

ATACs: Unique new mode of action to fight cancer

May 2024

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, or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements.

Such factors include, among others, the following: uncertainties related to results of our clinical trials, the uncertainty of regulatory approval and commercial uncertainty, reimbursement and drug price uncertainty, the absence of sales and marketing experience and limited manufacturing capabilities, attraction and retention of technologically skilled employees, dependence on licenses, patents and proprietary technology, dependence upon collaborators, future capital needs and the uncertainty of additional funding, risks of product liability and limitations of insurance, limitations of supplies, competition from other biopharmaceutical, chemical and pharmaceutical companies, environmental, health and safety matters, availability of licensing arrangements, currency fluctuations, adverse changes in governmental rules and fiscal policies, civil unrest, acts of God, acts of war, and other factors referenced in this communication.

Given these uncertainties, prospective investors and partners are cautioned not to place undue reliance on such forward-looking statements. We disclaim any obligation to update any such forward-looking statements to reflect future events or developments.

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Management team with strong pharma and R&D experience



Prof. Dr. Andreas Pahl
CEO

Heidelberg Pharma since 2012, CEO since 2024

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



Walter Miller
CFO

Heidelberg Pharma since 2023

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



Dr. András Strasz
CMO

Heidelberg Pharma since 2020

More than 15 years experience in clinical drug development including roles at Sandoz, Amgen and biotech companies



Dr. George Badescu
CBO

Heidelberg Pharma since 2018

More than 15 years experience in industry roles including leadership positions at Abzena



Dr. Jörg Kemkowski
COO

Heidelberg Pharma since 2023

More than 30 years experience in human and animal healthcare industry in different R&D leadership positions



Building a world class ADC pipeline



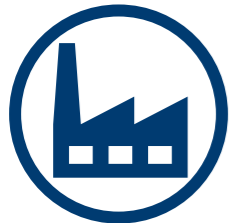
Differentiated ADC Technologies

- In Plug & Play mode
- 3 years from target to IND



Strong IP

- Several IP families
- Monopoly in the Amanitin/MoA space



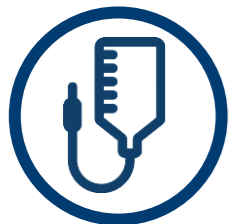
GMP Manufacturing

- Fully synthetic process for Amanitin
- 5 GMP batches completed



Partnerships

- Huadong: China-focused
- Takeda: ATAC technology
- Healthcare Royalty: Telix Pharma



Clinical Stage

- Data from HDP-101 dose escalation shows first objective responses and partial remissions
- HDP-102 CTA & FPI this year
- 2 additional CTAs in preparation



Corporate & Finance

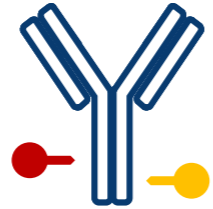
- Experienced leadership team; 105 employees
- Cash (runway): €32.6 million* (mid-2025)
- 75m USD milestone payment expected end of 2024

