Captor Therapeutics®

Promising research results in two flagship projects

20th January 2022

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Multistage studies are required before the drug can be administrated to the patient

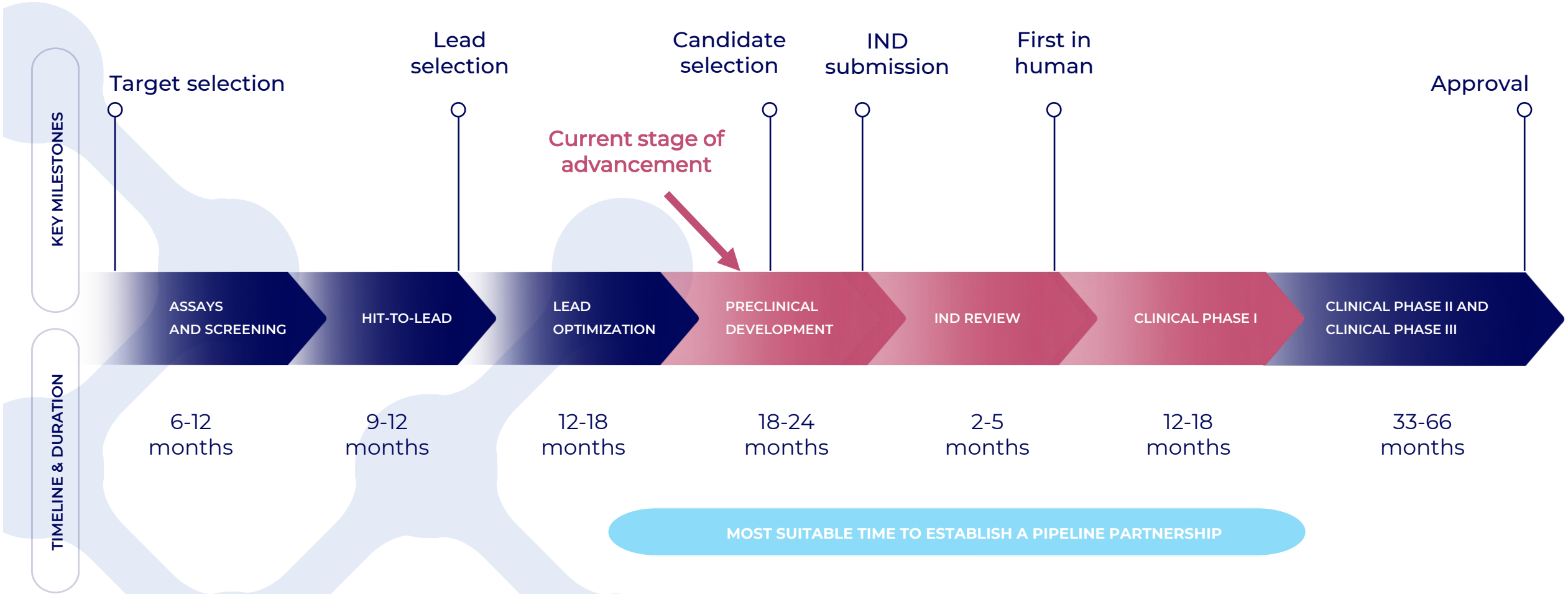
**Positive results of the animal studies –
a breakthrough towards clinical development**

Increasing predictive value of the data

The Captor pipeline

Preclinical stage include IND-enabling studies
***First in Human; at least 2 projects expected to enter Phase 1 by 2023*
***BID** – Bi-functional Degrader; **MG** – Molecular Glue*

CT-01 & CT-03 candidate selection in 2022



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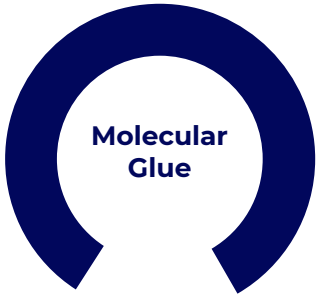
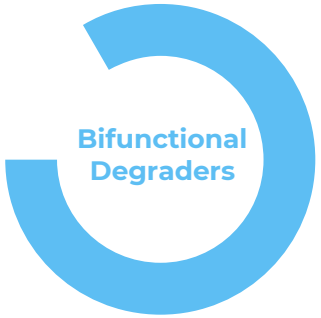
2 drug candidates advancing towards the clinics



