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H1 2024 Results

All images by Piotr Piatek

H1 2024 update – top line

- Captor submitted the application for clinical trial authorisation in Europe for the CT-01 project in August 2024
  - Site recruitment to the CT-01 clinical study in liver cancer patients has gone exceptionally well
- CT-02 (NEK7) and CT-03 (MCL-1) continue to advance
  - *In-vivo* proof of concept obtained in three different disease models for CT-02
  - Strong *in-vivo* data in non-human primates confirms the potential of CT-03 to potently degrade MCL-1 at doses with no signs of cardio-toxicity
  - Business discussions continue with interested parties, particularly in the area of inflammation (CT-02 and CT-05)
- In keeping with the focus on our leading projects, the net loss, cash outflow, and cash balance were improved compared to H1 2023

The Clinical Team taking CT-01 forward

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

Robert Dyjas, M.D. Ph.D.
Head of Medical Affairs
and Clinical Development

- Specialization in internal diseases
- PhD in medicine, Silesian Medical University
- 25 years' experience in clinical research, medical affairs and clinical development

EDUCATION

Trinity College Dublin
The University of Dublin

ŚLĄSKI UNIWERSYTET MEDYCZNY W KATOWICACH

PREVIOUS EXPERIENCE

Lilly
Roche
pharmacyclics
An AbbVie Company

OncoArendi Therapeutics
SGS
Roche
janssen

Fully owned pipeline

Program	Primary Target	Indications	Modality	Discovery	Preclinical*	IND Filing	Phase IA / IB	Phase II
CT-01	**GSPT1**	**Hepatocellular carcinoma**, Lung cancer, NET tumors	**MG**					
CT-02	**NEK7**	Autoimmunity, CNS, Metabolism, Oncology	**MG**					
CT-03	**MCL-1**	Liquid & solid tumors	**BIFD**					
CT-05	**PKCΘ**	Autoimmunity, Oncology, Transplantation, Metabolism	**BIFD**					
	New target projects	Autoimmunity, Cancer	**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

Clinical Research Organisation

ICON Clinical Research Limited

(Dublin, Ireland)

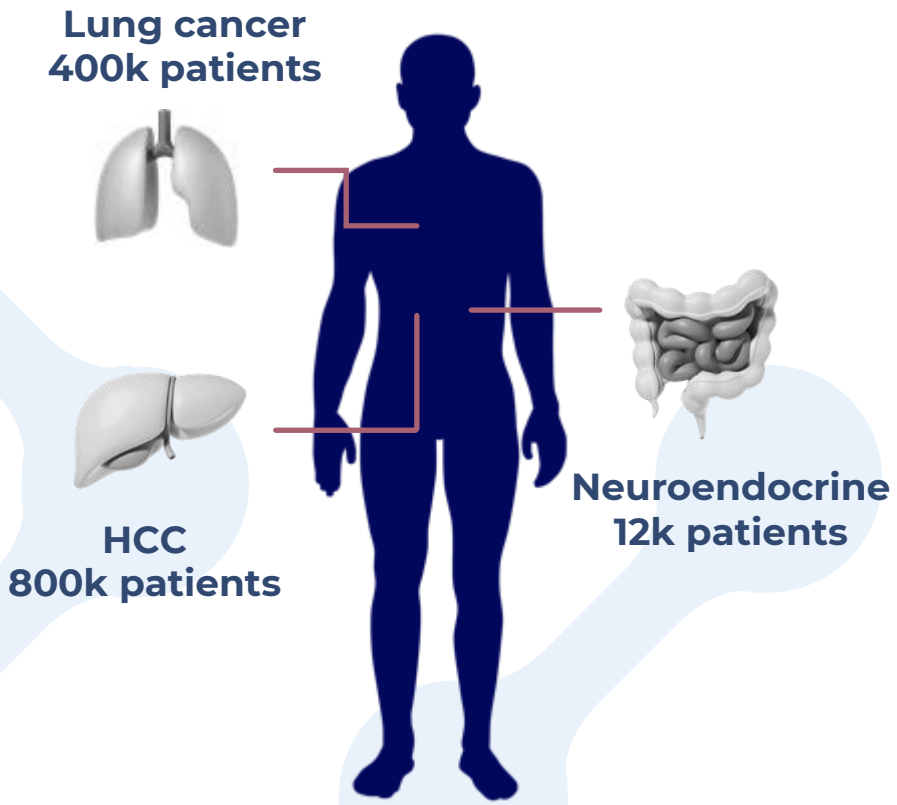
World leader in the field of providing innovative solutions in the healthcare system and CRO

