA and China
- Strengthened clinical, business and science teams with international hires

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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 (IBD, Gout, Dermatological diseases)	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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New members of the leadership team

Andrew Saunders DPM, FFPM
Chief Medical Officer

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

Donald Coppen, Ph.D.
Business Development Director

- PhD, University of Southampton
- MBA, Cranfield School of Management
- 20 years' experience in business development:
- Biocompatibles plc [Acquired by BTG plc for £177M]
- Algeta ASA [Acquired by Bayer for $2.9B]
- Consultant to various UK biotechs
- Mereo BioPharma plc [Ultragenyx >$300M out-license]

Tomas Drmota, Ph.D.
VP Early Discovery

- PhD, Charles University Prague
- University of Glasgow, Biochemistry and Molecular Biology
- Tufts University, School of Medicine Boston
- 25 years' experience in preclinical drug development for cardiovascular, metabolism, respiratory, autoimmunity and immuno-oncology therapeutic areas

EDUCATION

PREVIOUS EXPERIENCE

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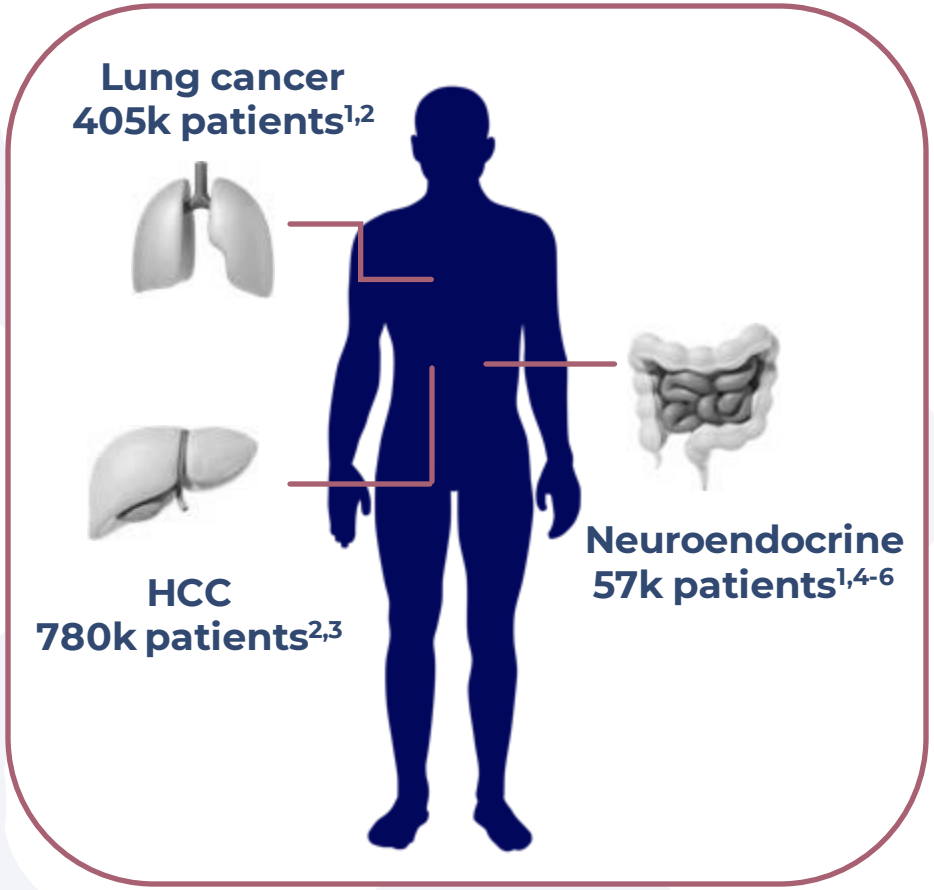
CT-01 (CPT-6281): First-in-Class GSPT1 Targeted Degrader for Hepatocellular Carcinoma (HCC)

CPT-6281 – first-in-class molecular glue degrader for hepatocellular carcinoma



The unique degradation profile of CPT-6281 leads to an Integrated Stress Response (ISR) and induction of apoptosis in HCC cells, while reduction of IL-1β levels in the tumor microenvironment may enable 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 tumors

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

(1) Semin Cancer Biol. 2006 Aug;16(4):253-64
(2) https://gco.iarc.fr/today/en/
(3) Nat Rev Dis Primers 7:6 (2021)
(4) Sci Rep. 2021 Apr 12;11(1)
(5) Endocr Connect. 2023 Nov 23;12(12)
(6) JAMA Oncol. 2017 Oct 1;3(10):1335-1342

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Epidemiology of Hepatocellular carcinoma