Project: CT-01
Target: Undisclosed
Main indication:
hepatocellular carcinoma

- ✓ Anticancer activity in different HCC models *in vitro**
- ✓ Good efficacy achieved after oral administration
- ✓ Strong tumor inhibition and tumor regression shown in mice bearing HCC tumors demonstrated with two candidate molecules *in vivo***



Project: CT-03
Target: MCL-1
Main indications:
blood cancers

- ✓ Anticancer activity *in vitro** in both liquid and solid tumors
- ✓ Potent and sustained MCL-1 degradation *in vivo* after single dose
- ✓ Cancer cells' killing *in vivo***

To enter clinical trials in 2023

** In vitro – outside of the living organism, **in vivo – in the living organism*

Captor Therapeutics®

DEMONSTRATING THE POTENTIAL OF CAPTOR'S TPD PLATFORM

CT-03: First-in-class MCL-1 degraders

CT-03 | MCL-1 – High potential target yet undrugged

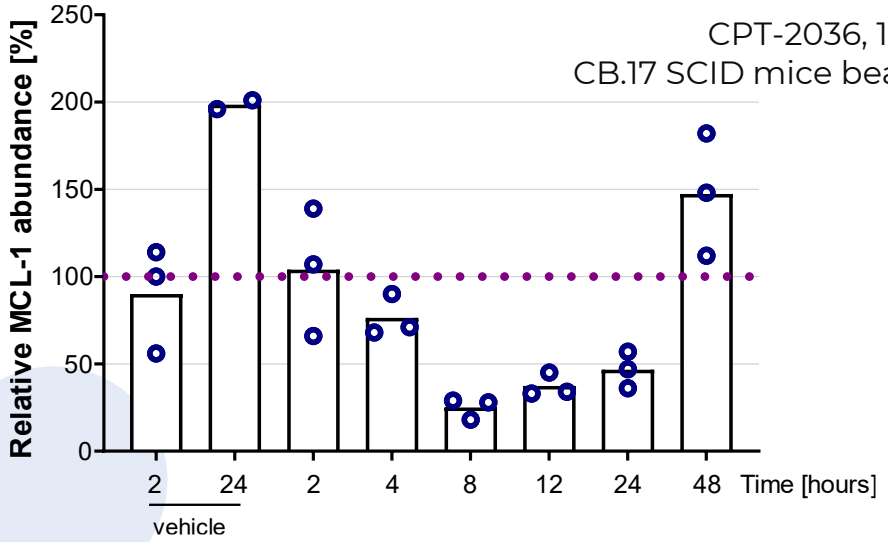
- MCL-1 is implicated in **cancer cells resistance** resistance to drugs
- Highly attractive target as it serves as a **major pro-survival signal** in:
  - Haematological malignancies (including Multiple Myeloma (MM), Acute Myeloid Leukaemia (AML), and non-Hodgkin Lymphoma (NHL))
  - Selected solid tumors (small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC) and triple-negative breast cancer (TNBC))
- Despite years of effort **no MCL-1 targeting drug** has been successfully developed

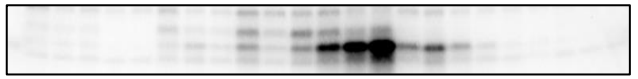
- **Classical approach has failed** to develop efficacious MCL-1 inhibitors
  - ➢ **Challenging for classical approaches** because of high affinity of MCL-1 for its natural ligands

Significant interest from large pharma on MCL-1 Inhibitors

Company	Inhibitor	Phase	Start date	Current state
Amgen	AMG 176	Phase 1	Q2 2016	Ongoing
	AMG 397	Phase 1	Q3 2018	Terminated in Q3 2019
	AMG 176 + Venetoclax	Phase 1	Q1 2019	Suspended in Q4 2020
Servier & Novartis (MIK665)	S64315	Phase 1	Q1 2017	Completed in Q2 2020
	MIK665	Phase 1	Q3 2017	Completed in Q3 2019
	S64315 + Venetoclax	Phase 1	Q4 2018	Ongoing
	S64315 + Azacitidine	Phase 1/2	Q1 2021	Ongoing
	S64315 + VOB560	Phase 1	Q2 2021	Ongoing
AstraZeneca	AZD5991	Phase 1	Q3 2017	Suspended in Q4 2020
	AZD5991 + Venetoclax	Phase 2	Q3 2017	Ongoing
AbbVie	ABBV-467	Phase 1	Q2 2020	Terminated in Q2 2021
Prelude	PRT1419	Phase 1	Q3 2020	Ongoing
	PRT1419	Phase 1	Q3 2021	Ongoing

