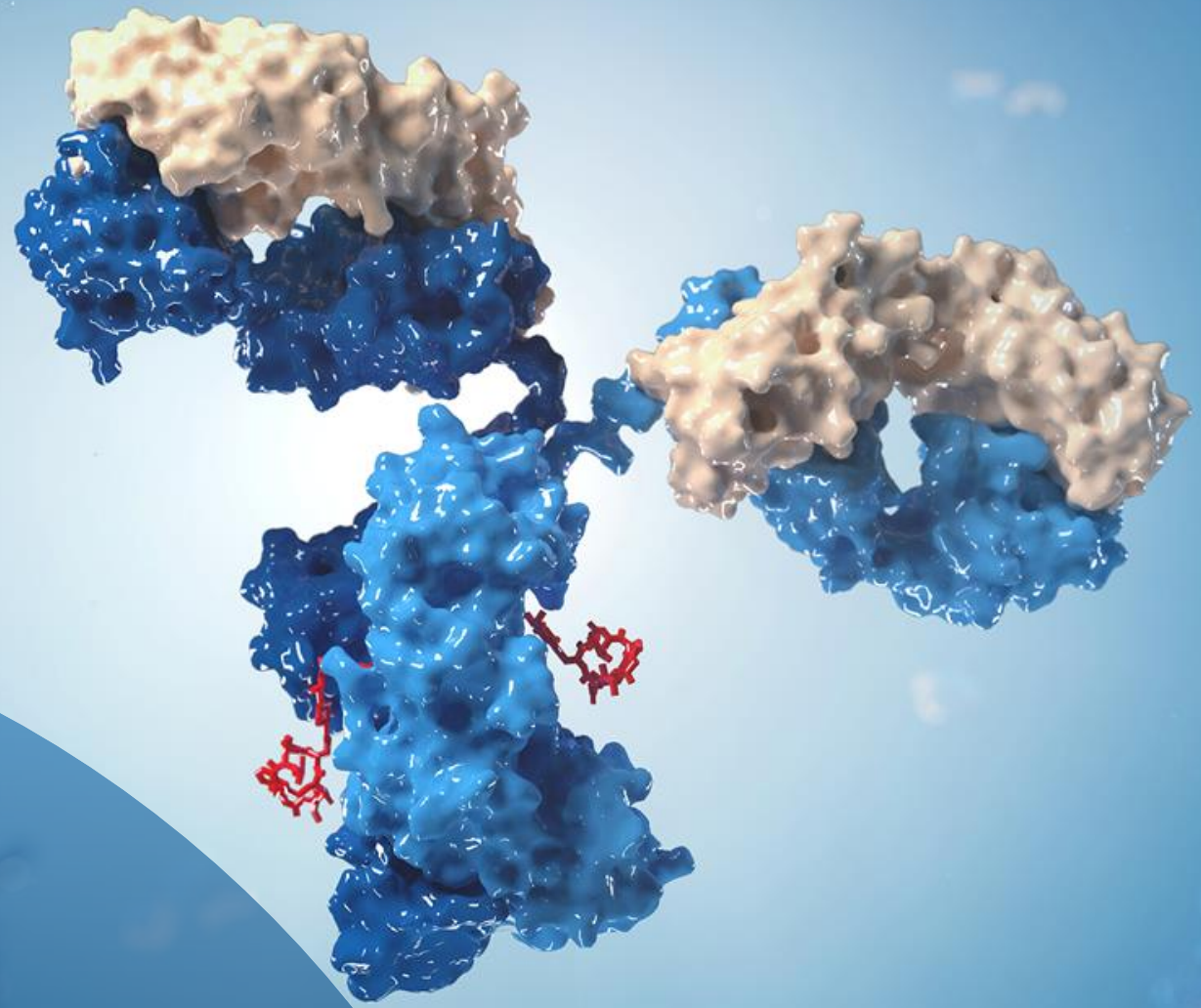
Heidelberg PHARMA



# THE LEADER IN NEXT GENERATION ADC PAYLOADS

**Company Presentation • February 2025**

# SAFE HARBOR

## FORWARD LOOKING STATEMENTS

This communication contains certain forward-looking statements, relating to the Company's business, which can be identified by the use of forward-looking terminology such as "estimates", "believes", "expects", "may", "will", "should", "future", "potential" or similar expressions or by general discussion of strategy, plans or intentions of the Company. Such forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause our actual results of operations, financial condition, performance, achievements or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements.

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# OVERVIEW

# CORPORATE HIGHLIGHTS

## PROPRIETARY PAYLOADS, WHOLLY-OWNED ASSETS & PARTNERED ADCs

### Lead ADC Program HDP-101 (BCMA-ATAC)

- Proprietary Amanitin Payload (patent exclusivity)
- Overcome resistance due to new MoA
- HDP-101 Phase I/IIa ongoing in RRMM
- 50% ORR in Cohort 5 with no signs of ocular or renal toxicities, myelosuppression or severe liver damage including one **complete remission**
- Delivering RP2D in mid 2025

### Amanitin & Exatecan based ADC pipeline in liquid & solid tumors

### Complete GMP manufacturing supply chain

### Technology and asset partnerships maximize value of pipeline

### Strong IP portfolio including platform, payload, assets, method of use and predictive biomarker

- Subcutaneous administration
- Patient stratification with 17p biomarker

### Cash runway through 2026*

*taking into account the milestone payment of $75 million from HealthCare Royalty

ADC = antibody-drug conjugate | MoA = mode of action | RRMM = Relapsed/Refractory Multiple Myeloma | ORR = overall response rate | RP2D = Recommended Phase 2 Dose | CTA = clinical trial application | FPI = first patient in

# MANAGEMENT TEAM

**Professor Andreas Pahl**
Chief Executive Officer

@ Heidelberg Pharma since 2012

Professor of Pharmacology and Toxicology at the University of Erlangen-Nuremberg (FAU) with 25 years experience in research and higher education

PhD in chemistry from the University of Berlin

**Walter Miller**
Chief Financial Officer

@ Heidelberg Pharma since 2023

20 years experience in corporate finance, M&A, strategic controlling, accounting and corporate development

MBA from the University of Aachen

**András Strassz, MD**
Chief Medical Officer

@ Heidelberg Pharma since 2020

**George Badescu, PhD**
Chief Business Officer

@ Heidelberg Pharma since 2018

**Jörg Kemkowski, VMD**
Chief Operating Officer

@ Heidelberg Pharma since 2023

# OUR MISSION

> Our mission is to build a world-class ADC pipeline by the use of differentiated ADC technologies.
>
> Professor Andreas Pahl, CEO

# STRONG IN-HOUSE R&D CAPABILITIES AND EXPERTISE

Synthetic chemistry

Antibody generation & bioconjugation

Preclinical testing

CMC

Bioanalytical sciences

Clinical Development

Best ADC candidate in the shortest time

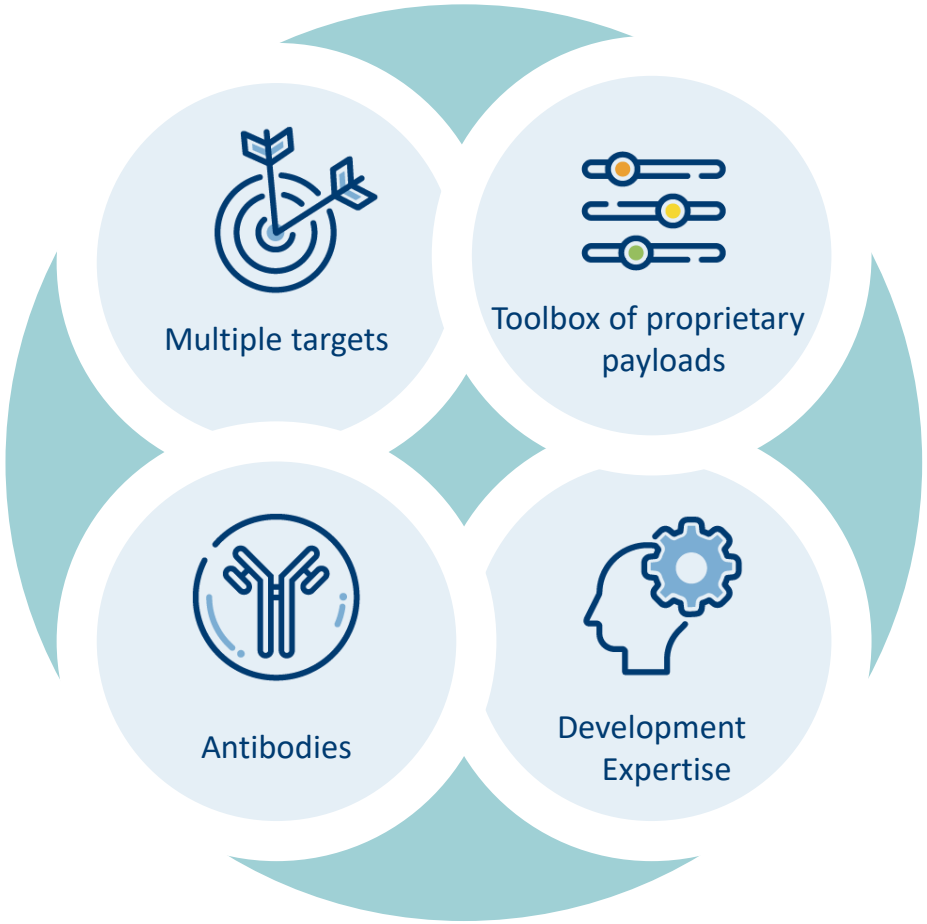
# VALUE CREATION THROUGH DEVELOPMENT OF BEST-IN-CLASS ADC ASSETS

## DISCOVERY & DEVELOPMENT ENGINE

Scouting

Partnering

In-licensing




Partnering at IND-ready, First clinical data, EOP1, Clinical POC

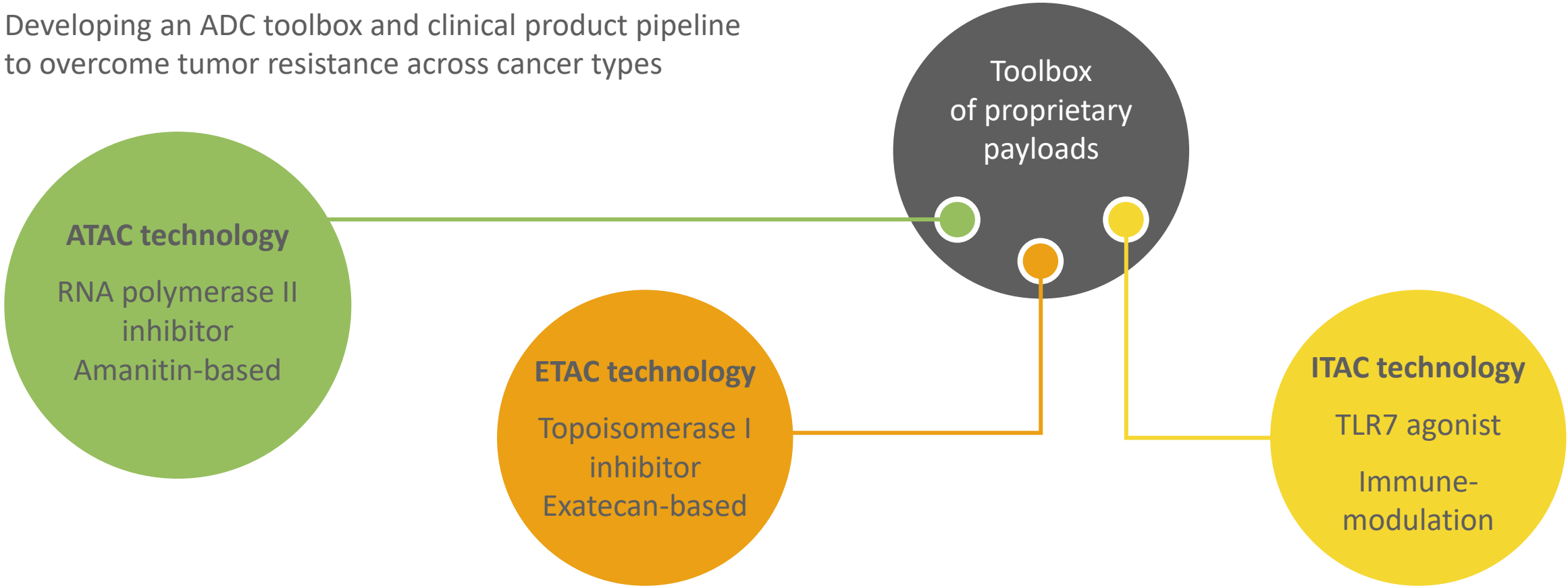
Co-Development

Upside: Retain territorial rights for potential commercialization

We are NOT a Target ID Company

# NEXT GENERATION ADC PAYLOAD PLATFORM

Developing an ADC toolbox and clinical product pipeline to overcome tumor resistance across cancer types