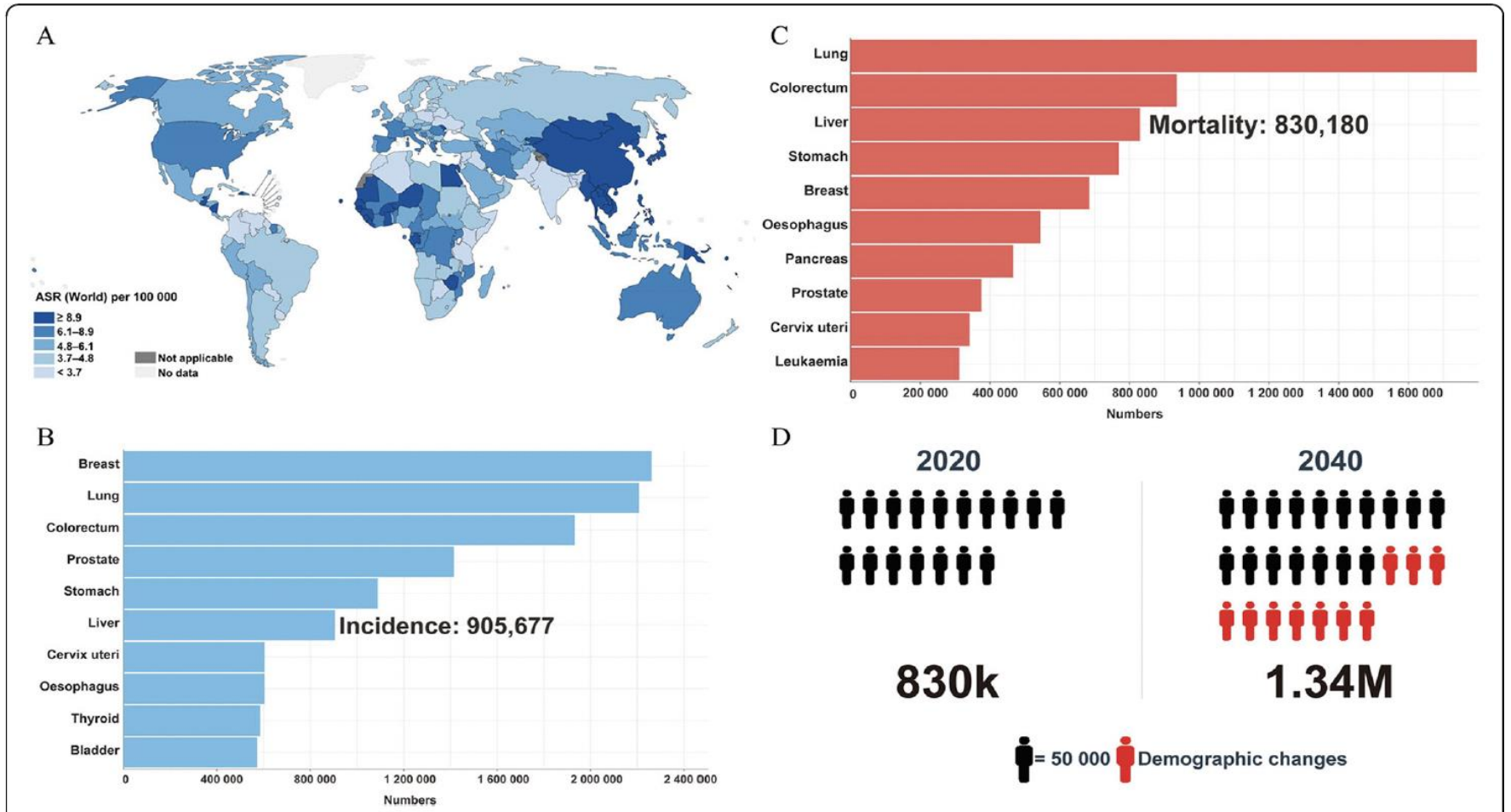

Fig. 1 Worldwide Epidemiology of Liver Cancer in 2020. Data source: GLOBOCAN 2020 (http://gco.iarc.fr/). (**A**) The estimated age-standardized incidences of liver cancer worldwide in 2020. (**B**) Bar charts of the estimated number of incident cases worldwide. (**C**) Bar charts of the estimated number of deaths worldwide. (**D**) WHO estimated the number of deaths from liver cancer from 2020 to 2040

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Current standard of care, changing causality, and opportunity

Line	Therapy	Survival Benefit vs Sorafenib	FDA Approval
1	TECENTRIQ atezolizumab + AVASTIN bevacizumab	+5.8 months[1]	Unresectable / metastatic HCC No prior therapy
1	IMFINZI durvalumab + IMJUDO tremelimumab-actl	+2.7 months[2]	Unresectable HCC
1 / 2	Nexavar (sorafenib) tablets	-[3]	Unresectable HCC
2	OPDIVO (nivolumab)	+1.7 months[4]	Unresectable HCC (Post sorafenib)
2	CABOMETYX (cabozantinib) tablets	+2.2 months[5]	Unresectable HCC (Post sorafenib)

Market projections are difficult as there are no truly effective therapies, however global market reports forecast around **15-20% CAGR**

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%

(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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Development status – 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	✓
Appointment of CRO to supervise clinical study	✓
GLP tox studies In-life phase -> completed Histopathology, TK, safety pharmacology analysis -> ongoing	✓
Drug Substance GMP manufacture	✓
Drug Product development and GMP manufacture	**Ongoing**
PK & PD assays development for the clinic	**Ongoing**
Investigator's brochure for clinical trials	**Final draft**