*In Vivo d*egradation and apoptosis induction





Cleaved form of caspase 3 indicated apoptosis activation

- Already after single dose of CPT-2036, a strong degradation of MCL-1 was achieved and sustained for 24 hours
- A strong apoptotic effect in cancer cells was demonstrated in addition to the degradation

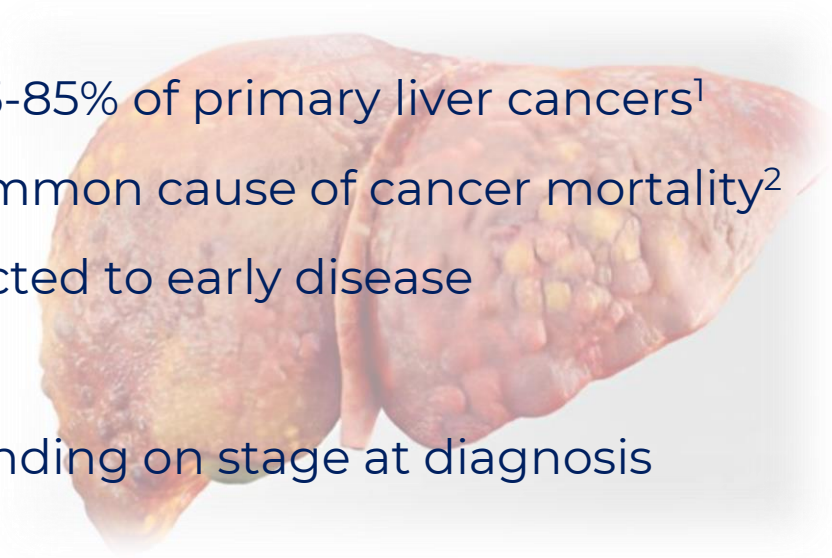
Captor Therapeutics®

DEMONSTRATING THE POTENTIAL OF CAPTOR'S TPD PLATFORM

CT-01: Addressing one of the deadliest cancers with Captor's molecular glue degrader drugs

CT-01: Addressing one of the deadliest cancers

- Hepatocellular Carcinoma (HCC) accounts for 75-85% of primary liver cancers[1]
- ~ 700 000 new cases each year, the 2nd most common cause of cancer mortality[2]
- Curative treatments (tumor resection) are restricted to early disease
- High rate of metastases
- 5-year Survival Rates[3] vary from 3% to 34% depending on stage at diagnosis



References: [1] Global Cancer Statistics 2018, [2] Data for the US, 2010-2016, ACS Cancer Facts & Figures, [3] DOI: 10.1200/JCO.2021.39.3_suppl.267

Approved drugs offer modest therapeutic benefit

- 2007 – **Sorafenib** approved as first-line treatment in HCC in 2007 – survival **2.8 months** longer as compared to no drug*
- 2020 - Combination of **Atezolizumab** (TECENTRIQ®) **plus Bevacizumab** (AVASTIN®) – **5.8 months** longer survival as compared to Sorafenib**

In overall, a patient with unresectable liver tumor treated with standard of care**:

- on average lives for 19.2 months,
- only 29.8% of patents respond to the treatment.