* as per end of February 2024

Strong in-house R&D capabilities and expertise



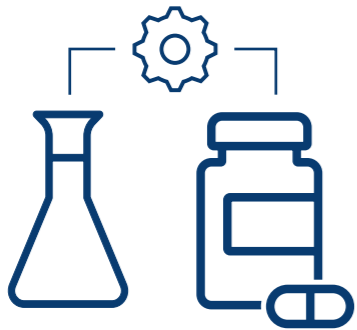
Synthetic chemistry



Antibody generation
& bioconjugation



Preclinical testing



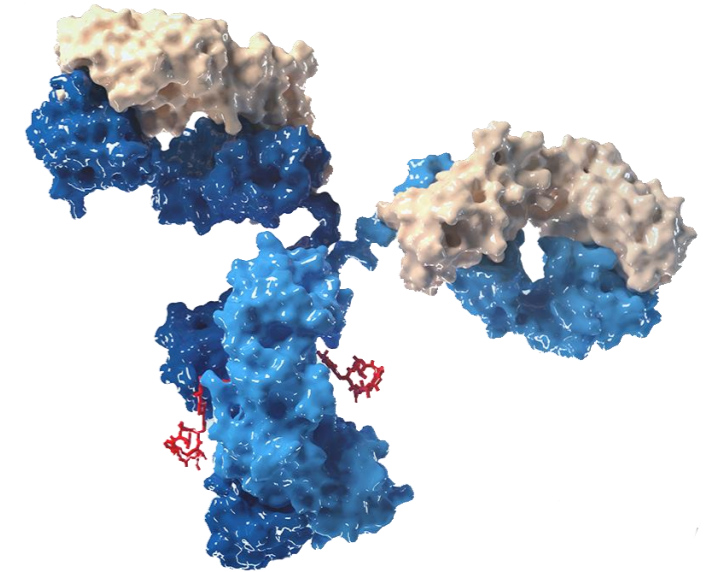
CMC



Bioanalytical sciences



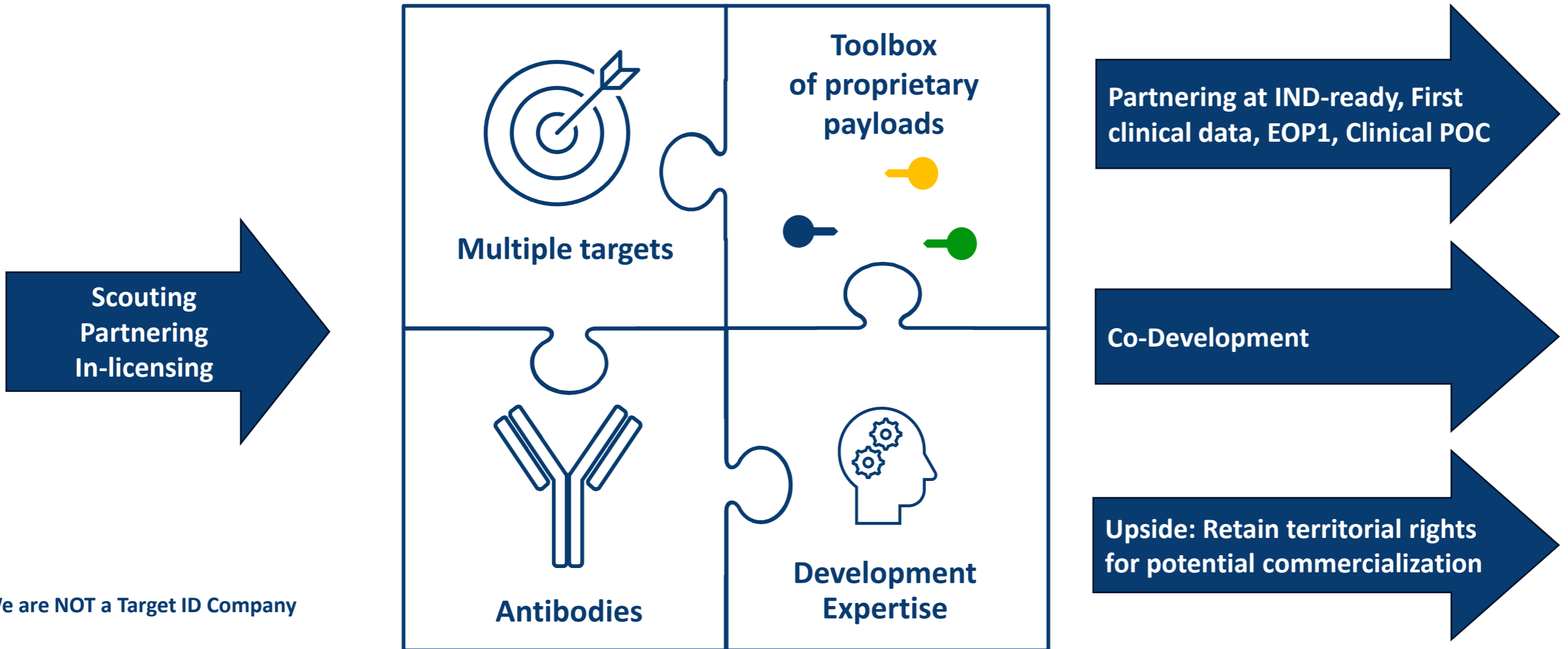
Clinical Development



Best ADC candidate in the shortest time

Value creation through development of best-in-class ADC assets

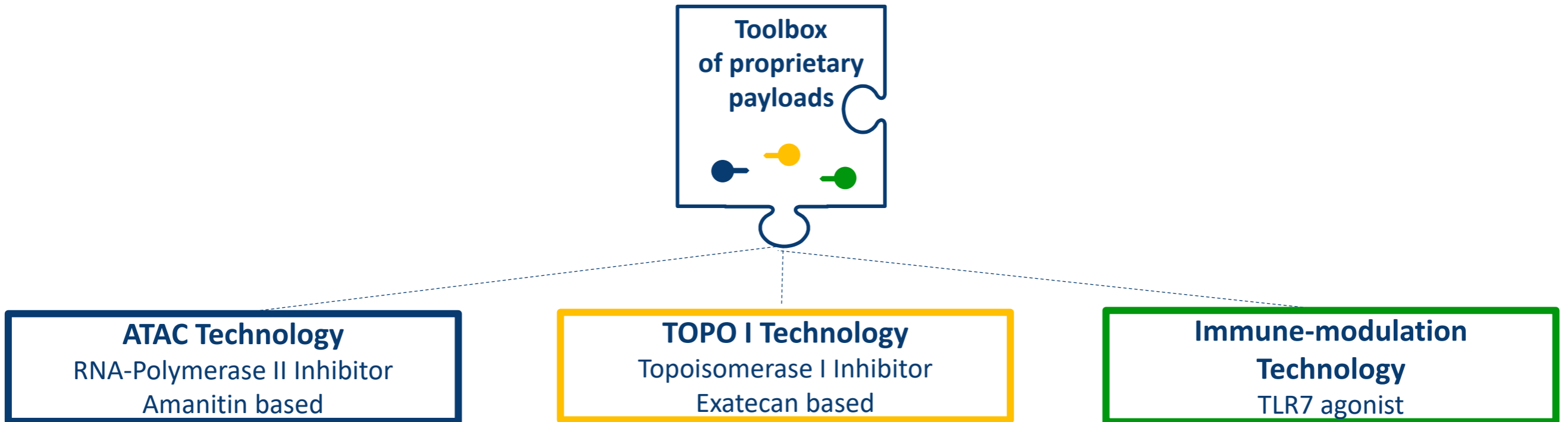
Discovery & development engine



We are NOT a Target ID Company

Payload Toolbox – Multiple MOAs

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



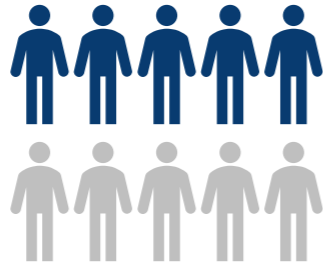
Different payloads and antibodies will lead to multiple development candidates with different modes of actions

Growing pipeline of proprietary and partnered programs

	Product	Target	Indication	Research	Preclinic	Phase I	Phase II	Phase III	Partner	