(Clinical Research Organization)

Design and conduct of the first phase of clinical trials of a new, innovative anticancer drug within the CT-01 project

CT-01: First-in-Class GSTP1 Targeted Degrader for Hepatocellular Carcinoma (HCC)

CT-01: Multi-target GSPT1, NEK7 & SALL4 degrader



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

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 and neuroendocrine cancers

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Liver cancer

Liver cancer

- Fifth most common cancer
- Second most frequent cause of cancer-related death globally
  - 905,000 new cases and 830,000 deaths per year
- 7% of all cancers

Hepatocellular Carcinoma (HCC)

- Accounts for approximately 90% of primary liver cancers
- Constitutes a major global health problem
- Metabolic diseases (e.g. obesity, T2D) are major drivers of new cases

Epidemiology of Hepatocellular carcinoma

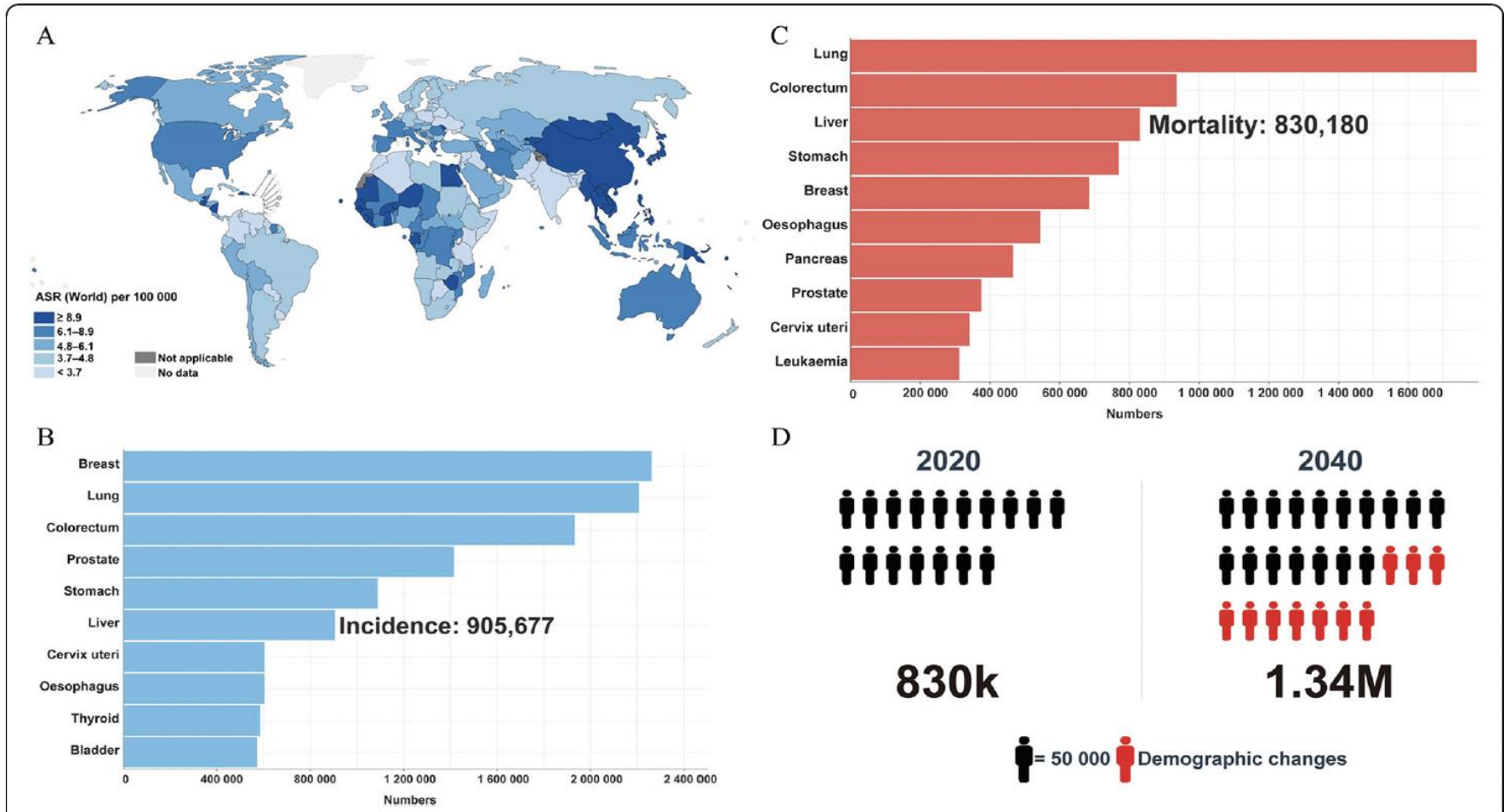

Fig. 1 Worldwide Epidemiology of Liver Cancer in 2020. Data source: GLOBOCAN 2020 (http://gco.iarc.fr/). (**A**) The estimated age-standardized incidences of liver cancer worldwide in 2020. (**B**) Bar charts of the estimated number of incident cases worldwide. (**C**) Bar charts of the estimated number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

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HCC: current standard of care 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%

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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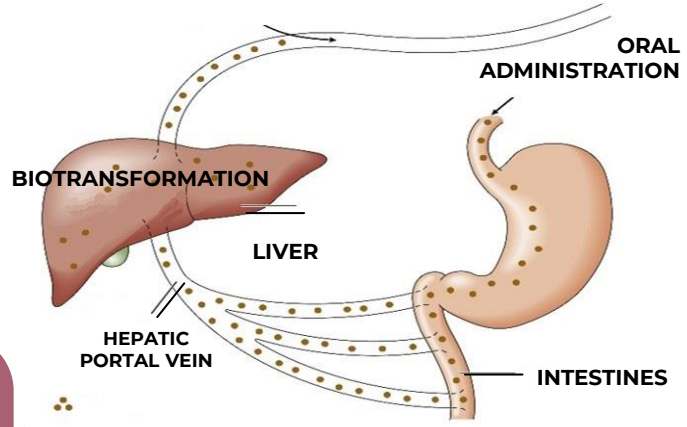
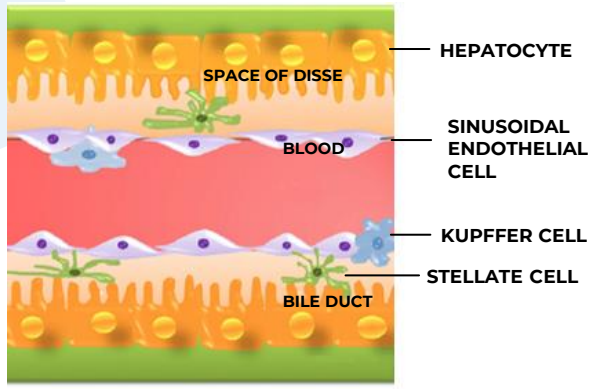
A key advantage of CT-01 for hepatocellular carcinoma

This should result in higher concentration of CT-01 active drug in HCC cells than other tissues