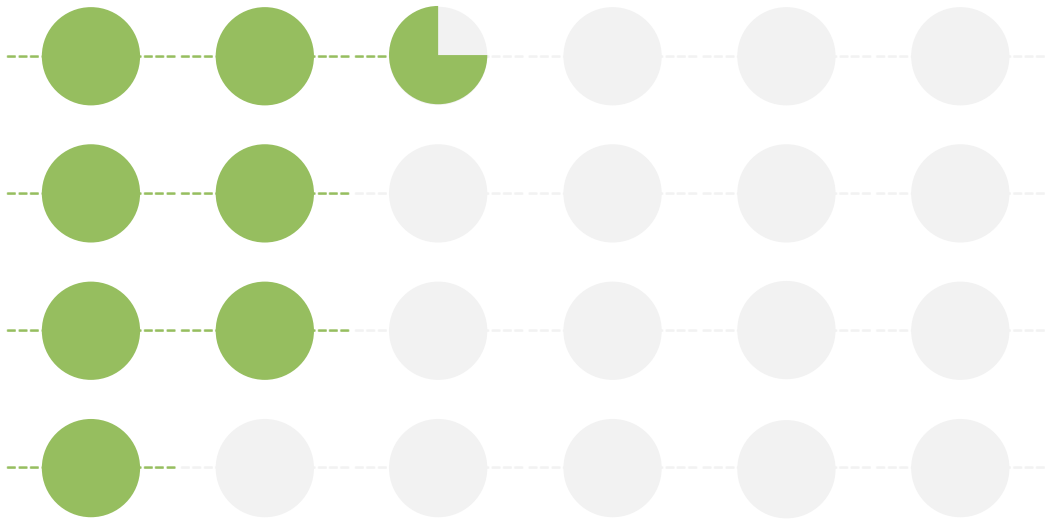



Different payloads and antibodies will lead to multiple development candidates with different modes of action

# GROWING PIPELINE OF PROPRIETARY PROGRAMS

**ATAC pipeline**

| Product | Target | Indication | Partner |
|---|---|---|---|
| **HDP-101** | BCMA | Multiple Myeloma | Huadong (China+) |
| **HDP-102** | CD37 | NHL (DLBCL/CLL) | Proprietary |
| **HDP-103** | PSMA | Prostate cancer | Huadong (China+) |
| **HDP-104** | GCC | Gastrointestinal cancers (e.g. CRC) | Huadong (Option China+) |




**TOPO I**

| Product | Target | Indication | Partner |
|---|---|---|---|
| **HDP-201** | GCC | Colorectal cancer | Proprietary |

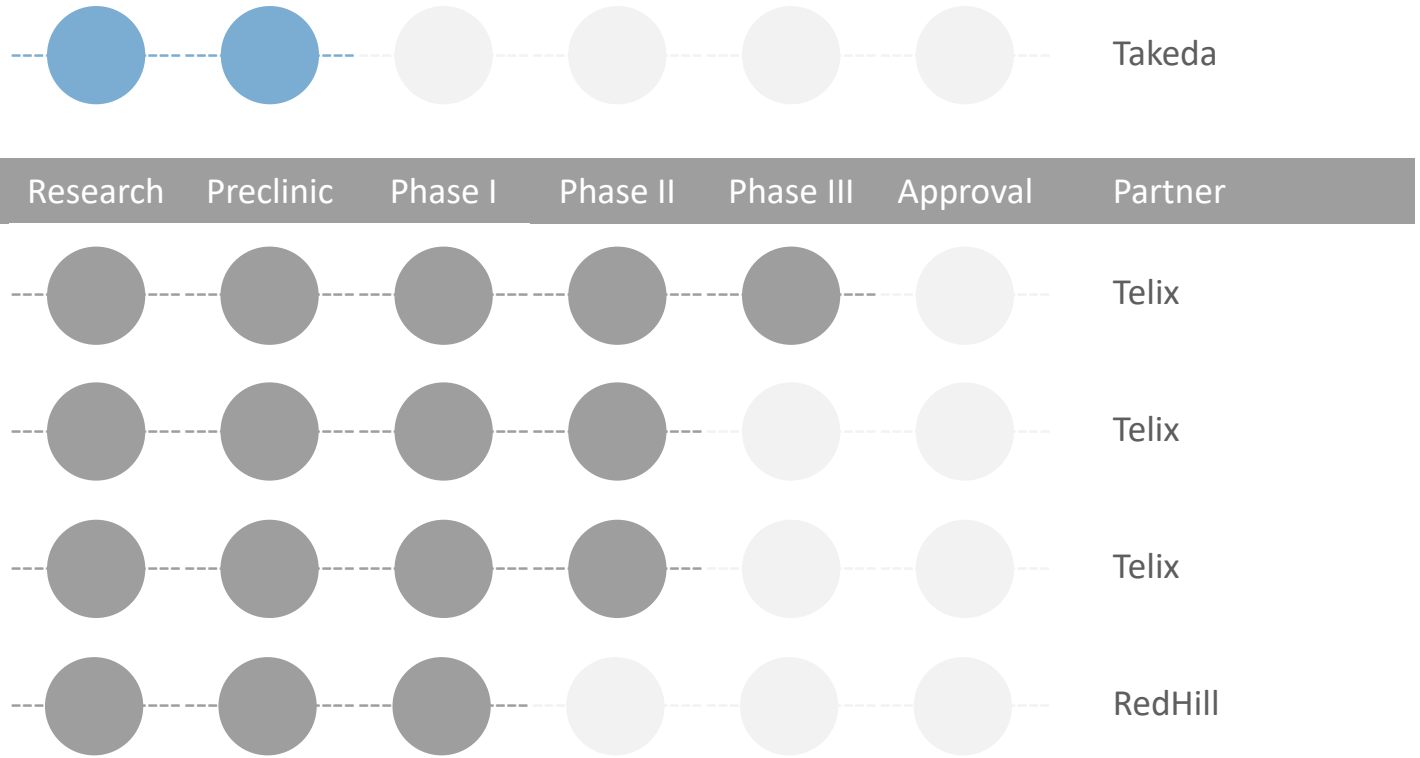
# GROWING PIPELINE OF PARTNERED PROGRAMS

**ATAC Partners**

| Product | Target | Indication | Partner |
|---|---|---|---|
| **TAK-ATAC** | n/a | Oncology | Takeda |

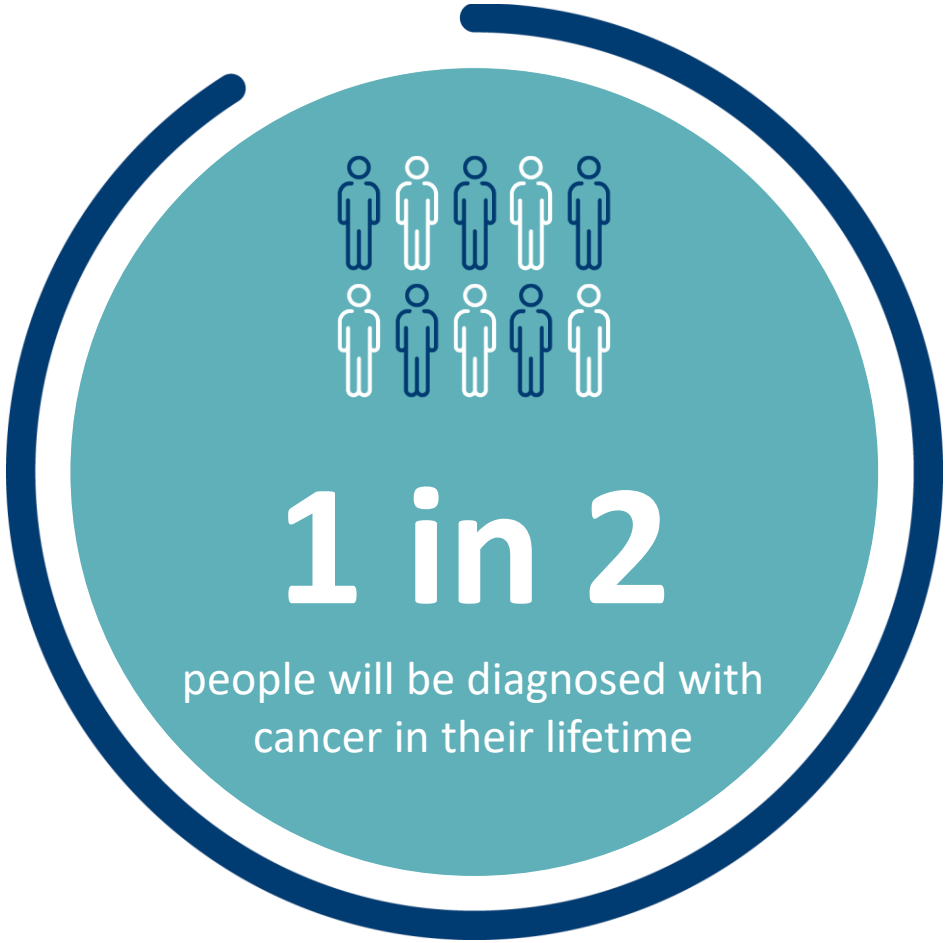
**Legacy Assets**

| Product | Target | Indication | Partner |
|---|---|---|---|
| **TLX250-CDx** | CA-IX | Kidney cancer | Telix |
| **TLX250-CDx** | CA-IX | Bladder cancer | Telix |
| **TLX250** | CA-IX | Kidney cancer | Telix |
| **RHB-107** | | COVID-19 | RedHill |

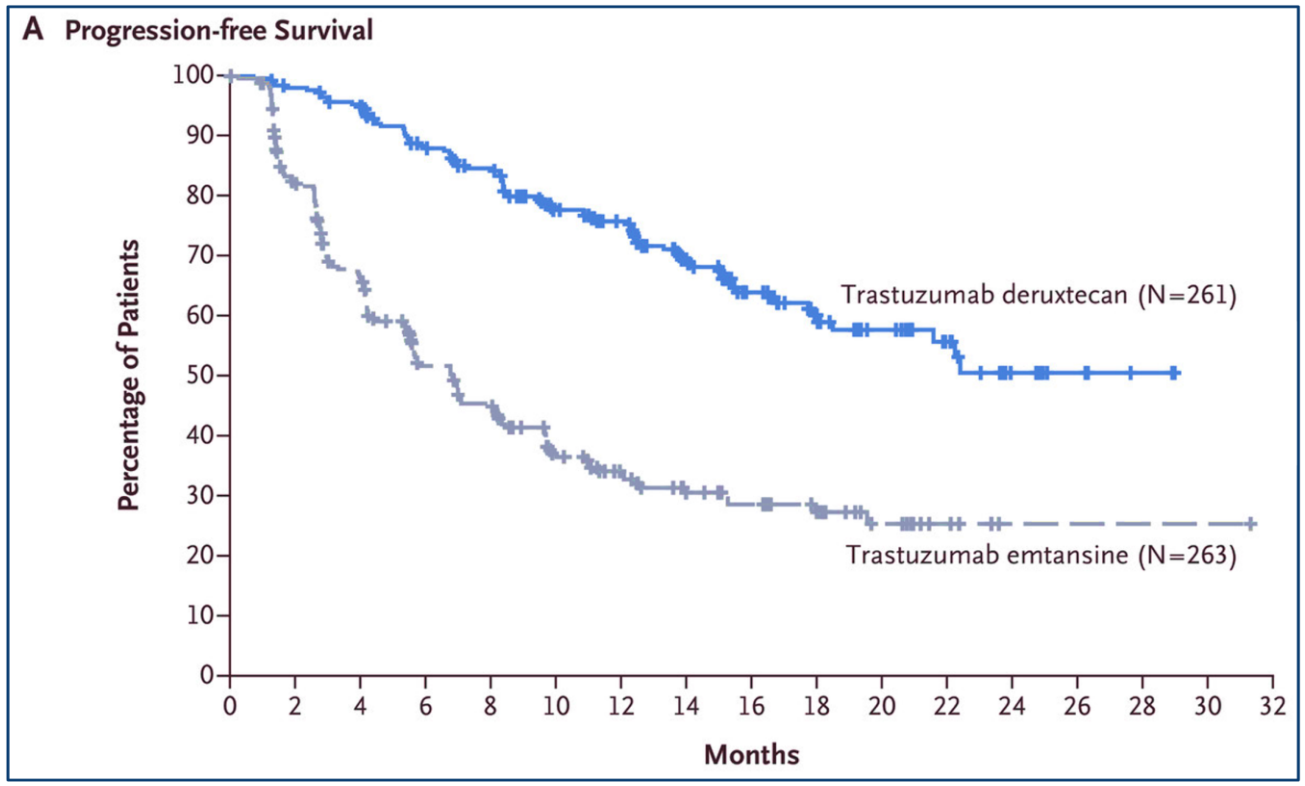


# ADC TECHNOLOGIES

# RESISTANCE IS ONE OF THE BIGGEST CHALLENGES IN ONCOLOGY




# THE PAYLOAD MOA IS WHAT MAKES THE DIFFERENCE!




Source: Cortés, J. et al, N Engl J Med 2022; 386:1143-1154

— Enhertu®
Payload: deruxtecan (Topo 1 inhibitor)