ATAC pipeline	HDP-101	BCMA	Multiple Myeloma	[Progress bar]					Huadong (China+*)	
	HDP-102	CD37	NHL (DLBCL/CLL)	[Progress bar]					Huadong (option China+)	
	HDP-103	PSMA	Prostate cancer	[Progress bar]					Huadong (China+)	
	HDP-104	GCC	Gastrointestinal (e.g., CRC)	[Progress bar]					Huadong (option China+)	
TOPO	HDP-201	GCC	Gastrointestinal	[Progress bar]					Proprietary	
ATAC partners	TAK-ATAC	n/a	Oncology	[Progress bar]					Takeda	
Legacy assets	TLX250-CDx	CA-IX	Renal Carcinoma Urothelial Carcinoma, TNBC	[Progress bar]						Telix
	TLX250	CA-IX	Renal carcinoma	[Progress bar]						Telix
	RHB-107		Oncology/GI, Covid-19	[Progress bar]						RedHill

* People’s Republic of China, Hong Kong, Macao, Taiwan, South Korea, Indonesia, Singapore, The Philippines, Thailand, Bangladesh, Bhutan, Brunei, Myanmar, Cambodia, Laos, Malaysia, Maldives, Mongolia, Nepal and Vietnam; excludes Japan, India, Pakistan, Sri Lanka