Thus improving therapeutic window





The enzyme is present in LSECs and stellate cells in the liver

Oral drugs pass through the liver before entering the systemic circulation

The first step of CT-01 conversion into the active metabolite is mediated by a specific enzyme

This enzyme is normally present at low levels but elevated in patients with diseased liver, including HCC

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CT-01: Progress to the clinic

- *In vitro & in vivo* pharmacology studies ✓
- Drug substance synthesis optimization and manufacture in a large scale ✓
- DMPK studies ✓
- Preliminary toxicology studies in 2 animal species ✓
- Toxicology studies under GLP (GLP Tox) ✓
- Drug substance manufacture under GMP ✓
- Drug product – capsule preparation ✓
- CTIS (Clinical Trial Information System) package preparation and submission ✓
- Clinical Trial Application Assessment

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Status: CT-01

Molecular Glue

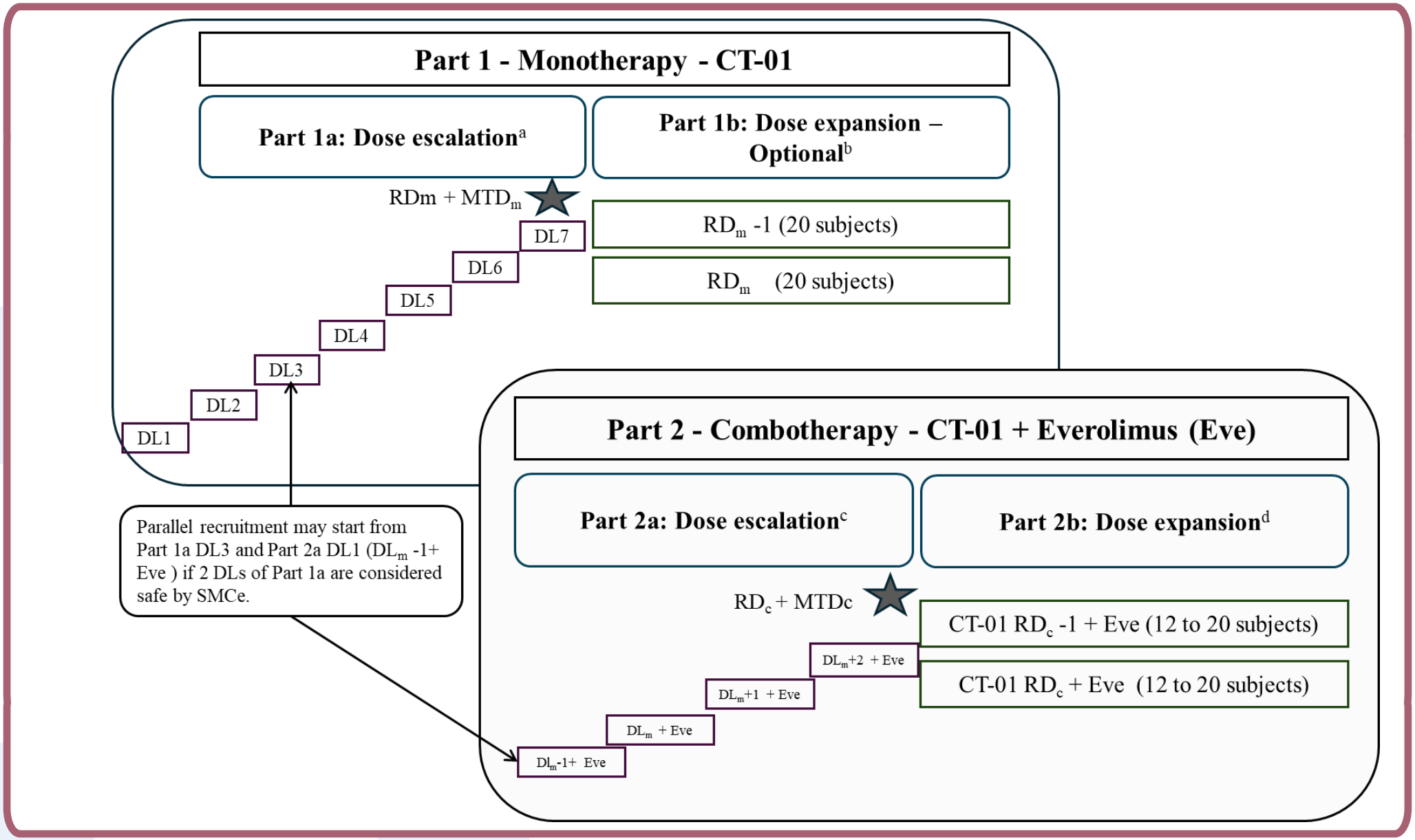
- **Initial indication**
  - Hepatocellular carcinoma
- **Degradation profile**
  - GSPT1, NEK7
  - Activated in diseased liver & lung
- **Differentiation from other GSPT1 degraders (BMS, Monte Rosa): potential for improved therapeutic window**
  - Oral pro-drug that goes to the target organ (liver) before entering the systemic circulation
  - Pro-drug is activated inside liver cells
  - Active degrader has poor cell membrane penetration (lingers inside cancer cells after activation)
  - Active degrader is rapidly cleared from the systemic circulation
- **Development activities**
  - DRF studies complete
  - GLP toxicology complete
  - Manufacturing scale-up complete
  - Clinical Trial Application submitted
- **Awaiting review by regulatory agency under the centralized procedure**