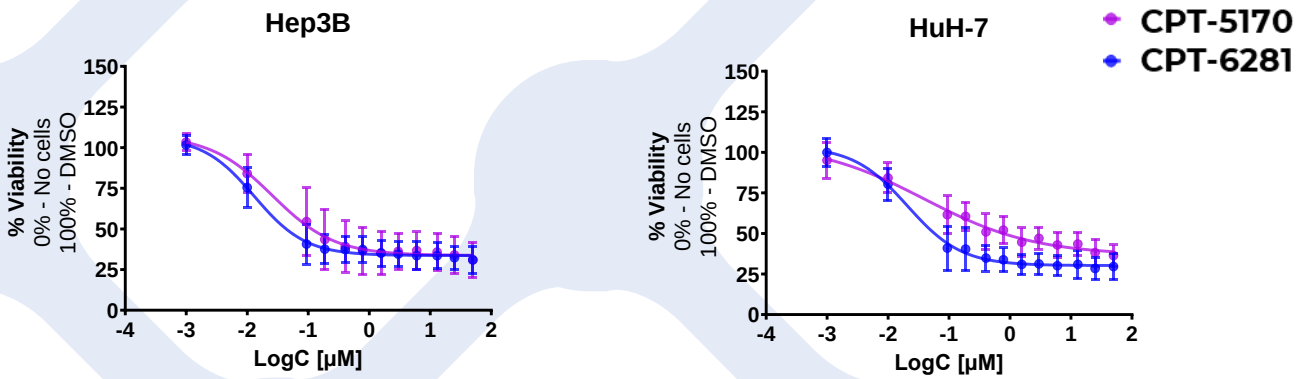
** Llovet J et al. 2007, DOI: 10.1200/jco.2007.25.18_suppl.lba1*

*** IMBrave 150, DOI: 10.1056/NEJMoa1915745, updated: DOI: 10.1200/JCO.2021.39.3_suppl.267*

CT-01 - molecular glue programme in HCC

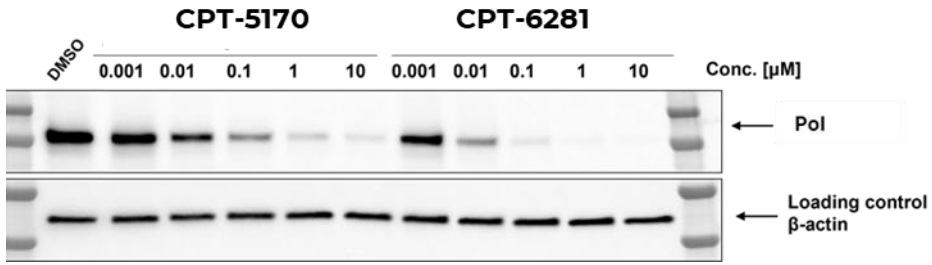
- Derived from the Captor proprietary library of molecular glues
- Active against a panel of HCC cell lines
- So far, no molecular glue drug has been approved in solid tumors