Resistance is one of the biggest challenges in oncology



1 in 2

people will be diagnosed
with cancer in their
lifetime



> 90%

of cancer deaths
are caused by drug
resistance

The journey of many cancer patients

Before Treatment



Treatment



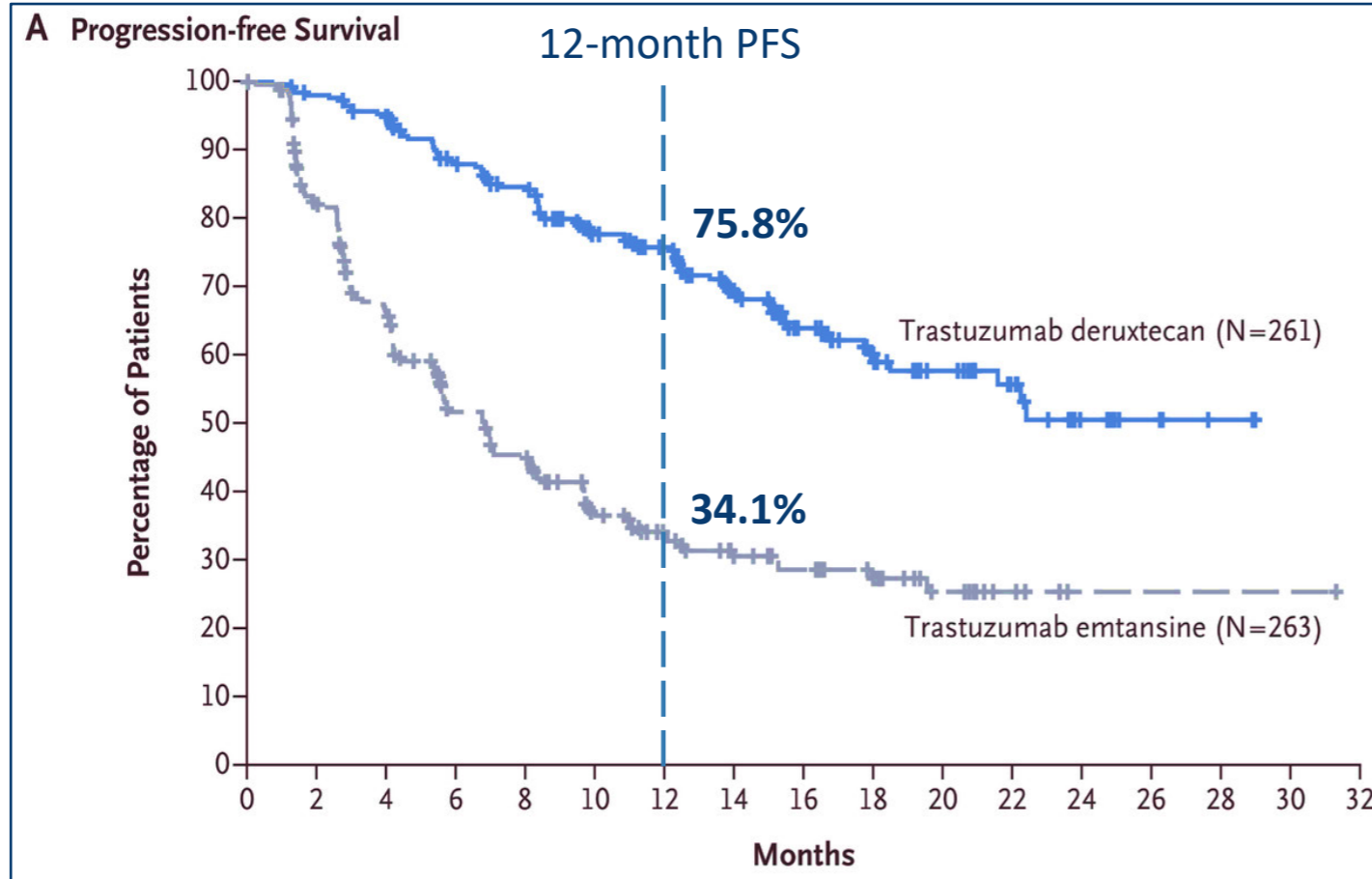
Resistance & Relapse



Wagke, N. et al, J Clin Oncol. 2011; 29(22): 3085–3096

We need new drugs with new mode-of-action to overcome resistance

The payload MOA is what makes the difference!