Phase 1a/b Clinical Plan

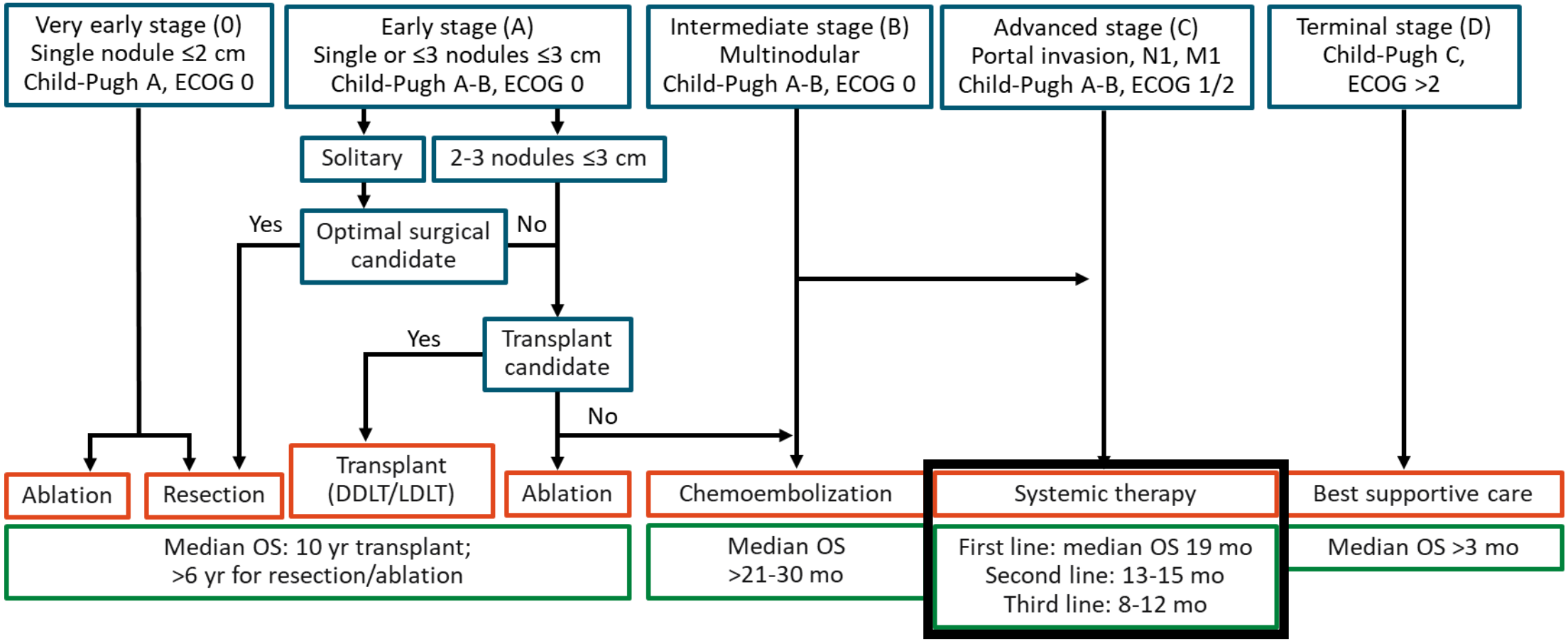
Protocol: CT-01-CD-01

A Phase 1, Open-Label, Dose Escalation, and Dose Expansion Study to Evaluate Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of CT-01 as Monotherapy and Combination Therapy with Everolimus in Subjects with Intermediate or Advanced Hepatocellular Carcinoma (BCLC Stage B or C) with Preserved Liver Function (Child-Pugh Class A)

Study design



Study design



- **Investigational group**: patients progressed/intolerant to SoC (ATZ/BEV), or Sorafenib/Lenvatinib
- Advanced HCC (BCLC-stage B-C), Child-Pugh A, ECOG 0-1

Endpoints in both parts of the study