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HCC treatment with a GSPT1 degrader - status

Molecular Glue

- **Initial indication**
  - Hepatocellular carcinoma
- **Degradation profile**
  - GSPT1, NEK7
  - **Liver and lung activated pro-drug**
- **Strong differentiation from other GSPT1 degraders (BMS, MonteRosa)**
  - Best-in-class degradation profile
  - Tissue restrained prodrug expands therapeutic window
- **Development activities**
  - GLP-tox and GMP manufacturing complete
  - Drug product (capsules) in finalization
- **Expected milestones in 2024**
  - Clinical Trial Application submission and approval in Europe
  - Initiation of Phase 1 clinical trials in hepatocellular carcinoma in H2

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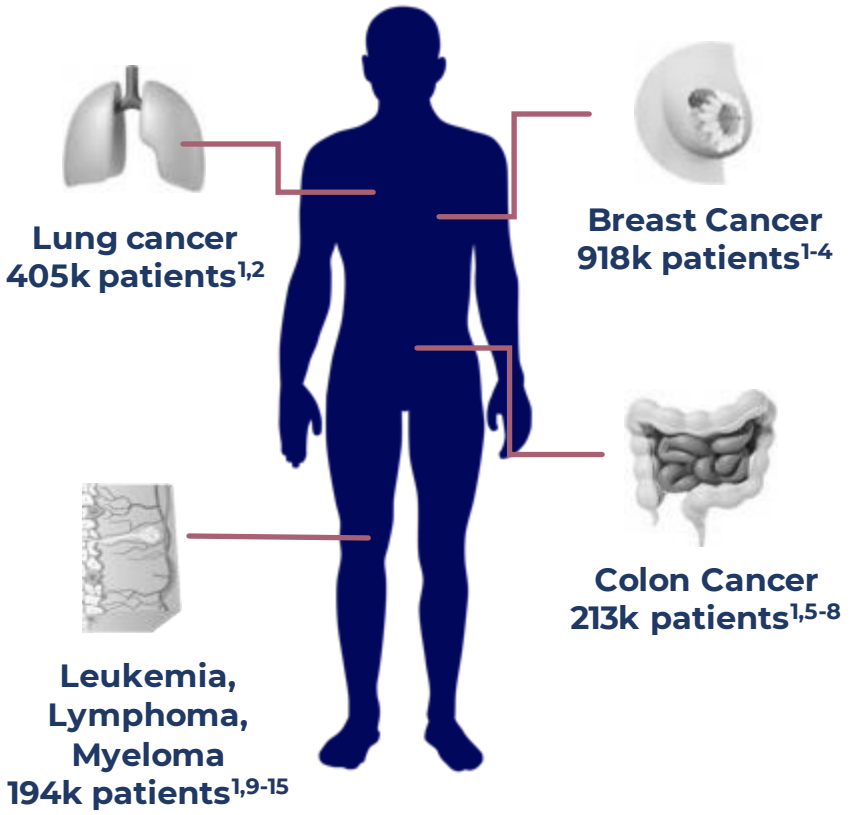
CT-03: First-in-Class MCL-1 Degraders for Liquid & Solid tumors

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



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

A critical resistance mechanism in haematological and solid tumors‡

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

Adequate ablation of MCL-1 requires rapid and sustained action & high target coverage

Use of inhibitors causes accumulation of MCL-1

Degraders have a different mode of action, without accumulation of MCL-1

Degradation of ~70% of MCL-1 induces apoptosis, while inhibitors require almost 100% of target coverage and cause accumulation of the MCL-1

This, together, with optimized clearance expands the therapeutic window from the perspective of toxicity

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

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MCL-1: a high potential cancer target

Highly attractive target with application in numerous cancer markets

Haematological malignancies

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

Acute Myeloid Leukaemia (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 from Pharma, no MCL-1 targeting drug has been approved and several inhibitors have been associated with toxicity

Captor has 2 lead degraders, CPT-908 and CPT-2036 and neither has shown any evidence so far of cardiotoxicity in keeping with their different mode of action from inhibitors