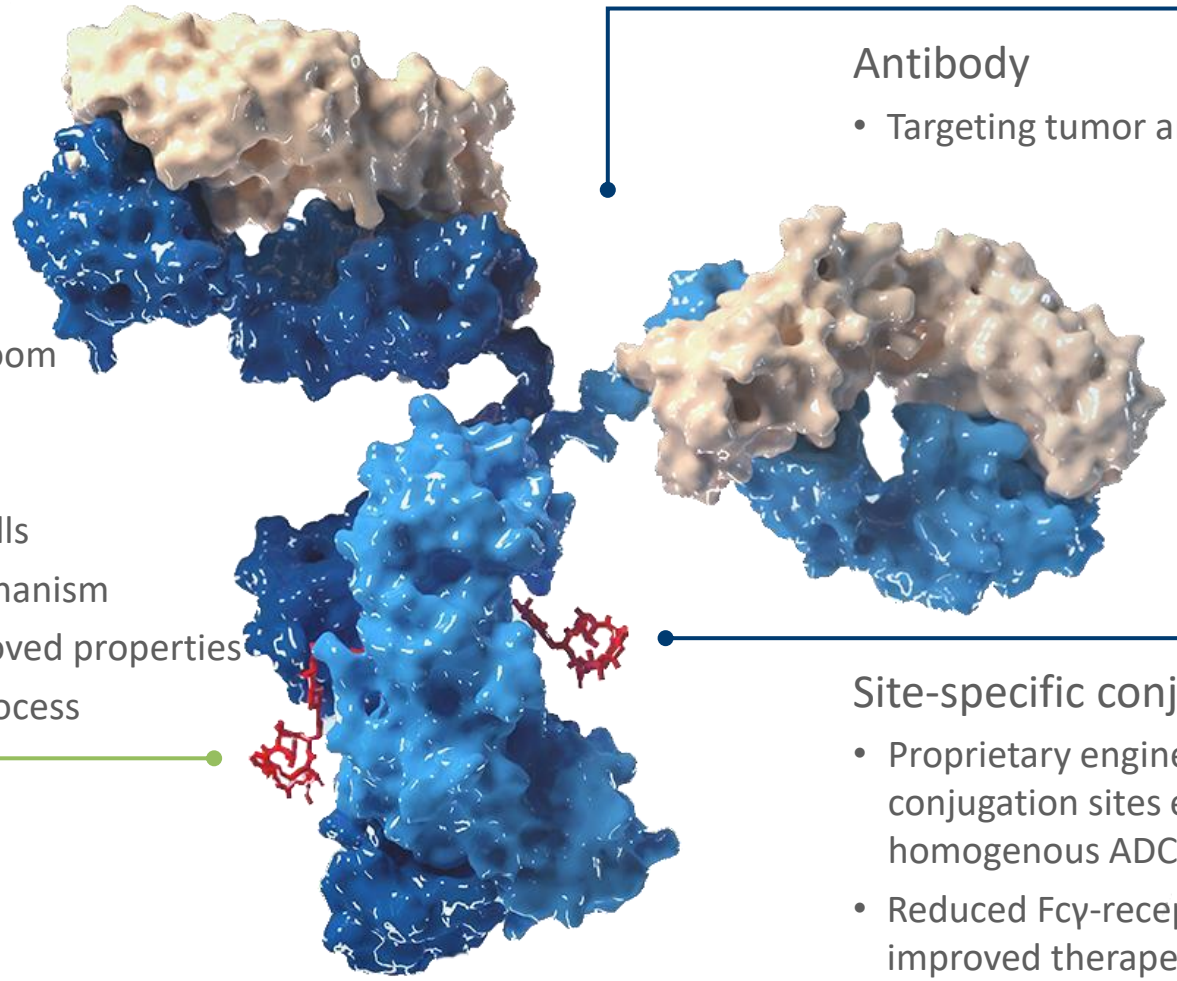
— Kadcyla®
Payload: emtansine (Tubulin inhibitor)

Same target (HER2), same antibody (Trastuzumab), same patient population

# ATACs ARE ADCs WITH AMANITIN AS A PAYLOAD

**Payload: α-Amanitin**

- Identified in Amanita phalloides mushroom
- Completely novel MoA:
  - Inhibition of RNA Polymerase II
  - Kills dormant/non-dividing tumor cells
  - Circumvents resistance via new mechanism
- Synthetic amanitin derivatives with improved properties
- GMP manufacturing via fully synthetic process



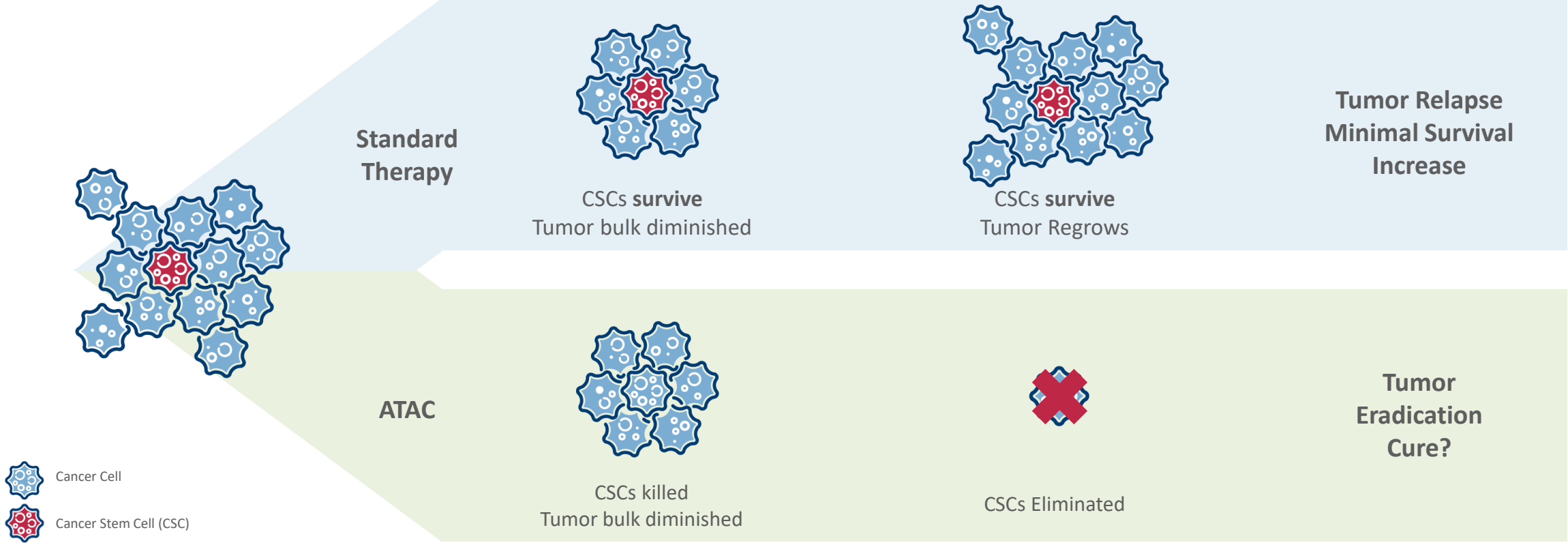
## Antibody

- Targeting tumor antigen

## Site-specific conjugation

- Proprietary engineered cysteine conjugation sites enable homogenous ADC production
- Reduced Fcγ-receptor binding for improved therapeutic index (TI)
- Drug-Antibody Ratio (DAR) = 2.0

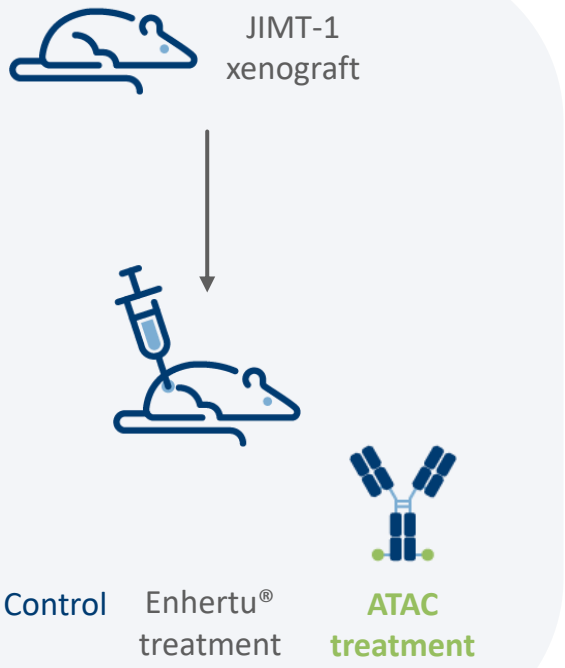
# ATACs ADDRESS THE LIMITATIONS OF CURRENT CANCER THERAPIES

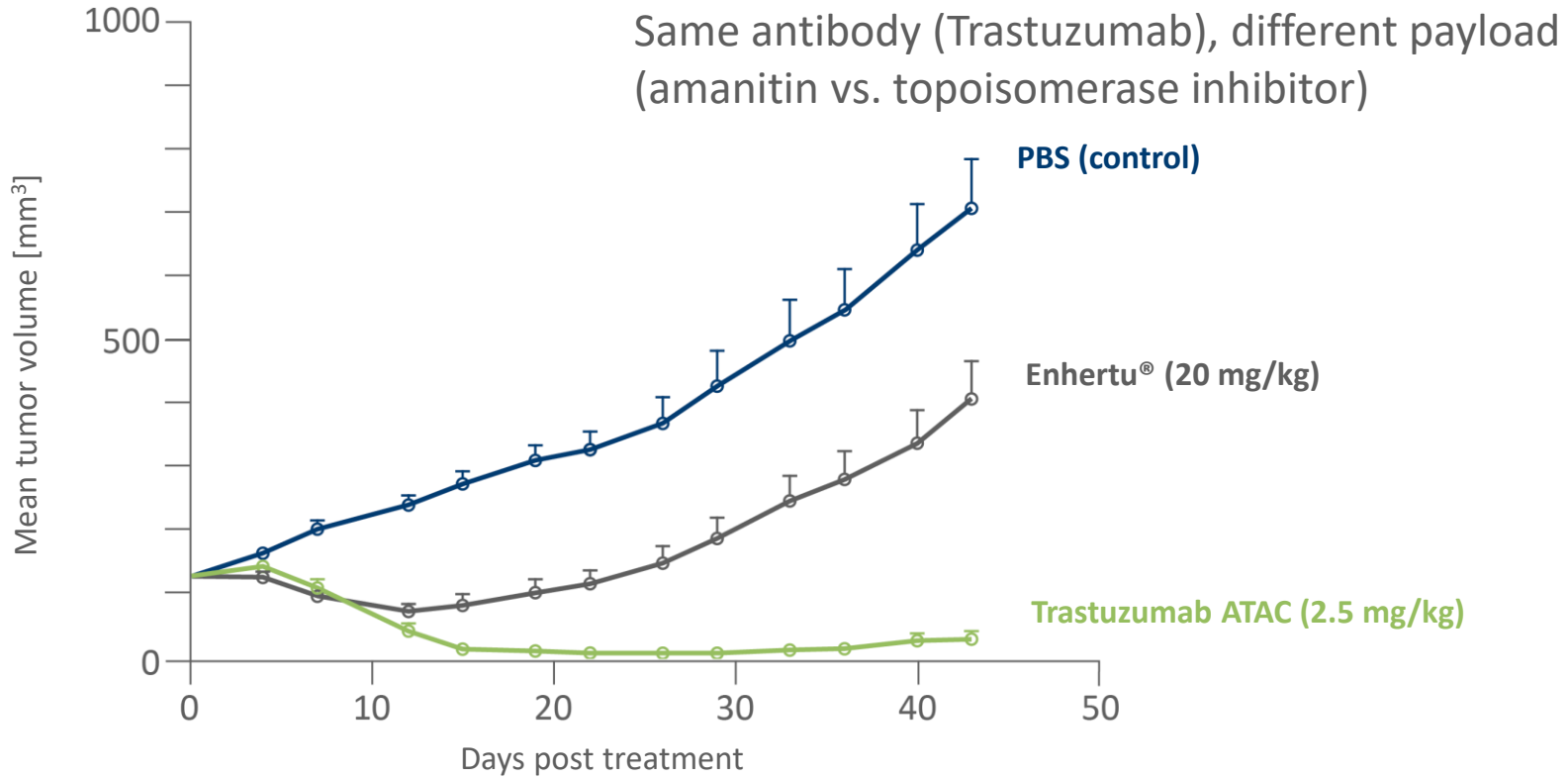



Amanitin has a mechanism of cytotoxicity that is radically different from that of conventional chemotherapy