Primary endpoints:

- Incidence of treatment-emergent adverse events (TEAEs), adverse events of special interest (AESIs), serious adverse events (SAEs)
- Incidence of DLTs
- Changes from baseline in vital signs, physical examinations, electrocardiogram (ECG), echocardiogram (including left ventricular ejection fraction [LVEF] assessment), and clinical laboratory tests
- MTDm/c which will be based on the incidence of DLTs of CT-01 monotherapy and combo
- RP2Dm/c which will be identified based on the assessment of safety and tolerability, efficacy, and PK

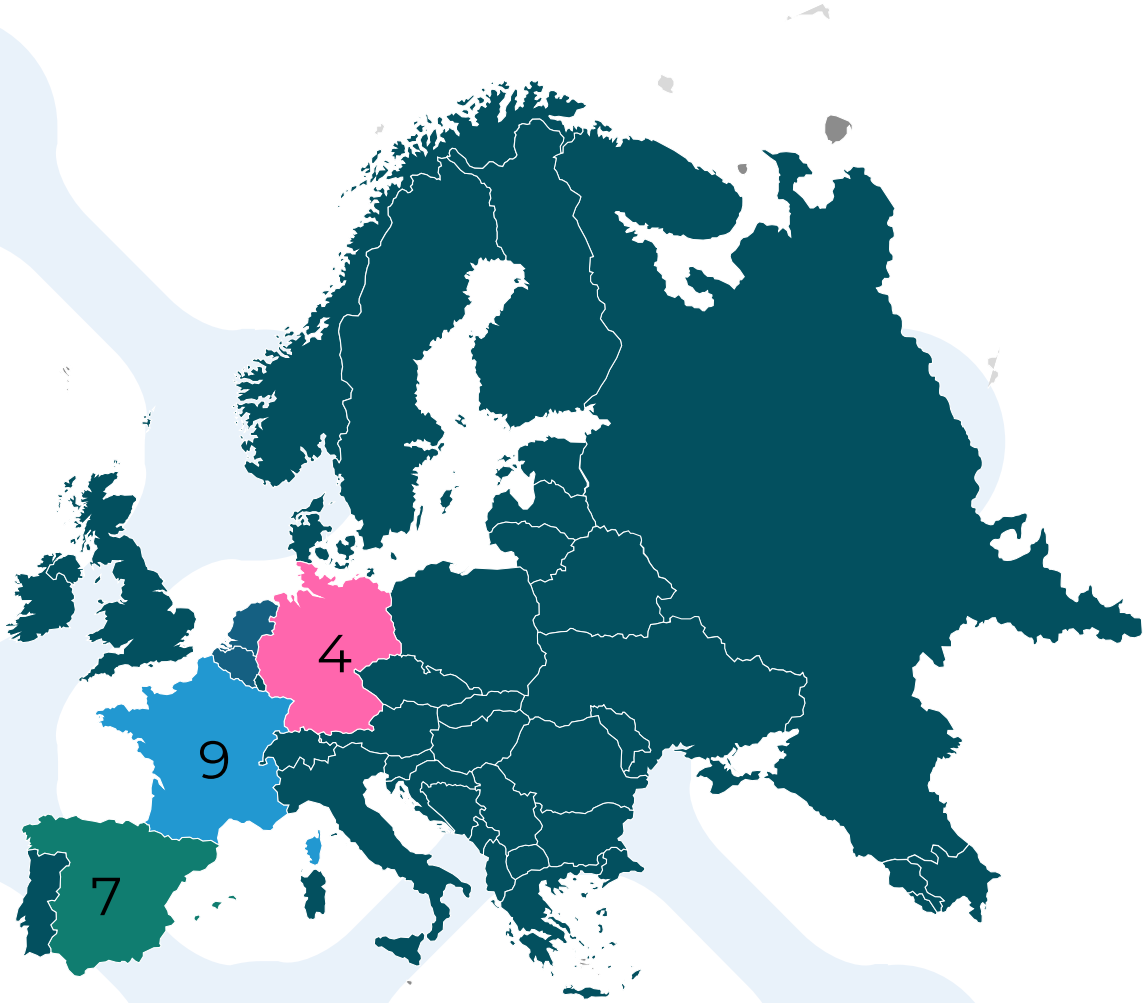
Secondary endpoints:

- Anti-tumor activity (ORR per RECIST), PK, changes in biomarkers (AFP, ALBI)

Exploratory endpoints:

- Changes of GSPT1 and NEK7 protein in blood samples in response to CT-01 monotherapy
- Changes of integrated stress response (ISR) genes (eg, activating transcription factor 3 [ATF3] and DNA damage inducible transcript 3 [DDIT3]) messenger RNA (mRNA) levels in blood samples in response to CT-01 monotherapy
- Correlation between systemic drug exposure and anti-tumor activity endpoints

Sites recruited to the Study



*20 selected sites on 17-Apr-24

Country	Site #	Institution name
Germany	GER-003	Universitätsmedizin der Johannes Gutenberg-Universität Mainz
	GER-005	Universitätsklinikum Bonn
	GER-002	Universitätsklinikum Leipzig
	GER-004	Universitätsklinikum Heidelberg

Country	Site #	Institution name
France	FRA-003	Centre Hospitalier Universitaire Nantes - Hôtel Dieu
	FRA-001	Centre Hospitalier Universitaire de Poitiers
	FRA-004	Centre Georges François Leclerc
	FRA-007	Institut Universitaire du Cancer de Toulouse Oncopole
	FRA-005	Les Hôpitaux Universitaires de Strasbourg
	FRA-006	Centre Léon Bérard
	FRA-008	Gustave Roussy
	FRA-002	Centre Eugène Marquis
	FRA-009	Hôpital Avicenne

Country	Site #	Institution name
Spain	SPA-002	Hospital Universitari Vall d'Hebrón
	SPA-005	Hospital Clinic de Barcelona
	SPA-007	Consorci Hospital General Universitari de València
	SPA-001	Hospital Universitario La Paz
	SPA-004	Hospital Universitario Fundación Jiménez Díaz
	SPA-003	Hospital Universitario Marques de Valdecilla
	SPA-006	Hospital Universitario Miguel Servet

Prof. Dr. Thomas Berg-Principal Investigator

- Head of the Division of Hepatology
- Department of Medicine II, Leipzig University Medical Center, Germany
- The Former Secretary General of the European Association for the Study of the Liver
- Leading the site with Early Phase Clinical Oncology Unit dedicated early phase clinical trials
- Very experienced in clinical research in hepatology, including hepato-oncology