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

Enhertu®

Payload: deruxtecan (Topo 1 inhibitor)

Kadcyla®

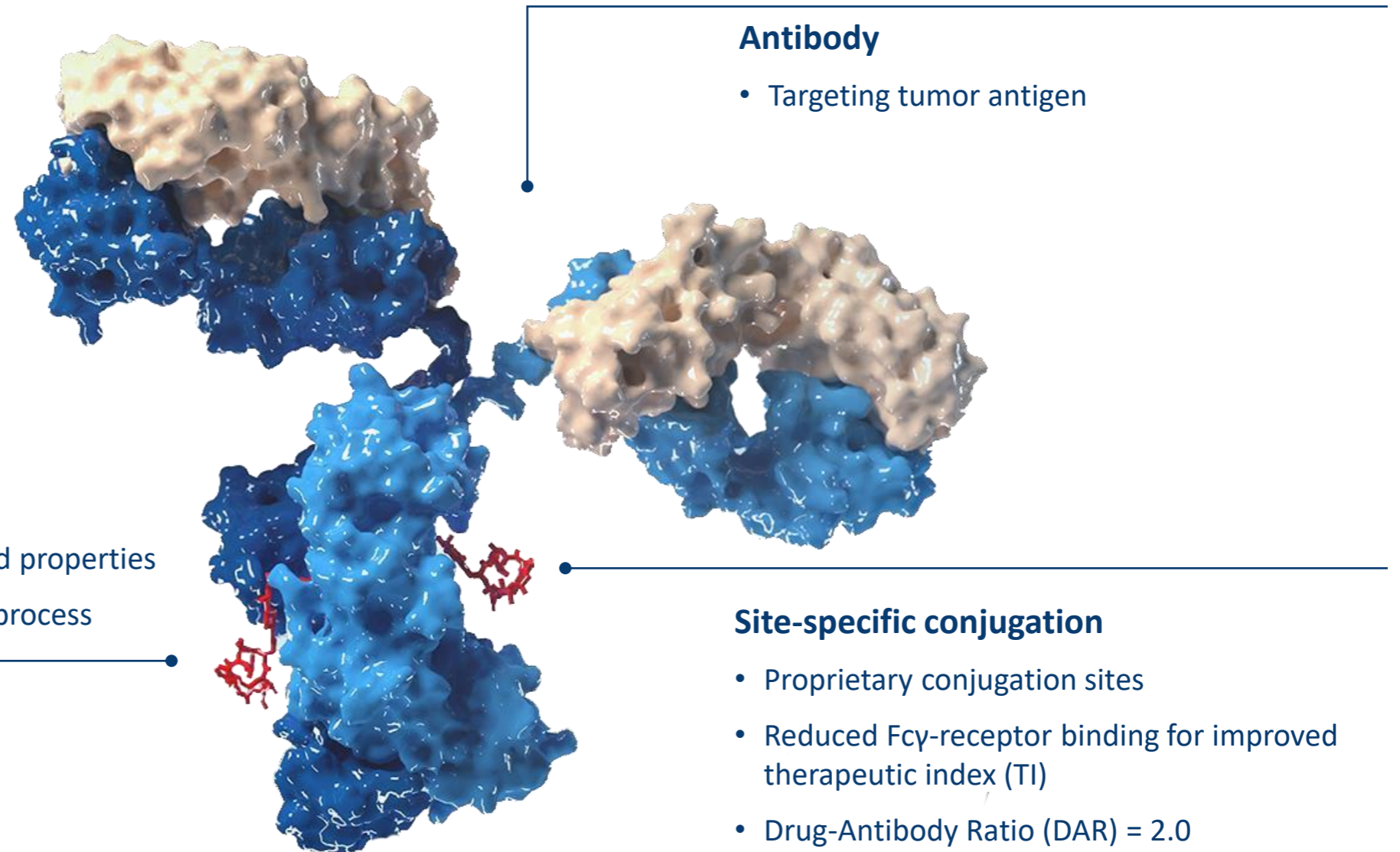
Payload: emtansine (Tubulin inhibitor)