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

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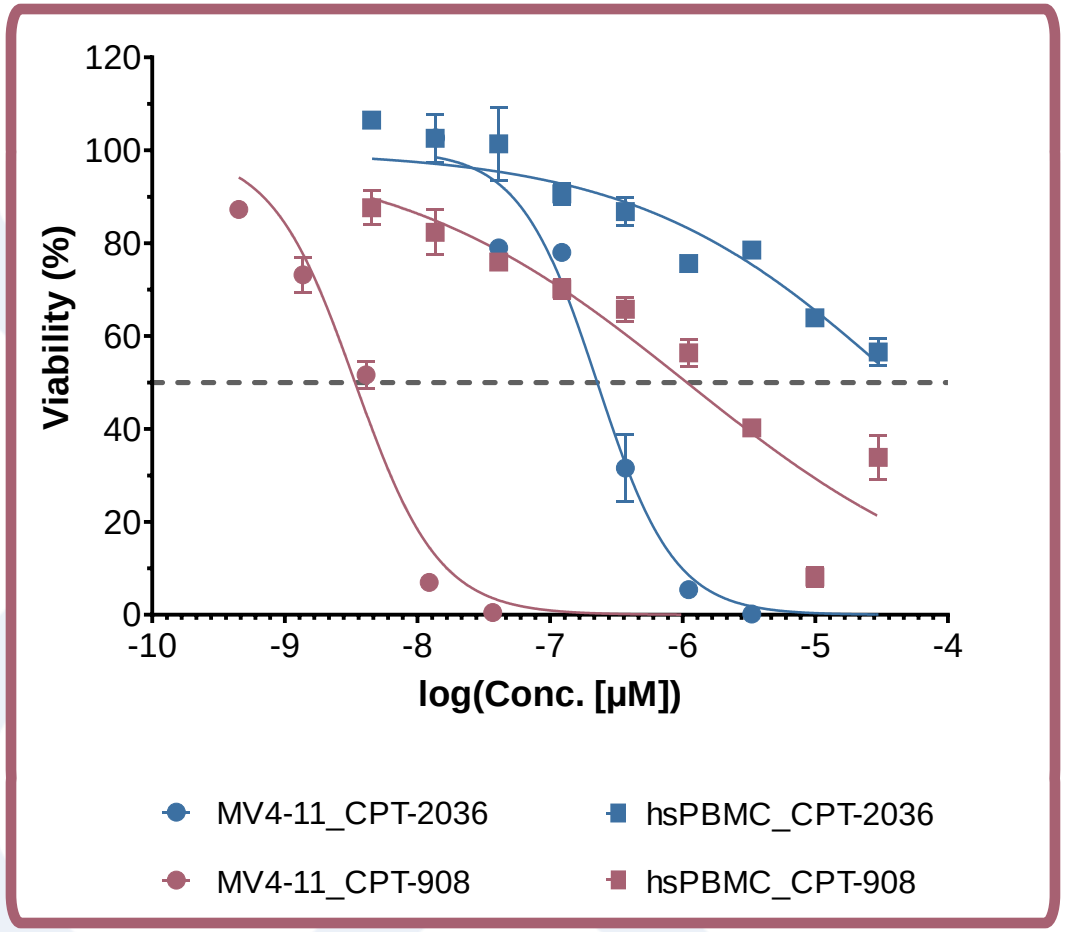
Human PBMCs and hiPSC-cardiomyocytes are much less sensitive to degradation



Cell line	IC_{50} [nM] CPT-2036	CPT-908
MV-4-11	119 +/-2.3 (N=21)	3 +/-1.1 (N=3)
MV-4-11 Ven-resistant	-	0.003
MV-4-11 Ven-resistant + Venetoclax	-	0.001
WSU-DLCL-2 (B-cell lymphoma)	3981 +/- 1.6	25 +/- 1.3
DMS 114	631+/-2.0	16+/-1.3
OPM-2 (MM)	251+/-1.6	<5 +/- 1.3
hsPBMC	12589 +/- 5.0	501 +/- 3.2
hiPSC-CM	15849 +/- 6.3	1585

PBMCs and hiPSC-cardiomyocytes are much less sensitive than cancer cell lines, even though MCL-1 is degraded

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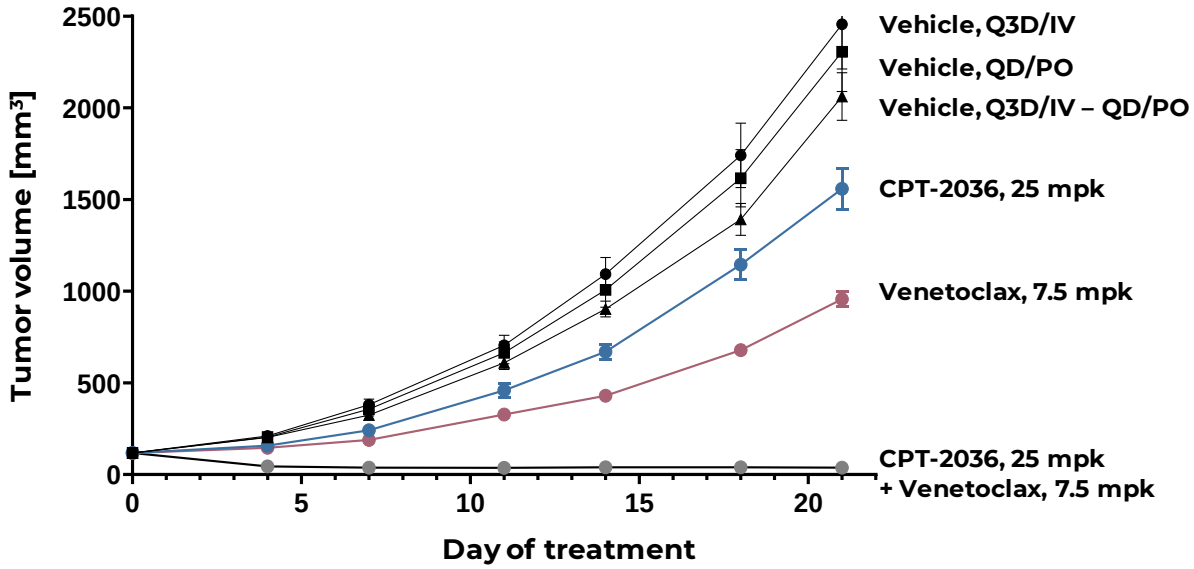
CPT-2036 regresses AML tumors in mice when combined with venetoclax