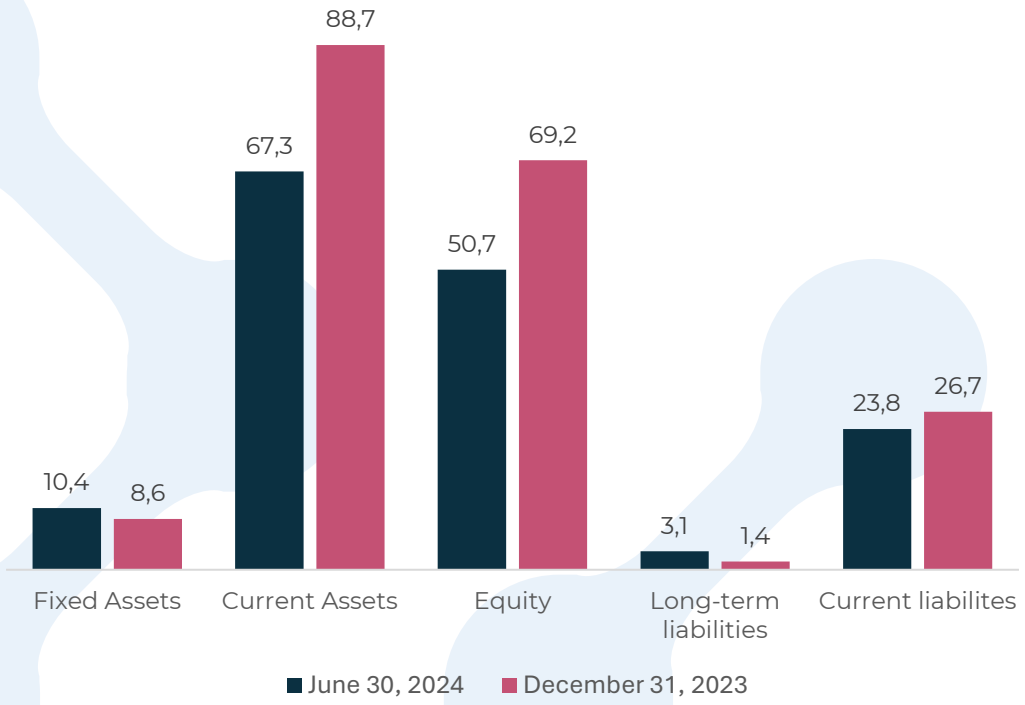
Results Highlights

Key points from the financial results in first half 2024

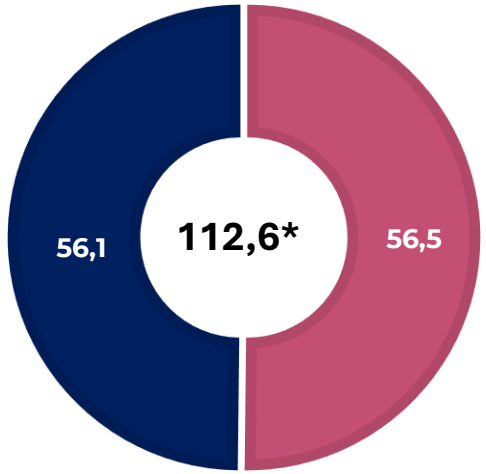
- Increase in revenues from collaborations from PLN **3,9M** to PLN **9,3M**
- Decrease in grant revenues from PLN **8,0M** to PLN **2,5M**
- Narrowing loss from PLN **43,3M** to PLN **19,6M** due to focus on lead projects, timing of expenditure on CT-01 costs, and lower employee benefit costs
- Reduced operational cash outflow from PLN **31,5M** in H1 2023 to PLN **17,5M** in H1 2024

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)

Captor Therapeutics®

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