Same target (Her2), same antibody (Trastuzumab), same patient population

ATACs are ADCs with amanitin as a payload

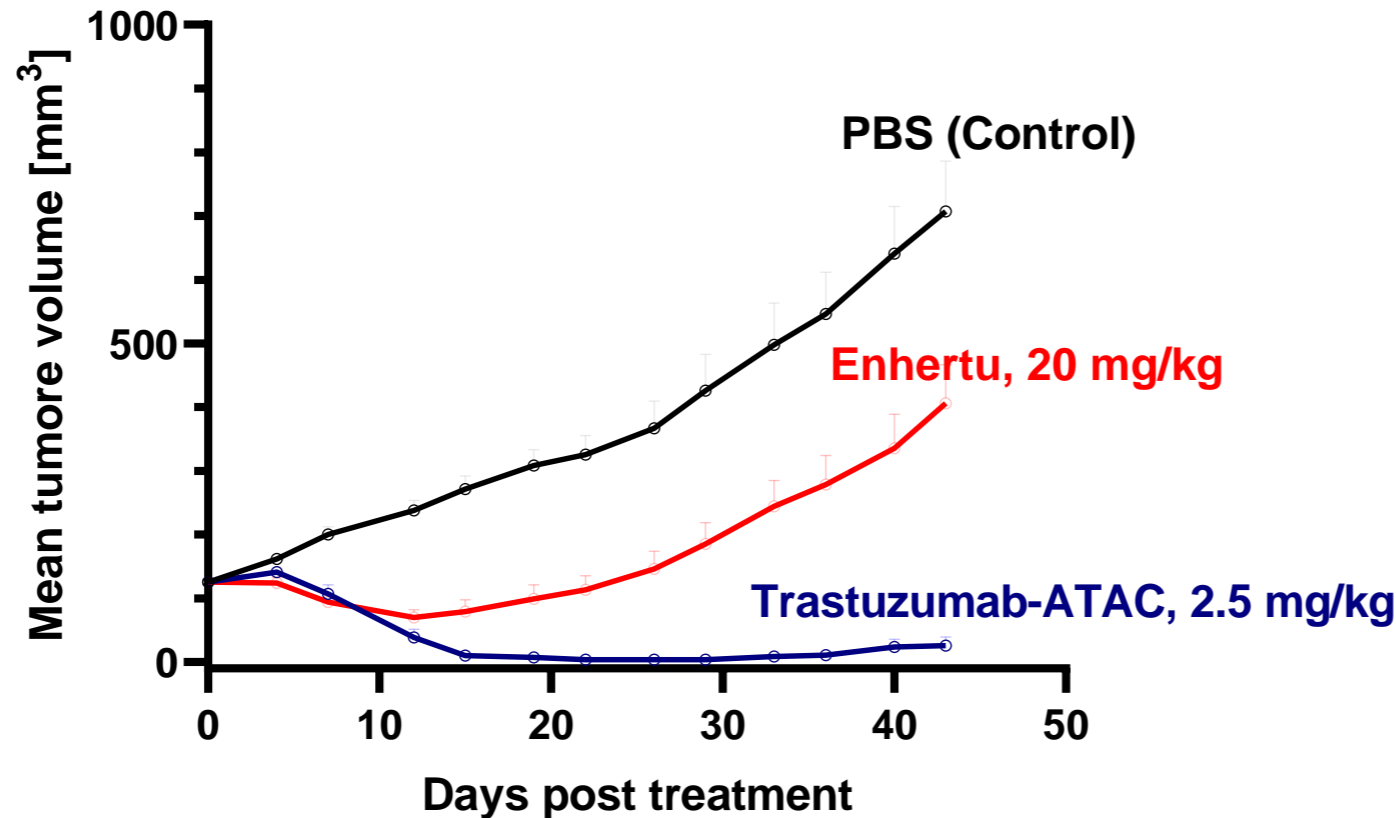
Amanitin as warhead

- Differentiated mechanism of action:
inhibition of RNA Polymerase II
 - Kills dormant tumor cells
 - Overcomes resistance
 - Predictive biomarker
- Synthetic amanitin derivatives with improved properties
- GMP manufacturing through fully synthetic process