# ATACs OVERCOME RESISTANCE

## BREAST CANCER MODEL (JIMT-1 XENOGRAFT) IS RESISTANT TO KADCYLA® AND ENHERTU®



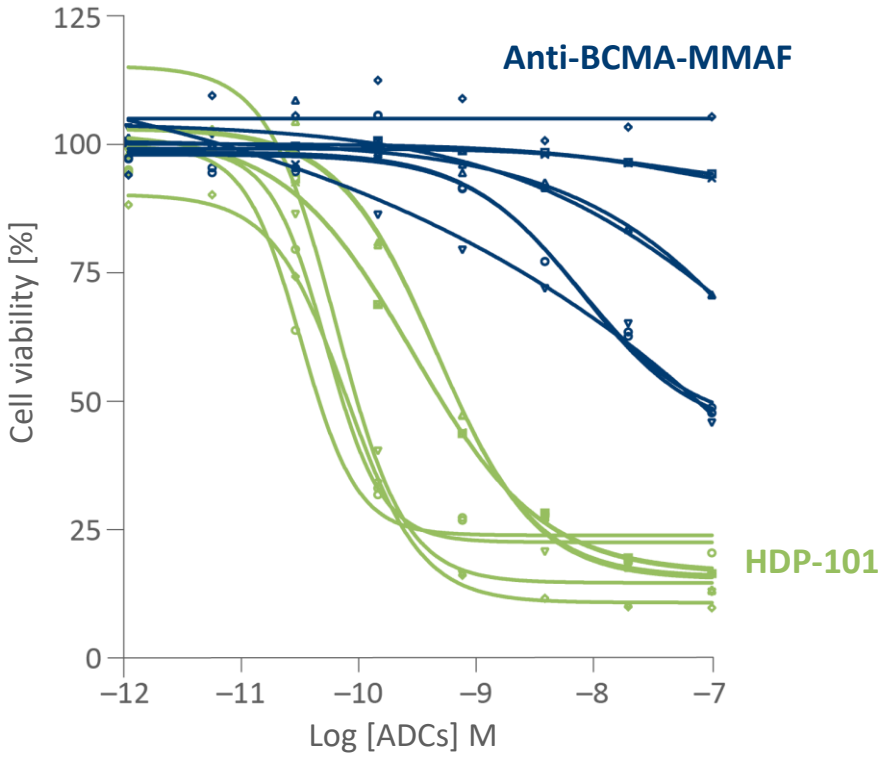

Trastuzumab ATAC leads to complete remission in resistant mouse model after single-dose

# HDP-101 OVERCOMES RESISTANCE IN MULTIPLE MYELOMA

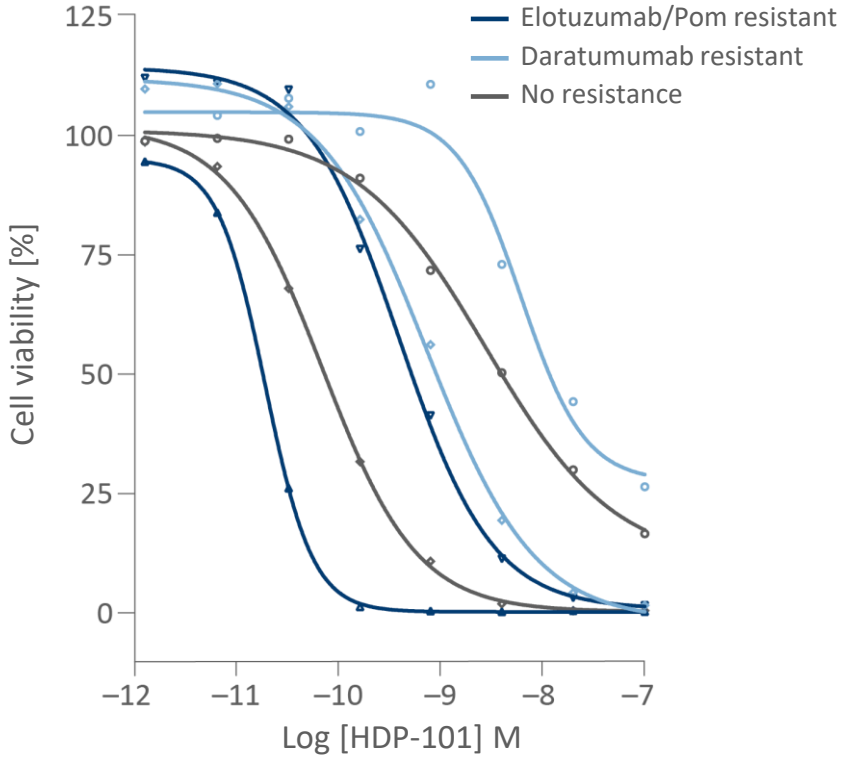
From bone marrow of patients obtained primary MM cells

Cytotoxicity assay with HDP-101 or Anti-BCMA-MMAF

**Kills non-dividing tumor cells unlike other ADC therapeutics**

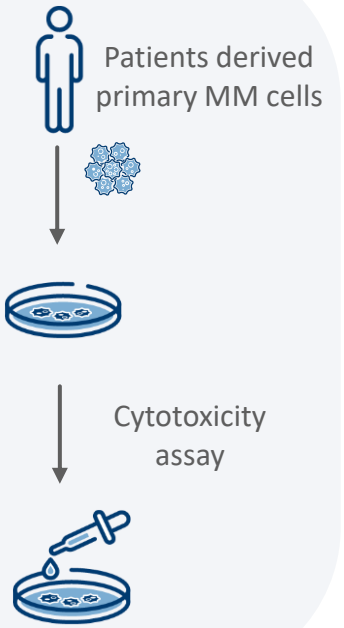



**Effectively kills cells from patients multi-refractory to SOC**

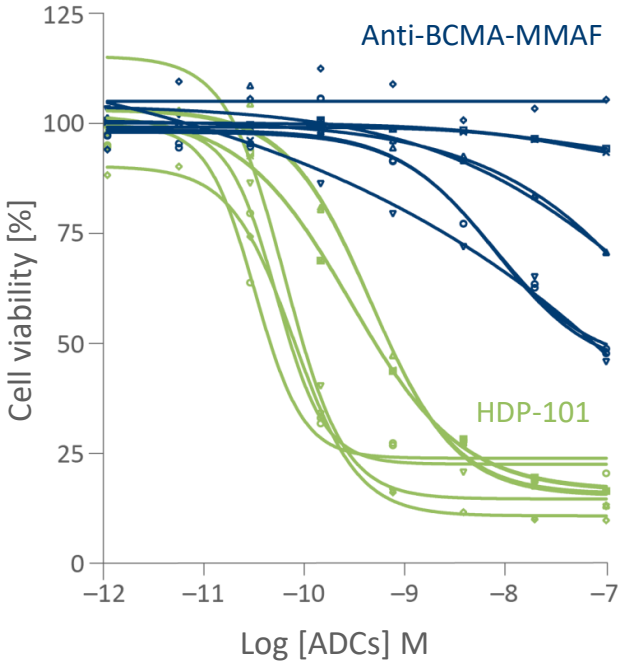



Collaboration with Heidelberg Myeloma Center, Marc-Steffen Raab |Source: Figueroa-Vazquez et al., Pahl, 2021; Mol Cancer Ther.

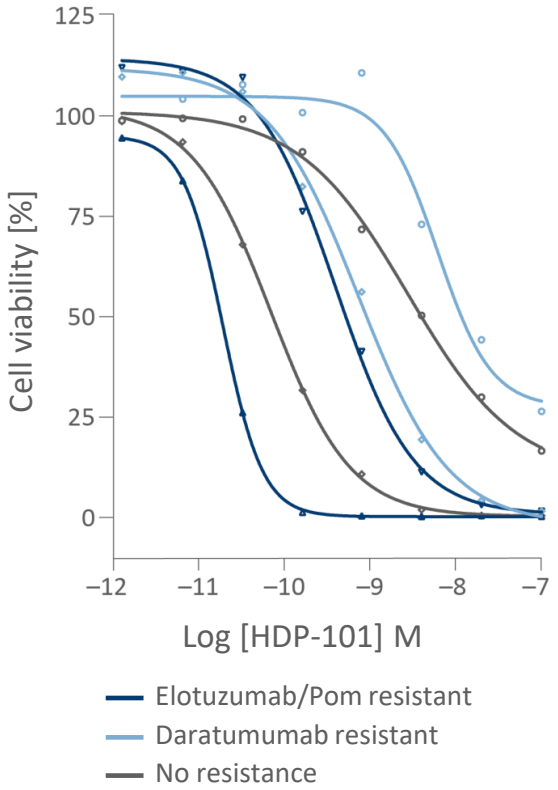
# HDP-101 OVERCOMES RESISTANCE IN MULTIPLE MYELOMA



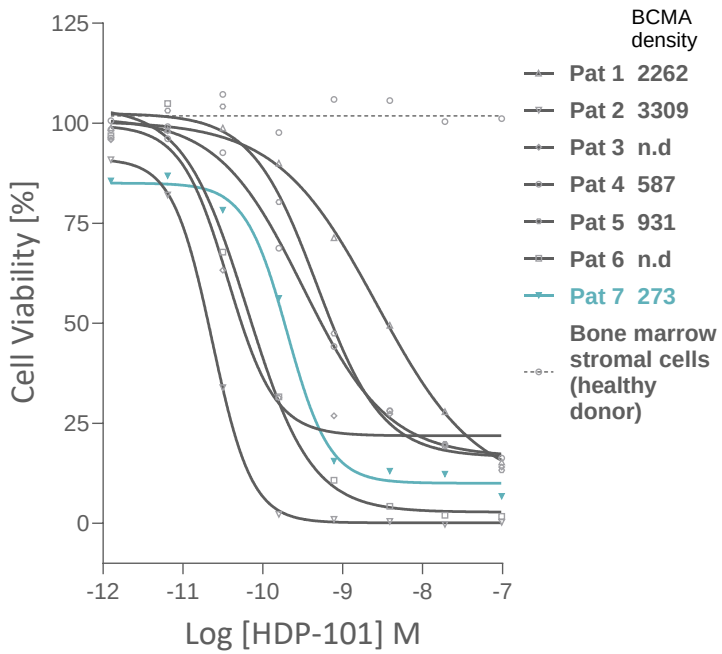

## Kills Non-Dividing Tumor Cells




## Effectively Kills Cells from Patients Multi-Refractory to SOC




## Kills cells with ultra-low antigen expression




Collaboration with Heidelberg Myeloma Center Marc-Steffen Raab
Source: Figueroa-Vazquez et al., Pahl, 2021; Mol Cancer Ther.