Regression of large tumors was observed for both CPR-2036 and venetoclax, with the combination providing the best outcome

CPT-2036 was administered 8 times, every 3 days (Q3D) intravenously and venetoclax was administered daily (QD) orally

CPT-2036 in combination with venetoclax strongly inhibits cancer growth in MV-4-11 Human Leukaemia Xenograft Model

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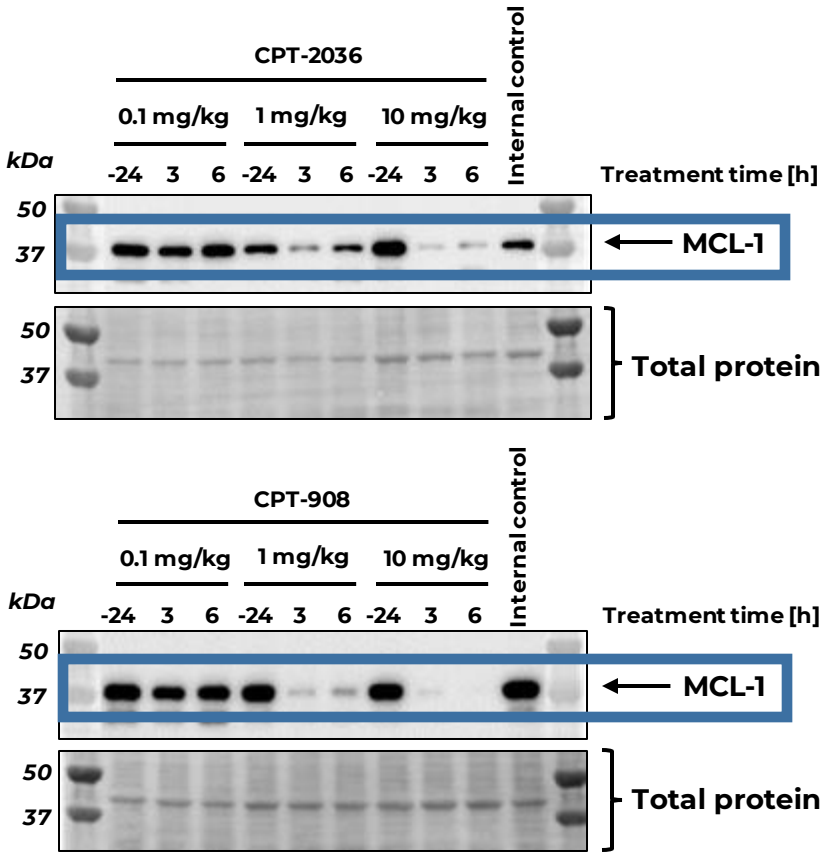
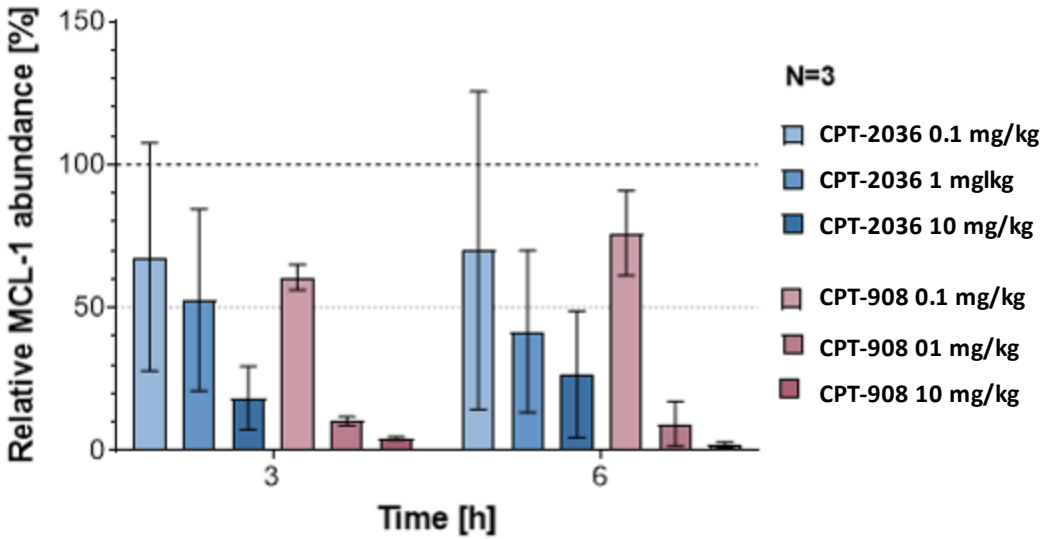
Strong PD effect of both CPT-908 & CPT-2036 *in vivo* (NHP PBMCs)