The Payload Makes The Difference

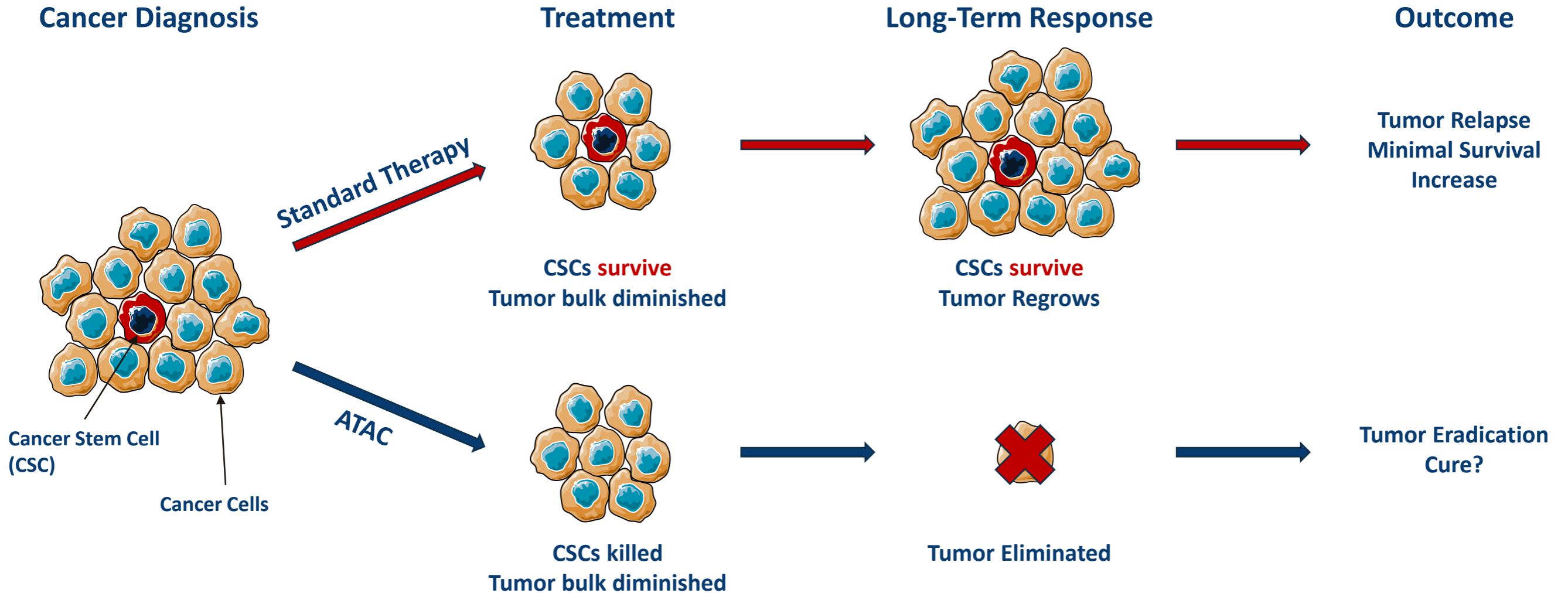
Breast cancer model (JIMT-1 Xenograft) is resistant to Kadcyła® and Enhertu®



- Same antibody (Trastuzumab), different payload (amanitin vs. topoisomerase inhibitor)
- **Complete remission after single-dose application of HER2-ATAC.**

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

ATACs address the limitations of current cancer therapies



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

Del(17p): Potential platform-wide predictive biomarker

Deletion of TP53 (tumor suppressor)

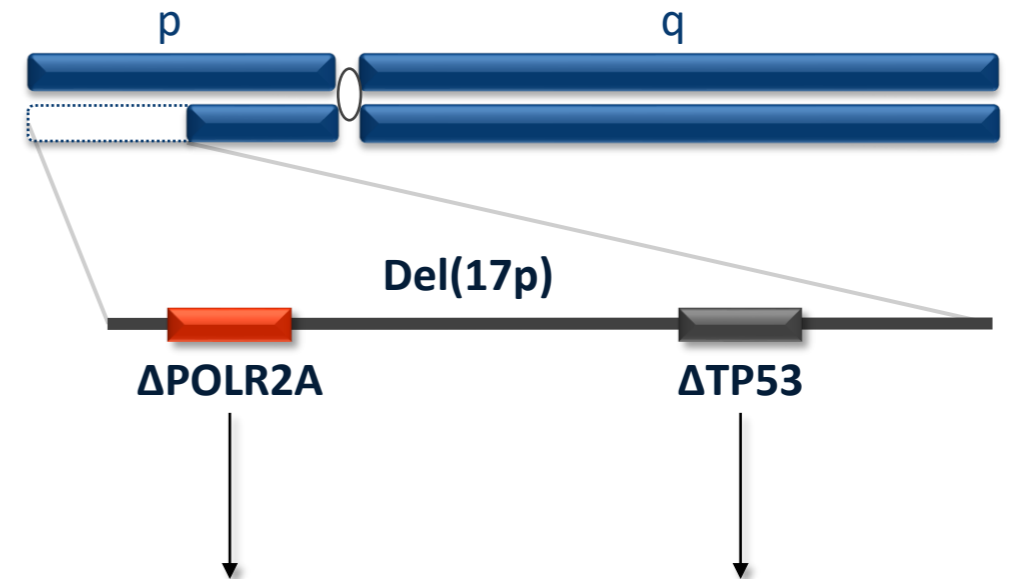
- High incidence
- More aggressive tumors **resistant** to SoC and poor prognosis