# DEL(17p): POTENTIAL PREDICTIVE BIOMARKER

Deletion of TP53 (tumor suppressor)

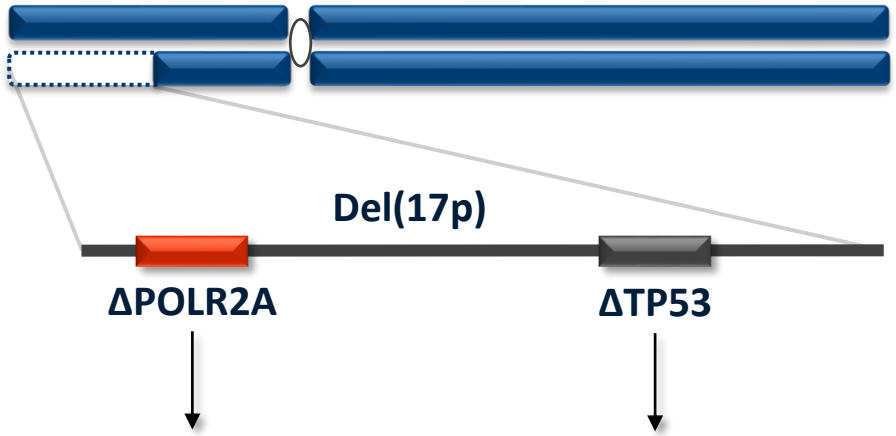
- High incidence
- More aggressive tumors resistant to SoC and poor prognosis

Deletion of RNA Polymerase II (POLR2A is co-deleted)

- Higher sensitivity to ATAC treatment

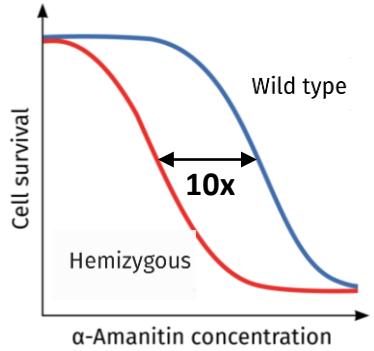
Occurs only in tumor cells

- Wider therapeutic window in patients with del(17p) tumors
- Across cancer indications and tumor types



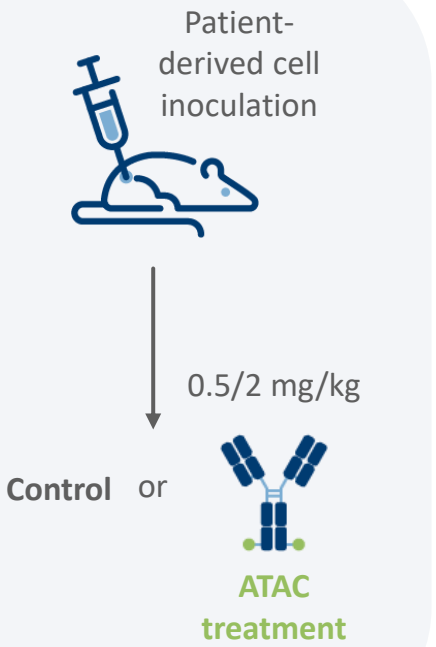

Intracellular target of amanitin: Increases ATAC sensitivity

Tumor suppressor: Increases tumor aggressiveness & resistance

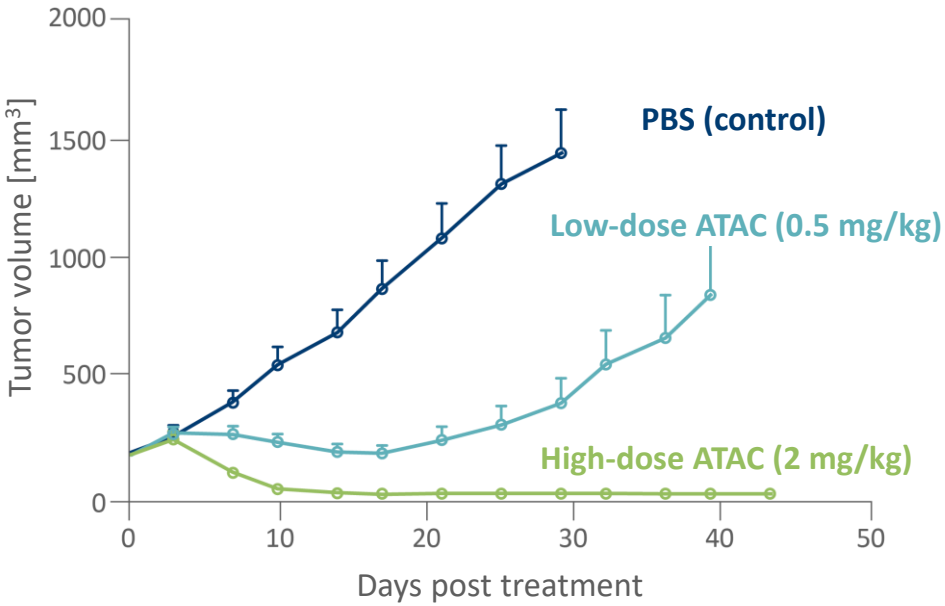



# DEL(17p): POTENTIAL PREDICTIVE BIOMARKER

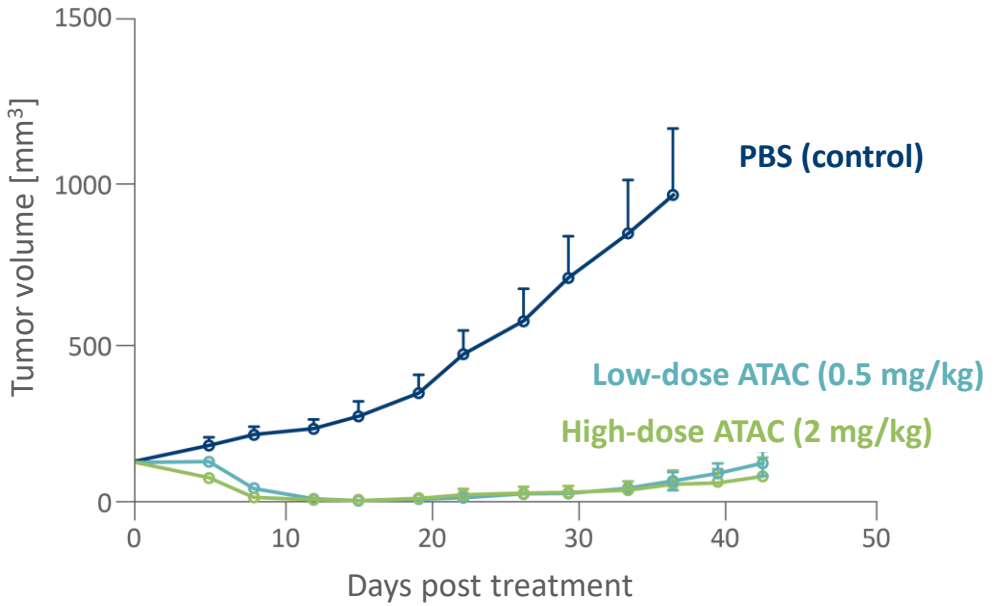
## HER2 1+ PATIENT-DERIVED XENOGRAFT MODELS




**Wild type** - normal RNA Pol II levels

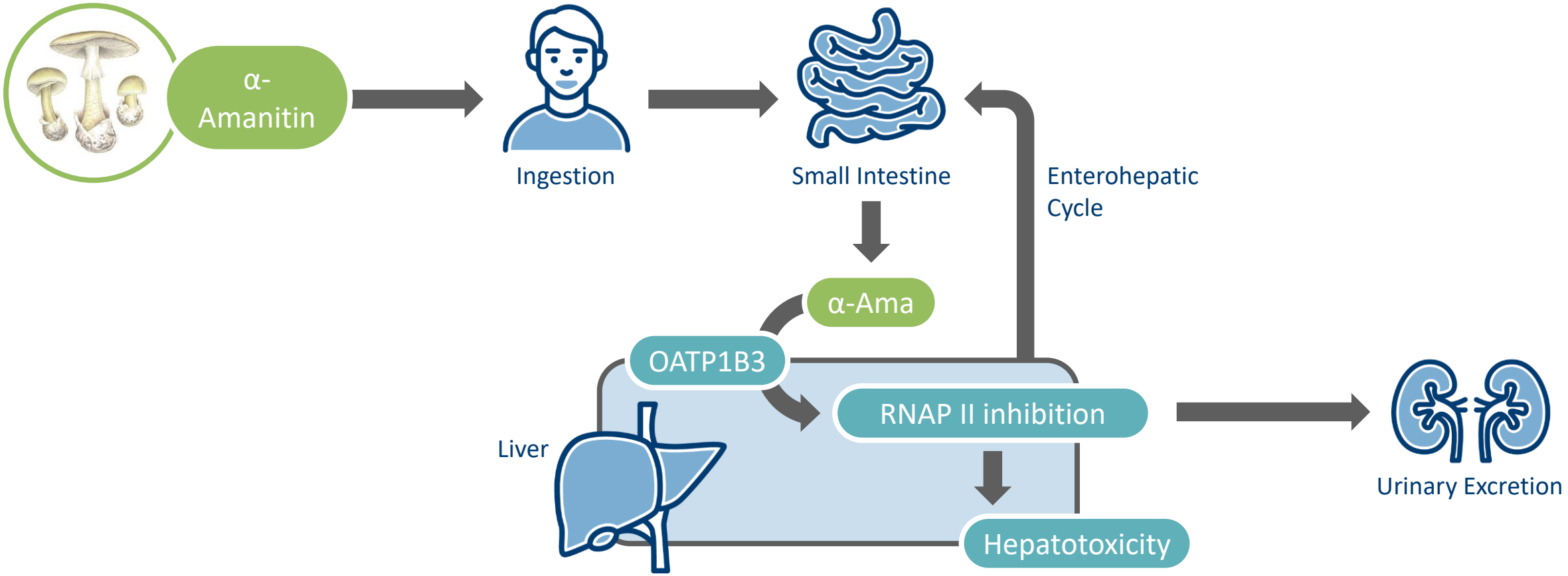



**del(17p)** - reduced RNA Pol II levels




Less amanitin is required to kill del(17p) cells → Wider therapeutic index in patients with del(17p) tumors

# TOXICITY MECHANISM OF α-AMANITIN IN HUMANS




Upon mushroom intoxication α-amanitin leads to hepatotoxicity
by specific uptake of the toxin into hepatocytes via the OATP1B3 transporter

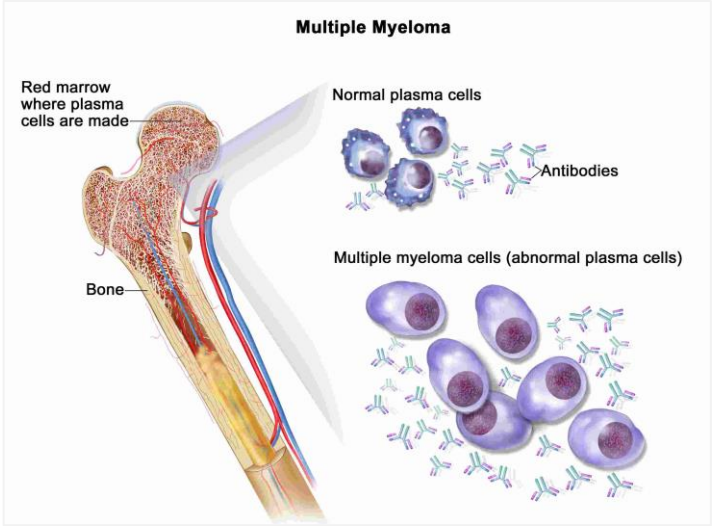
# MULTIPLE MYELOMA AND 17p DELETION

## MULTIPLE MYELOMA (MM)

- Malignancy characterized by clonal plasma cell expansion in the bone marrow
- Despite substantial improvements in PF and OS, MM patients eventually relapse

## DEL(17p) IN MM

- Deletion identified in app. 10% of newly diagnosed MM patients
- Alterations more frequent in late stages of the disease and associated with treatment resistance




Source:
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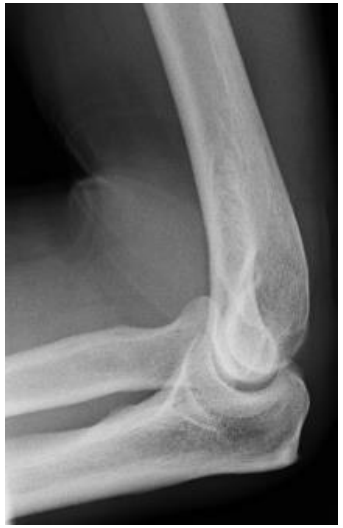
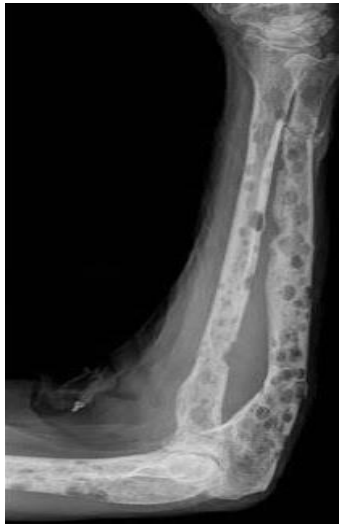


Source:
healthcare-in-europe.com



Source:
Heidelberg Pharma

# HDP-101 PHASE I/IIa: SUMMARY OF PRELIMINARY DATA

## Multiple efficacy endpoints show dose dependent and promising anti-cancer activity with intravenous doses of 20 - 100 µg/kg (median of 6.5, maximum of 15 prior lines of therapy):

- 56% (10/18) of patients responded to treatment with SD or PR
- Patient with 9 prior therapies including α-BCMA and α-GPRC5D treatment experienced a PR in cycle 2 (64 days of HDP-101), no detectable M-protein in blood from day 225, sCR confirmed at day 344 (bone marrow biopsy)
- Continues on treatment