Male Cynomolgus Monkey, IV injection

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

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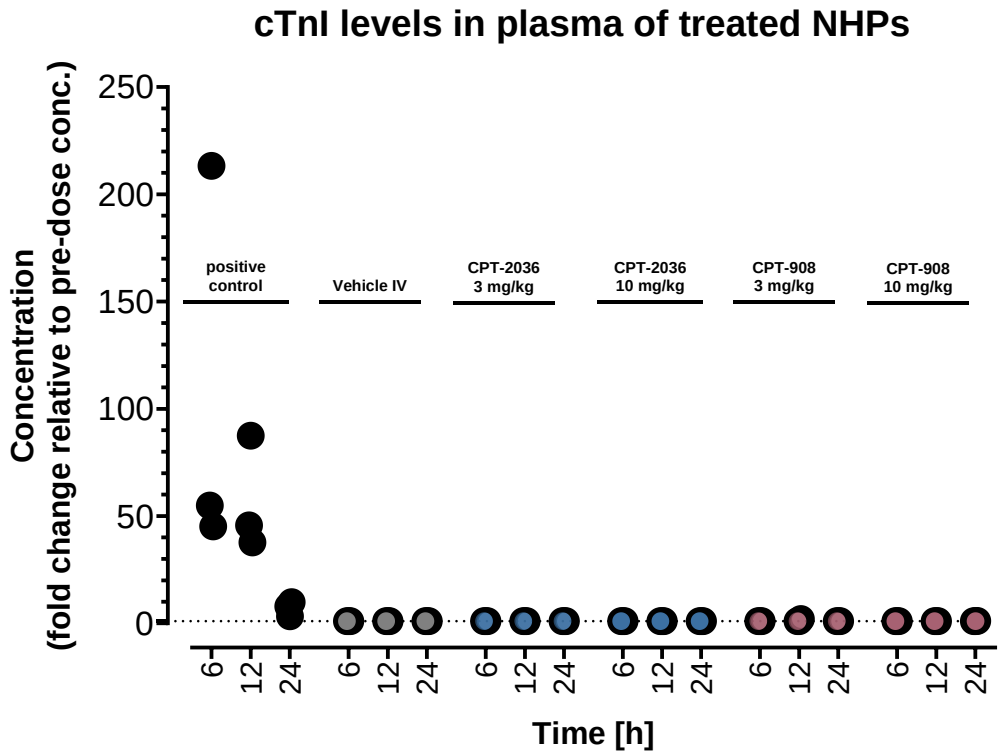
Cardiotoxicity marker Troponin I in plasma of NHPs after MCL-1 degrader dosing



No observed changes in cardiac troponin levels were significantly different from the vehicle control

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

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Status: CT-03

Bifunctional Degrader

- **Initial indications**
  - Blood cancers, subsequently solid tumors
- **Degradation profile**
  - Selective first-in-class MCL-1 degraders
- **Development activities**
  - Efficacy proven *in vivo*
  - Candidate selection studies underway
  - No indicators of cardiac safety issues
- **Expected milestones**
  - Candidate selection planned for 2024
  - IND-enabling studies 2024

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CT-02: First-in-Class NEK7 Degraders for Autoimmune & Neurodegenerative Diseases

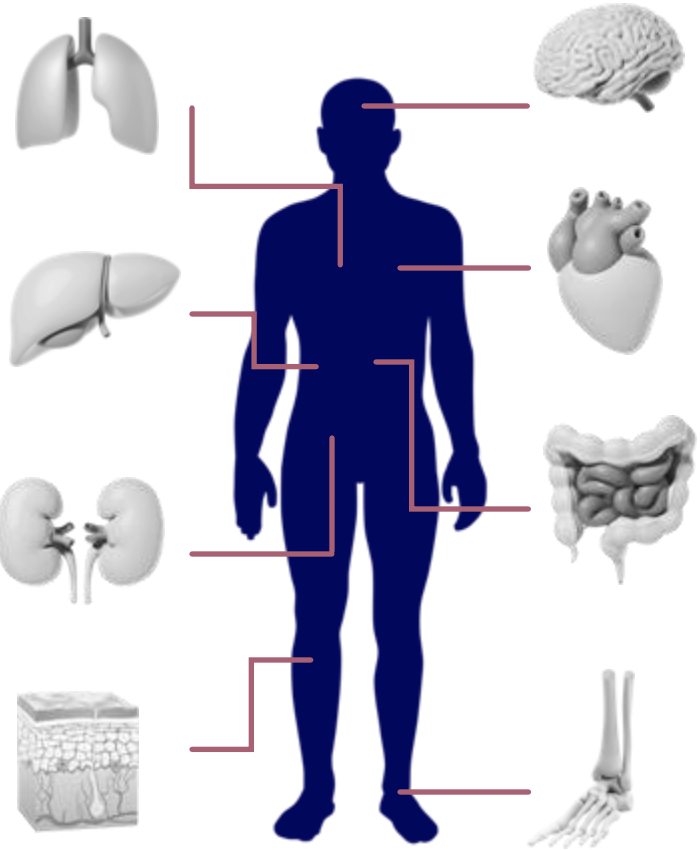
CT-02: Vast market potential for inflammasome modulators