Cytotoxic effect in liver cancer cell lines



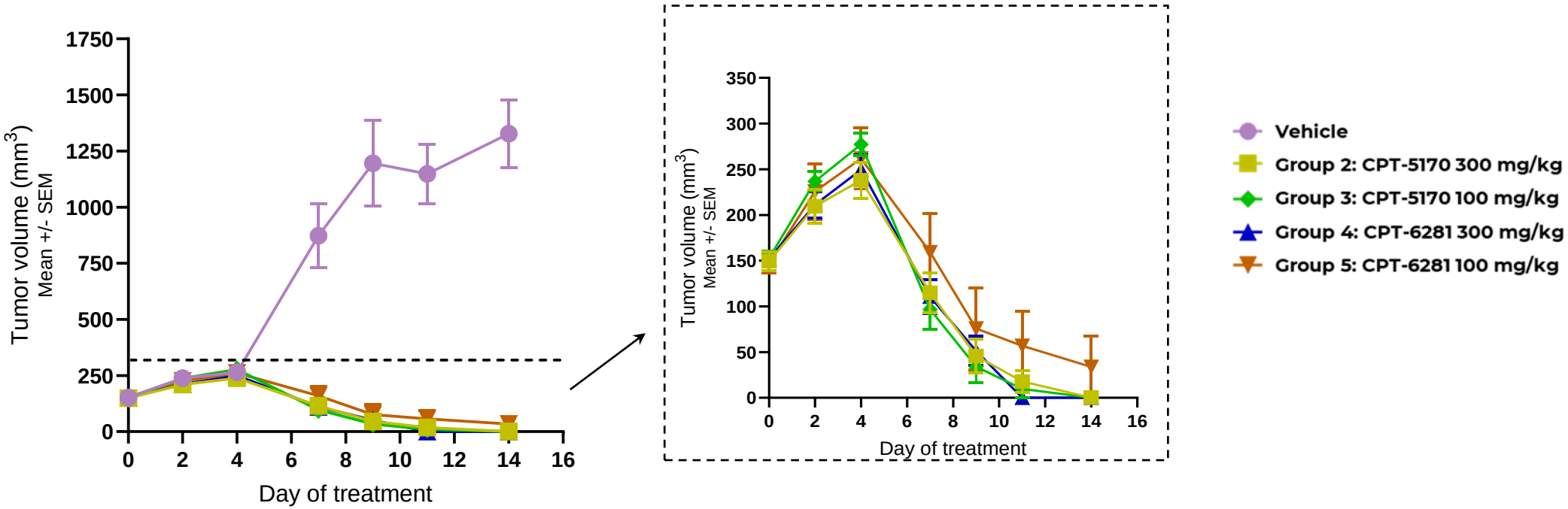
72 hours, CTG assay

Potent degradation of PoI with CT-01 compounds



HEP3B cells, 24 hours

In vivo proof-of-concept – tumor regression

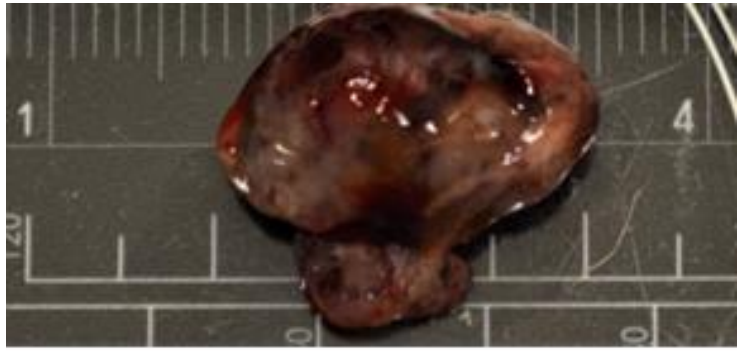


Human liver cancer model - Hep 3B2.1-7 (NSG mice)
The study performed by reputable subcontractor Covance/LabCorp

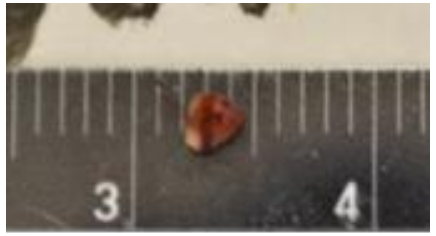
- 2 CT-01 degraders induced **tumor regression** following **oral administration**
  - Both compounds were very **well tolerated** by the animals

In vivo proof-of-concept – tumor regression

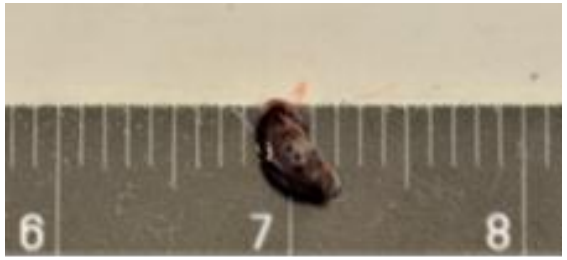
Representative exampled of tumors after study termination



Vehicle
Group 1, animal #7



CPT-5170, 100 mg/kg
Group 3, animal #2



CPT-6281, 100 mg/kg
Group 5, animal #1

CT-01 and CT-03 candidate selection in 2023

Recent ***in vivo*** results demonstrate:

- ✓ **tumor regression (depletion)** in the mouse model of hepatocellular carcinoma, following treatment with **CT-01 degraders ,** and **high tolerability** of the compounds
- ✓ Achievement of the goal – **protein degradation and cancer cell death** – in mouse model of acute myeloid leukemia following treatment with **CT-03 degraders**

build our confidence in further development of the compounds, and constitute milestones towards the **clinical development**

Next steps in 2022:

- ✓ Further *in vivo* testing and selection of the best compounds for **clinical candidates**
- ✓ **Synthesis upscale** of the selected compounds
- ✓ Initiation of **the IND-enabling studies**

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Thank you!

All images by Piotr Piatek