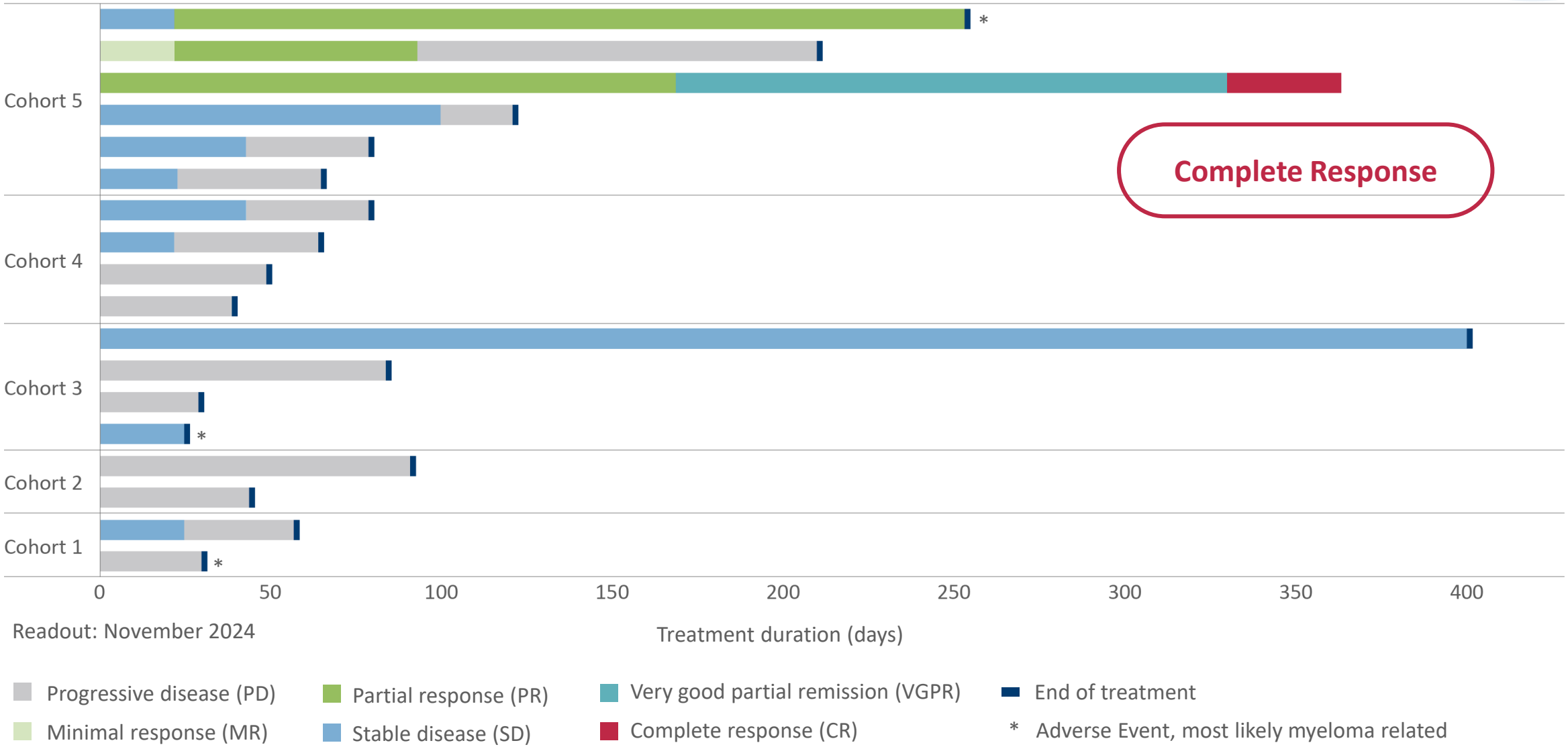
## Safety & tolerability observed across 18 patients at all dose levels tested:

- No signs of ocular or renal toxicities, infusion reactions, myelosuppression or severe liver damage
- No TRAEs leading to drug discontinuation*
- No DLTs in cohort 1-4, no Grade 5 AEs
- Thrombocytopenia Grade 3-4 only observed in cycle 1; short-lived and without clinical symptoms

In a heavily pretreated patient population, HDP-101 monotherapy showed favorable safety and demonstrated efficacy, with stabilization of disease and partial responses in patients who progressed on FDA-approved treatments including anti-BCMA CAR-T and daratumumab

*One patient experienced a G3 AE at 100 µg/kg, and resumed dosing with 80 µg/kg since 2nd treatment

# HDP-101 – PHASE I PRELIMINARY EFFICACY DATA



# CASE SUMMARY: COHORT 5 COMPLETE RESPONSE

## 70 Year Old Female with Stage II IgG-Ķ Myeloma Since 2002

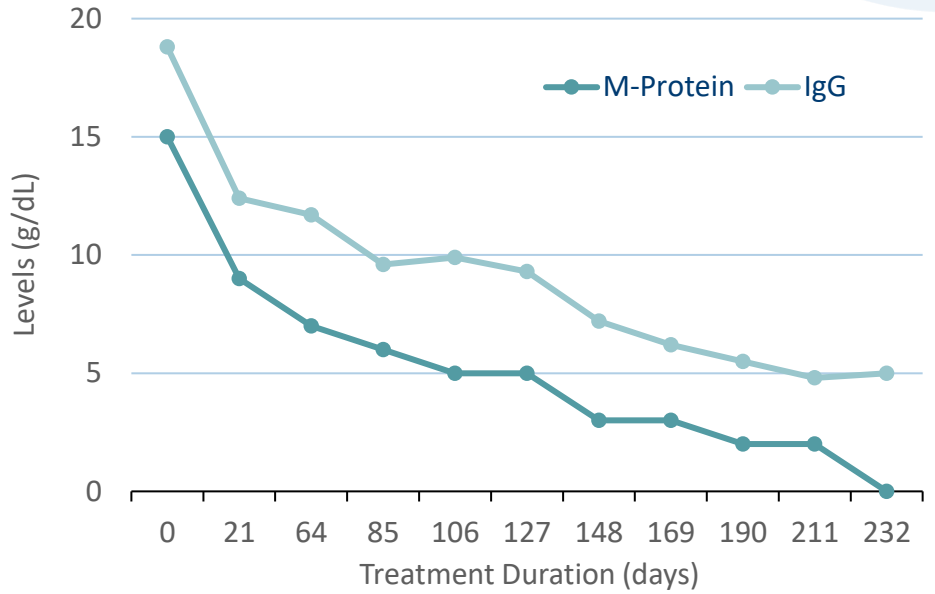
- 9 prior lines of therapies including transplant, IMiDs, PIs, and Daratumumab
- Last 3 treatment regimens & response:
  - **7th line**: BCMA CAR-T (Aug-2018) VGPR
  - **8th line**: GPRC5D/CD3 Bi-specific Antibody (Jul-2020) CR
  - **9th line**: Iber-Dex (Jan 2022) PR

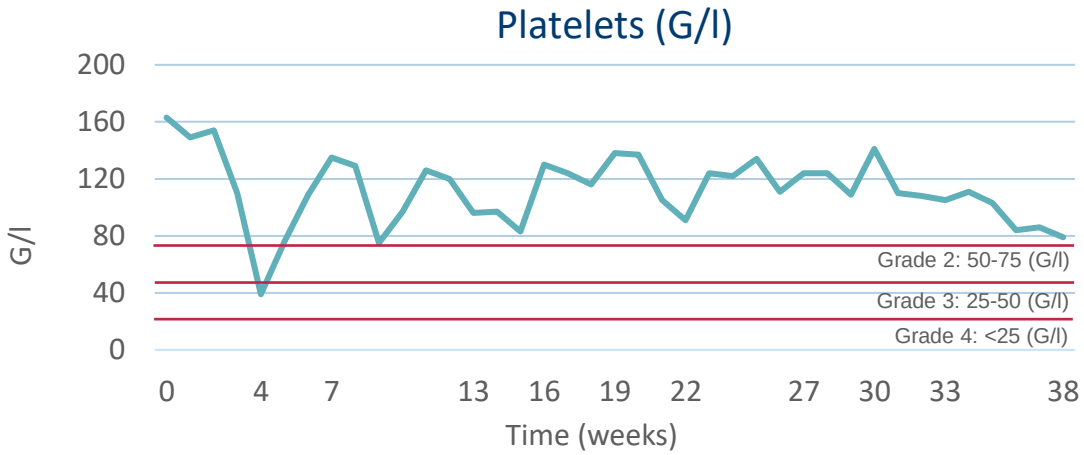
## Started HDP-101 (100 µg/kg) in Oct 2023

- PR in cycle 2 (64 days of HDP-101)
- No detectable M-protein in blood from day 225
- sCR confirmed at day 344 (bone marrow biopsy)
- Continues on treatment

## Treatment well tolerated

- Overall mild AEs: No AESI, no DLT, no SAE
- No keratopathy, liver damage or lung toxicity
- No signs of ocular or renal toxicities
- Transient Grade 3 thrombocytopenia in cycle 1




VGPR = very good partial response (>90% reduction from baseline of m-protein) | IMiDs = immunomodulatory drugs; PIs = protease inhibitors| CR = complete response | PR = partial response | sCR = stringent complete response – absence of clonal plasma cells in bone marrow | AESI = adverse event of special interest | DLT = dose limiting toxicity | SAE = serious adverse events

# DOSE OPTIMIZATION STRATEGIES FROM COHORT 6

After Cohort 5 a detailed safety analysis was performed

The Safety Review Committee (SRC) recommended

- to continue the clinical study and
- mitigate the transient platelet reductions after the first dose

  - Arm A: premedication with corticosteroids and antihistamine
  - Arm B: weekly dosing
  - Arm C: splitting the first cycle dose

Additional changes include adjustment of dose escalation and additional safety measures

**Dose optimization:**

| Arm A | Arm B | Arm C |
|---|---|---|
| 1Q3W with premed | 1Q1W weekly dosis | Split first dose (Day 1-8) than 1Q3W |

Further cohorts with the most promising dose regimens will be continued and the dose will be increased

# HDP-101 PHASE I/IIa TRIAL DESIGN IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

## Phase I: Dose Escalation

Q3W intravenous dosing, BLRM Design

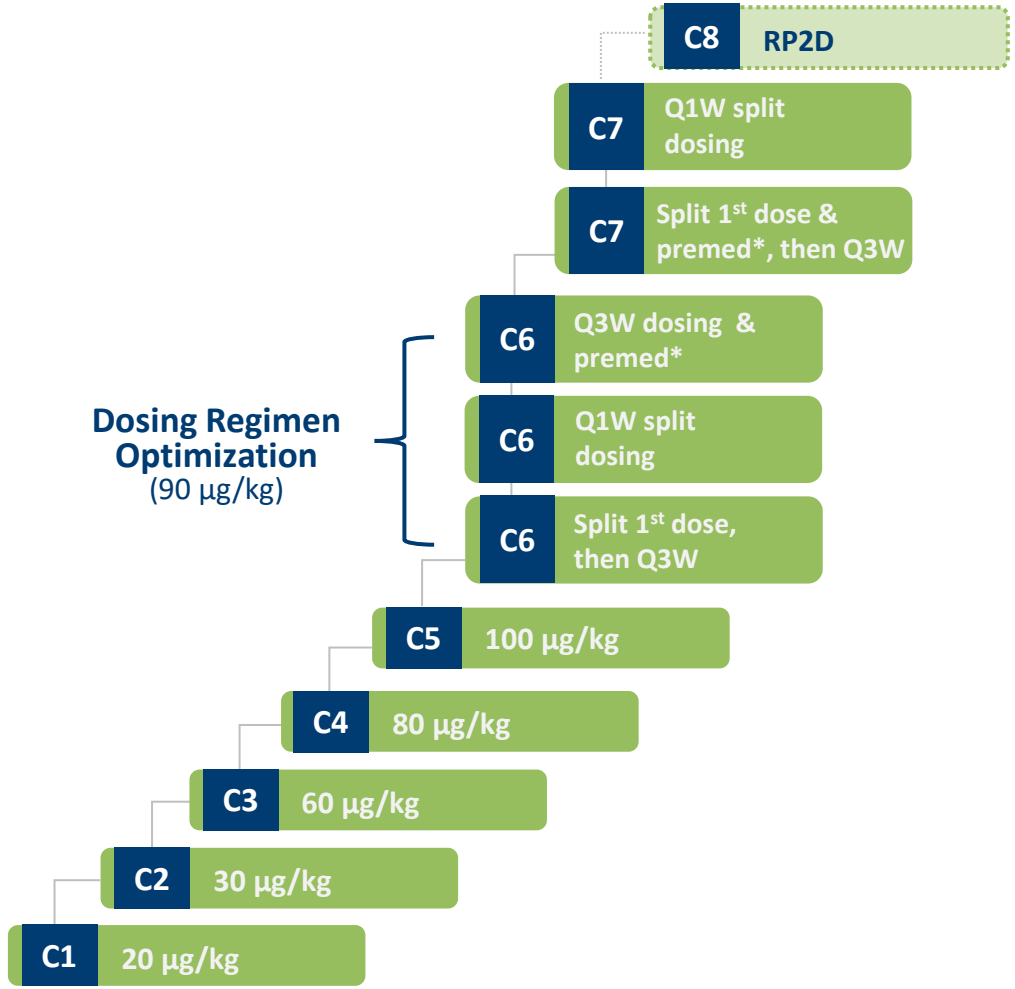
### Objectives

**Primary:** DLT in cycle 1, ORR

**Secondary:** Safety, Tolerability, PFS/OS

**RP2D Identification**

## Phase IIa: Dose Expansion




### Key Eligibility Criteria

- Prior SCT or transplant ineligible
- Prior treatment with an immunomodulatory drug, proteasome inhibitor, and α-CD38 treatment, alone or in combination
- Refractory or intolerant to any established standard of care therapy providing a meaningful clinical benefit for the patient