Allergy
Asthma

Fibrotic diseases

Lupus nephritis

Psoriasis



Neuroinflammation
(AD, PD, MS, ALS)

Myocardial infarction
Diabetic cardiomyopathy

Inflammatory Bowel Disease

Gout
Rheumatoid Arthritis

NEK7 degradation inhibits inflammasome formation and, consequently, the production of inflammatory cytokines leading to the reduction of symptoms of immune-related diseases.

Recent publications demonstrate the potential role of CNS inflammasome in weight loss

Two series of potent NEK7 degraders:

CPT-513 - systemic therapy for the treatment of **autoimmune disorders**

CPT-101 - therapy of inflammatory **neurodegenerative disorders**

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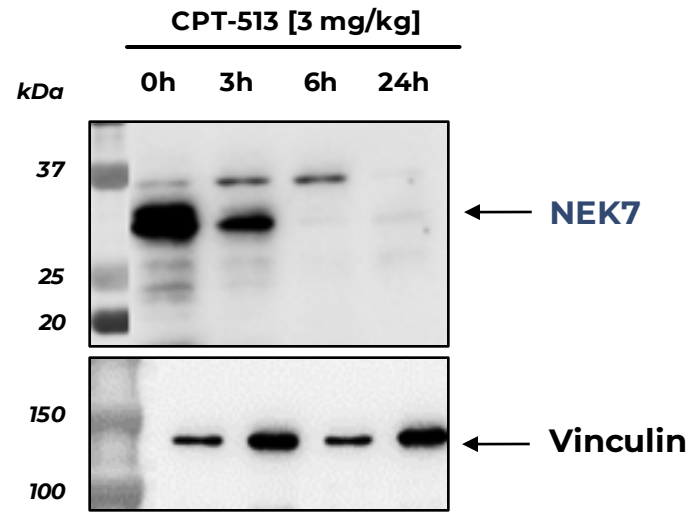
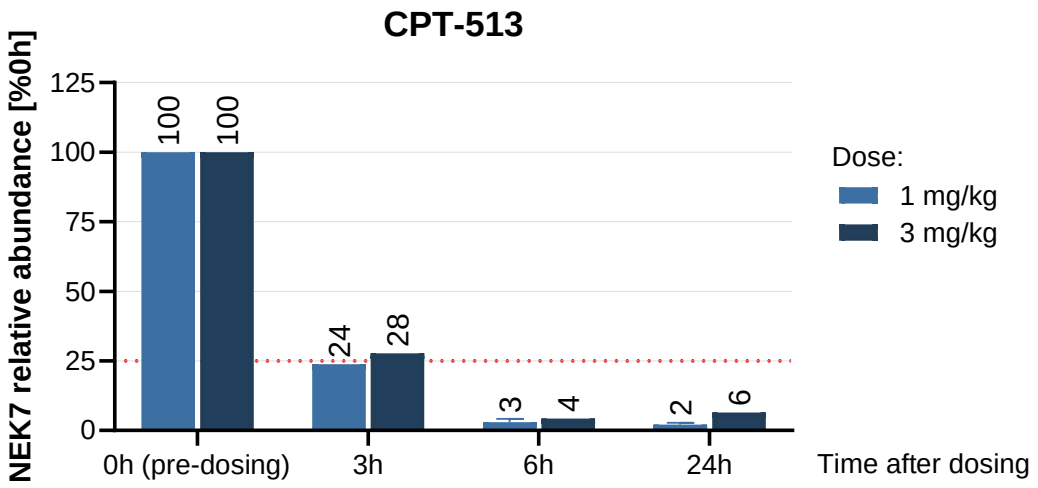
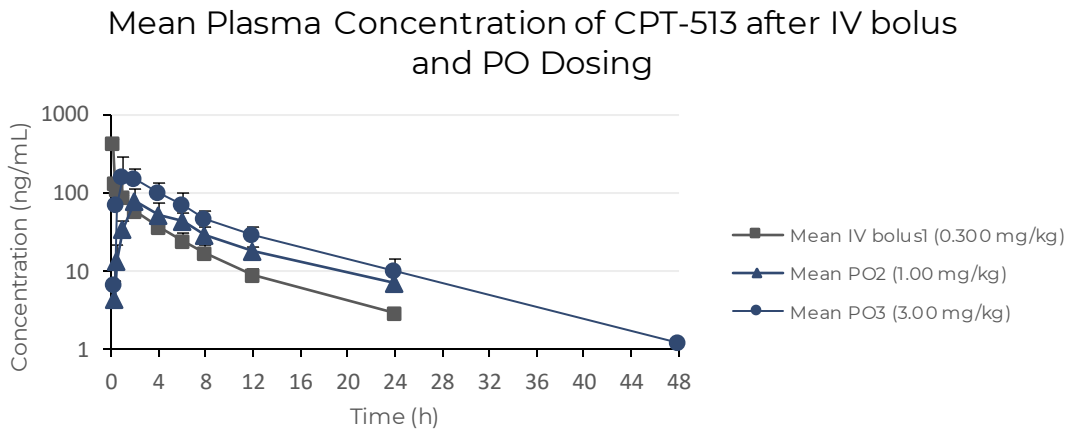
CPT-513 efficiently covers and degrades NEK7 in NHPs