**Patients in Phase IIa will be stratified by del(17p) status**

* NCT04879043 | BLRM = Bayesian logistic regression model | DLT = dose-limiting toxicity |PFS = progression free survival | OS = overall survival | Premed = premedication with corticosteroids and antihistamine

# COHORT 6 SUMMARY AND COHORT 7 OUTLOOK

## Cohort 6 has been fully recruited

- 10 patients treated (3-4 patients per arm)
- No DLT observed
- The Safety Review Committee unanimously confirmed that 90µg/kg is safe and recommended to escalate the dose
- All three new treatment strategies had a positive effect on the transient thrombocytopenia
- Responses were seen at the dose of 90µg/kg, corresponding to the expectations (treatments and assessments are still ongoing)

## Cohort 7 has been opened beginning of December 2024

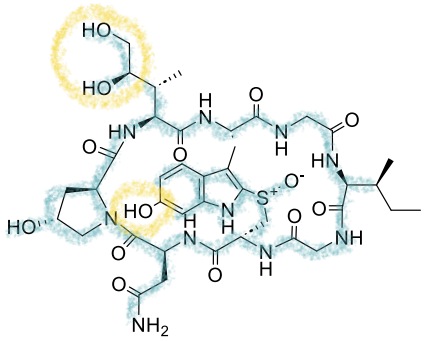
- The dose level is at maximum escalation according to study protocol using dose distribution
  - Weekly dose (amendment planned to allow switch between weekly and 3 weekly dosing)
  - Split first dose combined with premedication, followed by every 3-week dosing
- The cohort is open, and first patients are under treatment

# HDP-101 OVERVIEW

| Unique preclinical features | Potential clinical benefit |
| --- | --- |
| Efficacious against dormant tumor cells | Stronger & longer lasting tumor response |
| Efficacious in ultra-low BCMA-expressing tumor cells | Deeper responses and higher response rate |
| Novel mechanism to which all patients will be naïve | Overcome resistance |
| No ocular toxicity seen thus far | Superior safety profile |
| del(17p) tumors → Predictive Biomarker | Breakthrough designation and accelerated approval |

HDP-101 Has Best-In-Class Potential

# STRONG IP PORTFOLIO – AMONG OTHERS FOR MOA



## PAYLOAD

**Amatoxin synthesis & derivatives**

- WO2014009025 – building block (DHIle)
- WO2019030173 – hydroxy-tryptophane
- WO2017149077 – synthetic variants
- WO201997654 A1 – tryptophane linker
- WO2017149077 – synthetic amatoxins
- WO2020216947 – Amatoxin derivative

## ATAC Platform

**Linker attachment**

- WO2010/115629 – linker attachment
- WO2016/142049 – antibody linkage site

## Antibodies & Products

**HDP-101**

- WO18115466 – $\alpha$-BCMA ATAC
- WO2015166073 – hu $\alpha$-BCMA mAbs

**HDP-102**

- WO2022194988 – $\alpha$-CD37 ATAC

**HDP-103**

- WO20025564A1 – $\alpha$-hPSMA-mAbs
- WO2020216947 – $\alpha$-PSMA ATAC

**HDP-104**

- WO2024094688 – anti-GUCY2C ATAC

## Patient & Tumor

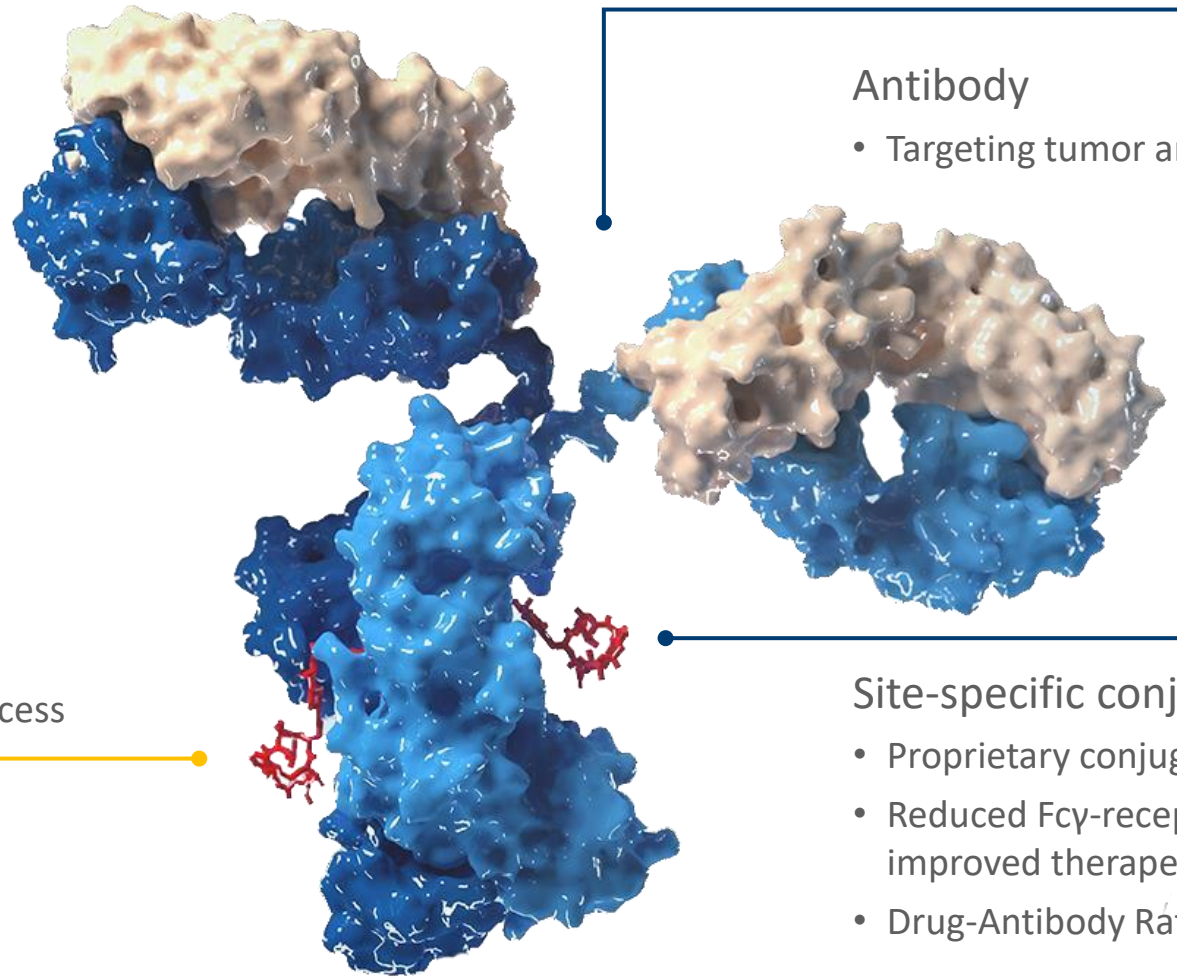
**Biomarker**

- WO16141185 – TP53/POLAR2A

**Dosing & treatment regimes**

- WO2024189048 – subQ administration
- WO2023194539 – tolerance induction
- WO2022096604 – ICI+ATAC combo

# ADCs WITH TOPO I AS A PAYLOAD



## Payload: TOPO I inhibitor

- Clinically validated mechanism of action: Inhibition of Topoisomerase I
- GMP manufacturing via fully synthetic process

## Antibody

- Targeting tumor antigen

## Site-specific conjugation

- Proprietary conjugation sites
- Reduced Fcγ-receptor binding for improved therapeutic index (TI)
- Drug-Antibody Ratio (DAR) = 4.0 (2 x 2)

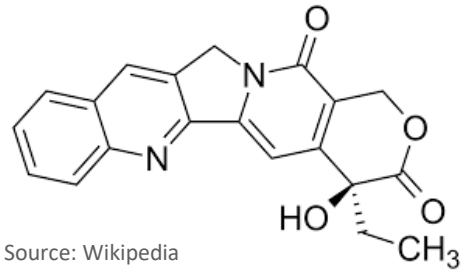
# ADC CANDIDATE WITH NEW PAYLOAD: HDP-201

## HDP-201: ANTI-GCC EXATECAN-BASED ADC

- New payload: Exatecan (Topoisomerase Inhibitor I)
- Guanylyl cyclase C (GCC) is a transmembrane receptor protein (GUCY2C) for regulation of intestinal electrolyte homeostasis
- (Over-) Expressed in > 95% of colorectal cancers and in ~ 65% of esophageal, gastric, and pancreatic tumors
- Indication: Colorectal cancer
- *In vitro/in vivo* tests show tolerability and efficacy at least comparable to approved Exatecan ADCs

## EXATECAN – CAMPTOTHECIN

- From the Tree of Life (Camptotheca acuminata)




Source: Wikipedia

GCC antibody produced in sufficient quantities to supply two ADC projects: HDP-201 & HDP-104

# FINANCIALS

# FINANCES – AS OF 31 AUGUST 2024

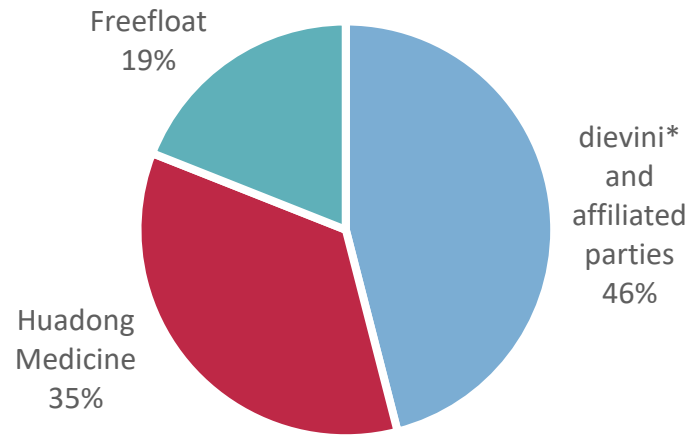
| | |
|---|---|
| **Total Assets (including cash)** | €65.8M |
| **Healthcare Royalty agreement** | $75M available upon approval* |
| **Equity** | €35.8M |
| **Common shares** | 46.6M |
| **Major Shareholders** | dievini & affiliated parties 46%, Huadong Medicine 35% |

Cash as of 31 August 2024 expected to fund operations into mid-2025

*USD 75.0 million from HealthCare Royalty expected to extend operations until the end of 2026

# FINANCIALS AND SHAREHOLDINGS

| In € m | Guidance 2024 | 9M 2024 | 9M 2023 |
|---|---|---|---|
| Sales revenue and other income | **10.0 – 12.0** | 7.6 | 13.9 |
| **Operating expenses** | **30.0 – 33.0** | **22.8** | **30.0** |
| Cost of sales | | 1.5 | 3.1 |
| R&D costs | | 15.7 | 22.1 |
| Administrative costs | | 4.7 | 3.6 |
| Other expenses | | 1.0 | 1.2 |
| **Operating result (EBIT)** | **(19.0) – (22.0)** | **(15.2)** | **(16.1)** |
| **Net loss for the period** | | **(14.3)** | **15.8** |




- Cash inflow of € 22.8 million due to the transaction with HealthCare Royalty
- Repayment of the final tranche in the amount of € 5 million of the shareholder loan to dievini
- Taking into account a further expected payment of USD 75.0 million from HealthCare Royalty, the company assumes that financing will be available until the end of 2026

# BALANCE SHEET AND CASH AS OF AUGUST 2024

| **Assets** (€ m) | **31.08.2024** | **30.11.2023** |
|---|---|---|
| Non-current assets | 13.4 | 13.7 |
| Other current assets | 15.8 | 13.3 |
| Cash | 36.6 | 43.4 |
| | **65.8** | **70.4** |

| **Equity and liabilities** (€ m) | **31.08.2024** | **30.11.2023** |
|---|---|---|
| Non-current liabilities | 21.2 | 1.3 |
| Current liabilities | 8.7 | 19.8 |
| Equity | 35.9 | 49.3 |
| | **65.8** | **70.4** |

- Cash balance at 31 August 2024: € 36.6 (2023: € 43.4 m)

- Equity end of August 2024 decreased to € 35.9 m (2023: € 49.3 m)
- Equity ratio was 54.5%  (2023: 70.1%)

# OUTLOOK

# LEADING ADC PIPELINE IN LIQUID & SOLID TUMOR INDICATIONS

## HDP-101

**BCMA-ATAC for Relapsed/Refractory Multiple Myeloma**

- 50% ORR in Cohort 5 with no signs of ocular or renal toxicity, myelosuppression or severe liver damage including one CR
- Phase I/IIa Study dose escalation Cohort 7 ongoing
- Recommended Phase II dose (RP2D) expected in mid 2025*
- Phase IIa expected to start in 2025

## HDP-102

**CD37-ATAC for Non-Hodgkin Lymphoma**

- CTA filed in Q4 2024
- Phase I dose escalation study NHL
- Extension cohorts for most promising NHL indications

## HDP-103

**PSMA-ATAC for metastatic & castration resistant Prostate Cancer**

- IND-enabling and GLP tox studies completed
- CTA planned for Q4 2025

## HDP-104

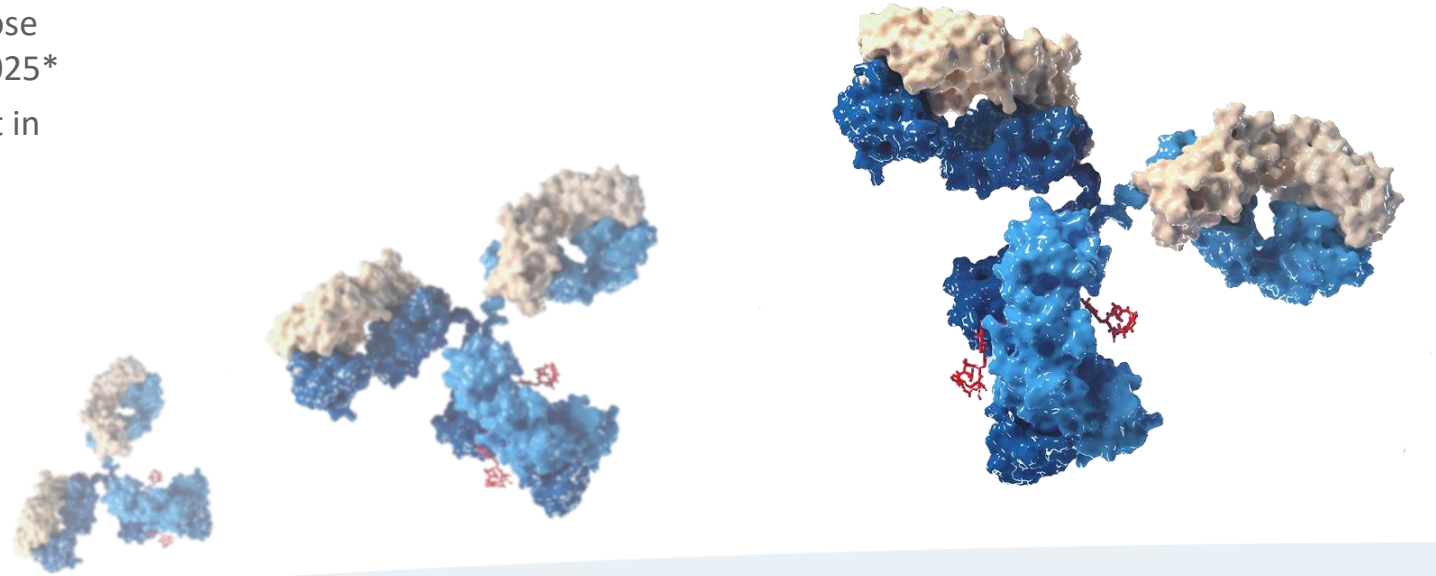
**Guanylyl cyclase C (GCC)-ATAC for colorectal cancer**

- IND-enabling and GLP tox studies starting in 2025

## HDP-201

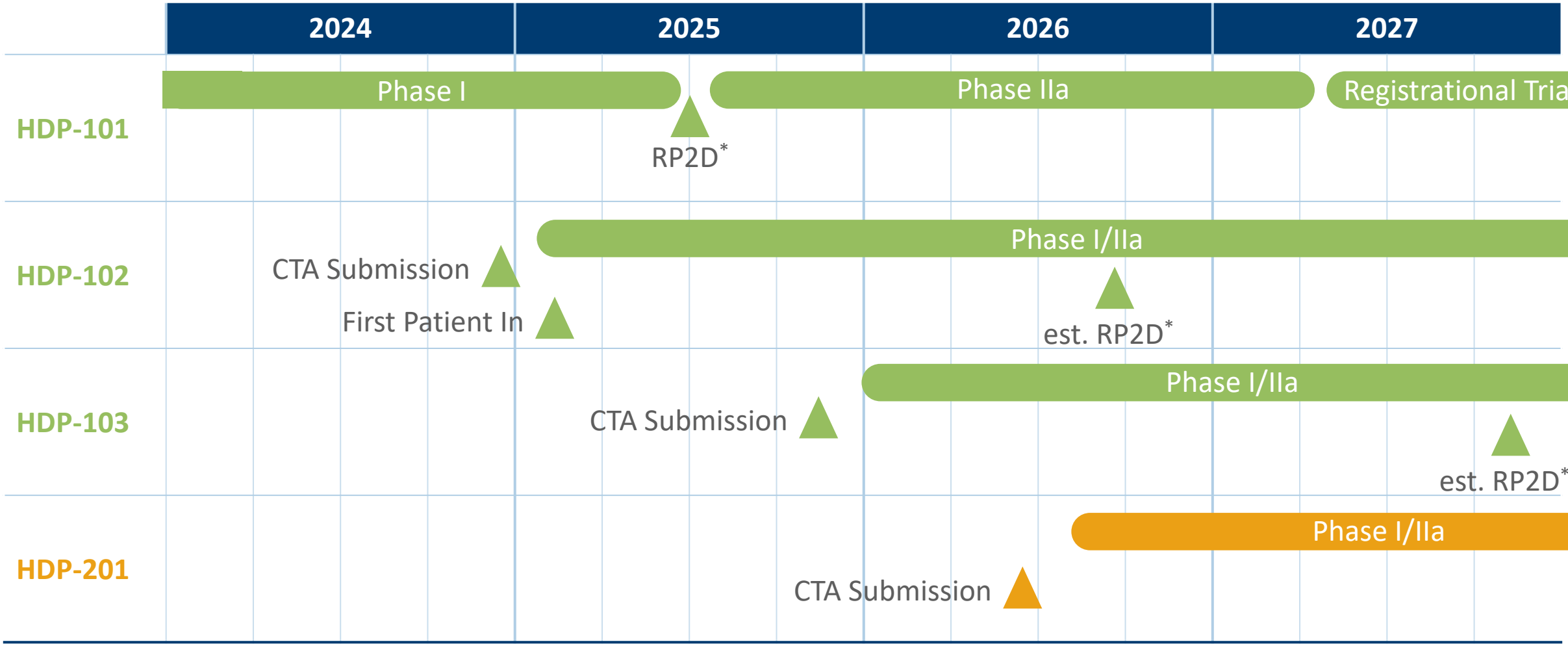
**Guanylyl cyclase C (GCC)-ETAC for colorectal cancer**

- ADC with payload Exatecan
- Preclinical studies demonstrate large therapeutic index & superiority versus known Deruxtecan ADCs
- CTA planned for 2026



*data driven timeline

# UPCOMING CATALYSTS: MULTIPLE VALUE-CREATING MILESTONES




**Partnered programs:**

- **Huadong Medicine** HDP-101 IND in China approved; starting Phase II in China in 2025
- **Takeda** conducts IND-enabling studies

*data driven timelines

# GOOD REASONS TO INVEST IN HEIDELBERG PHARMA

HDP-101 with first positive efficacy data and excellent potential for indication with high unmet medical need

Highly dynamic ADC environment with an attractive global market that is expected to grow to USD 19 billion in 2030

Expansion of partner network to increase the number of innovative ADCs, broaden indications and regions in the interests of patients

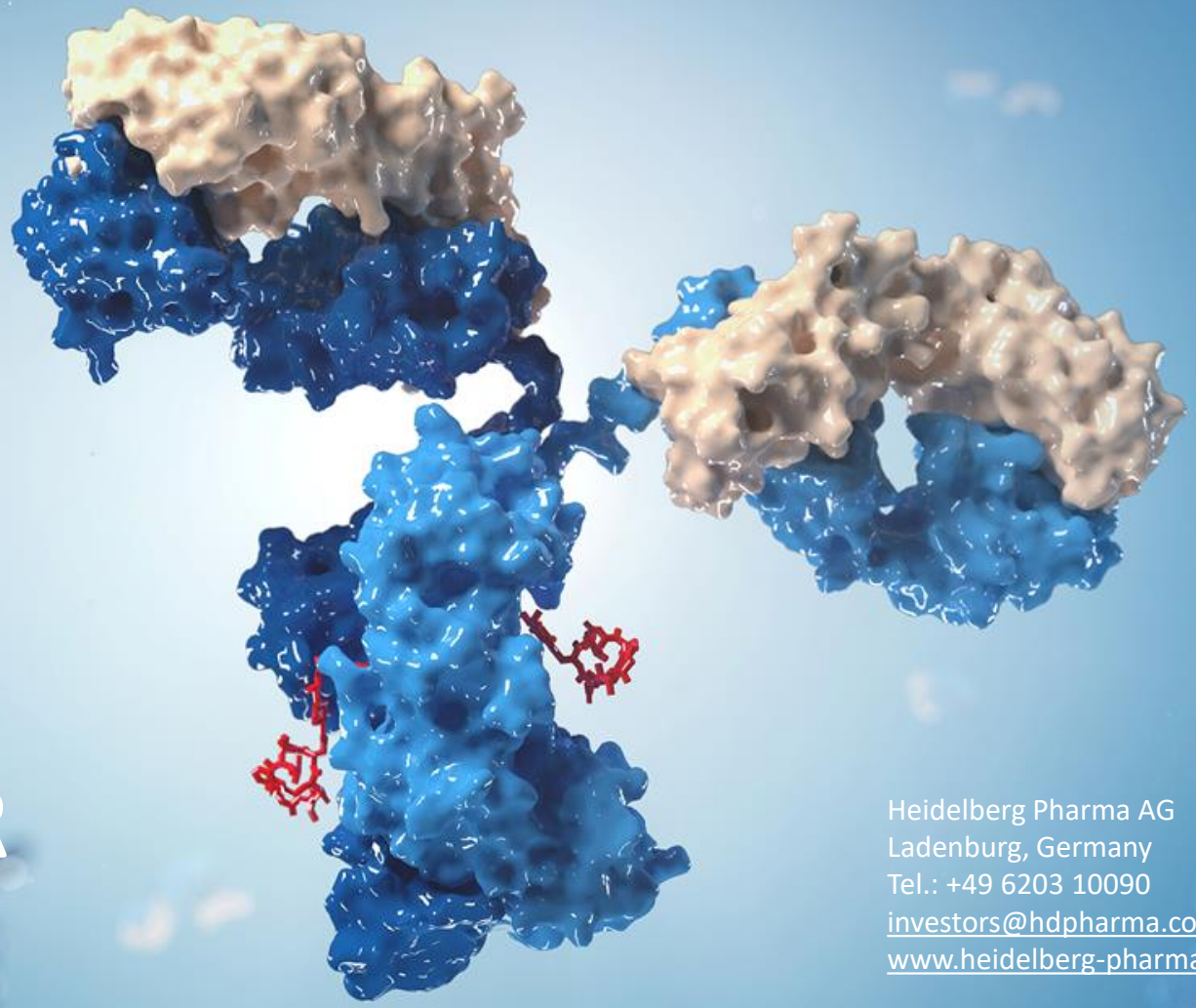
Numerous milestones in the next 36 months offer potential for a significant increase in the company's valuation

Solid cash reach until the end of 2026* ensures implementation of ongoing programs and clinical validation of ADCs

*taking into account the milestone payment of USD 75 million from HealthCare Royalty

We want to become a leading global ADC company with our clinical program

Heidelberg PHARMA



# THANK YOU FOR YOUR ATTENTION!

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