NEK7 degradation is observed in monkey PBMCs isolated at 3, 6, and 24 h after CPT-513 PO [1 & 3 mg/kg] administration

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CT-02: Excellent degraders from two different strategies

Two series of potent NEK7 degraders - in **autoimmune diseases** (CPT-513) and **neurodegenerative disorders** (CPT-101, brain-penetrant series)

Activity confirmed both *in vitro* on 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

SCHEDULED H1 2024

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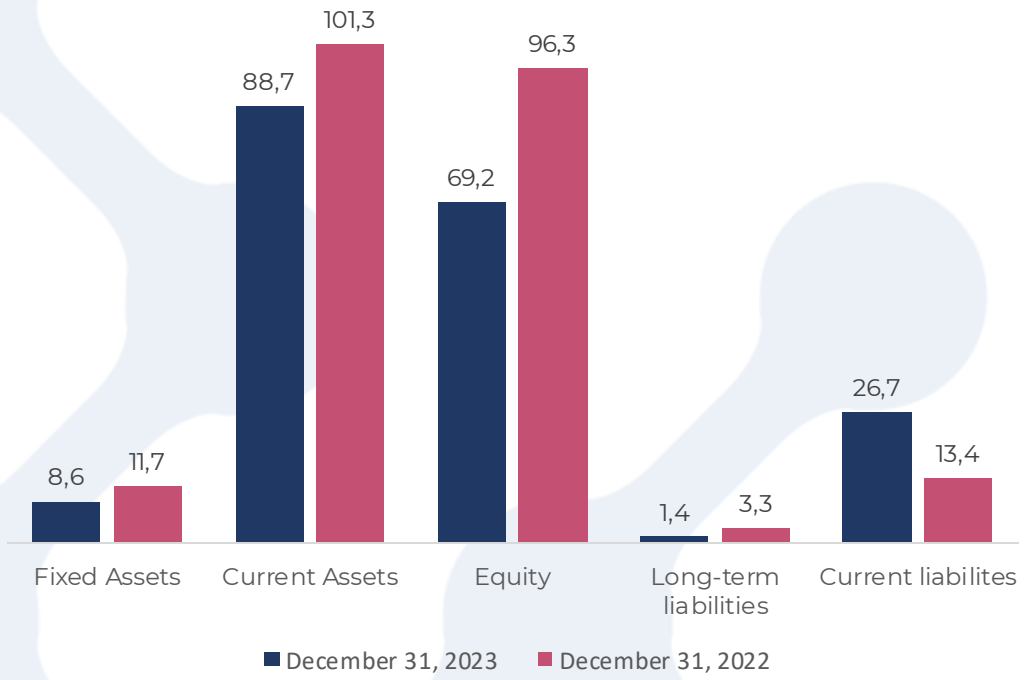
Finance Highlights

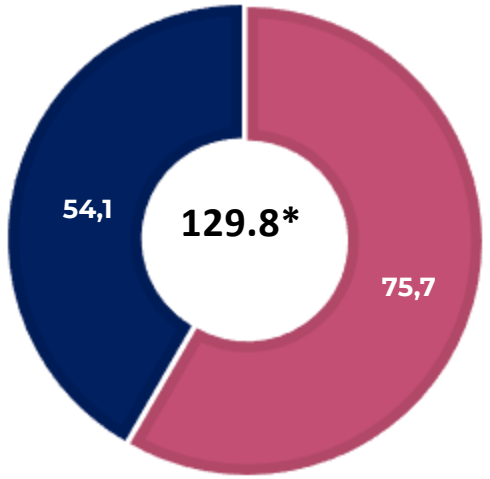
Balance sheet and cash position

Consolidated statement of financial position (PLN, M)



Cash position

Available funding secured
(PLN, M; as of December 31, 2023)



Total : PLN 129.8 M*

- PLN 75.7 cash
- PLN 54.1 available grants (NCBR; ABM)

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

R&D costs in 2023

Total : PLN 77.1 M

Net Operational Cash Flow
(excluding equity Investment)
Total: PLN 52.2 M

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

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

Captor Therapeutics GmbH
Hegenheimermattweg 167A
4123 Allschwil, Switzerland

Contact: investor.relations@captortherapeutics.com