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

- Higher sensitivity to ATAC treatment

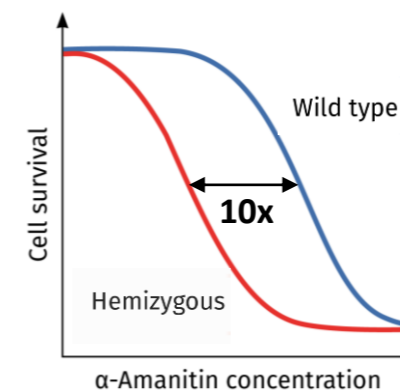
Occurs only in tumor cells

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



Intracellular target of amanitin: Increases ATAC sensitivity

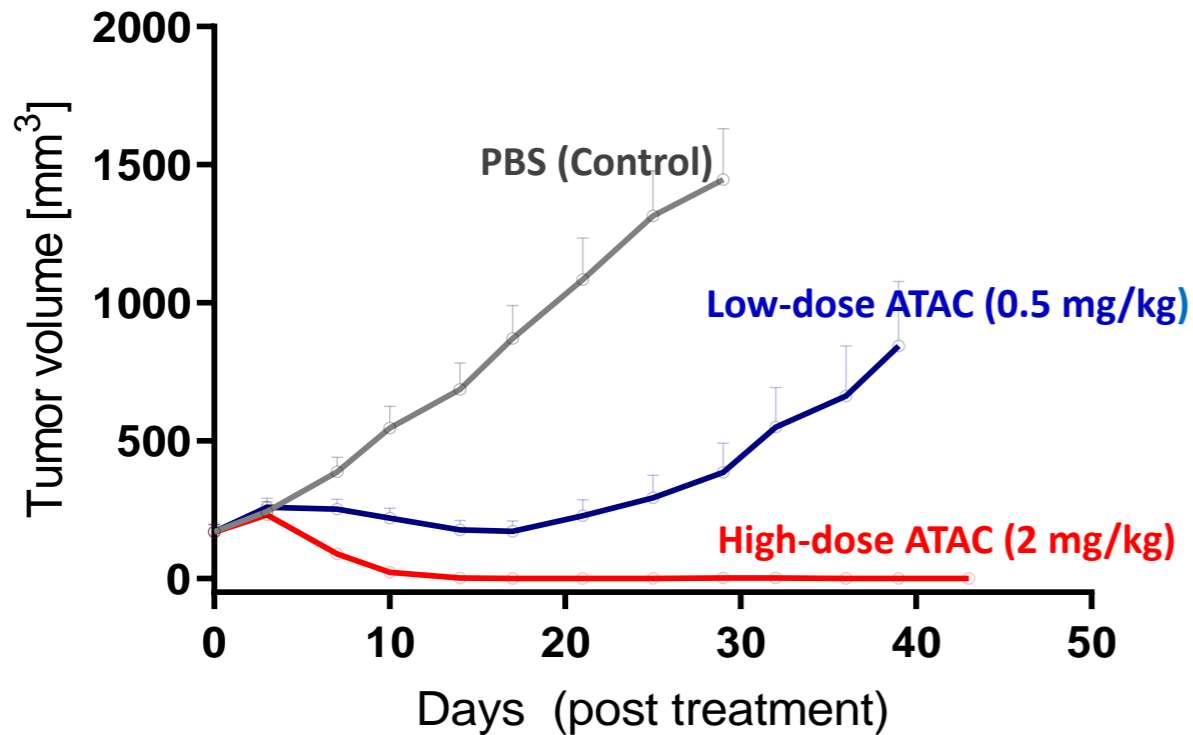
Tumor suppressor: Increases tumor aggressiveness & resistance



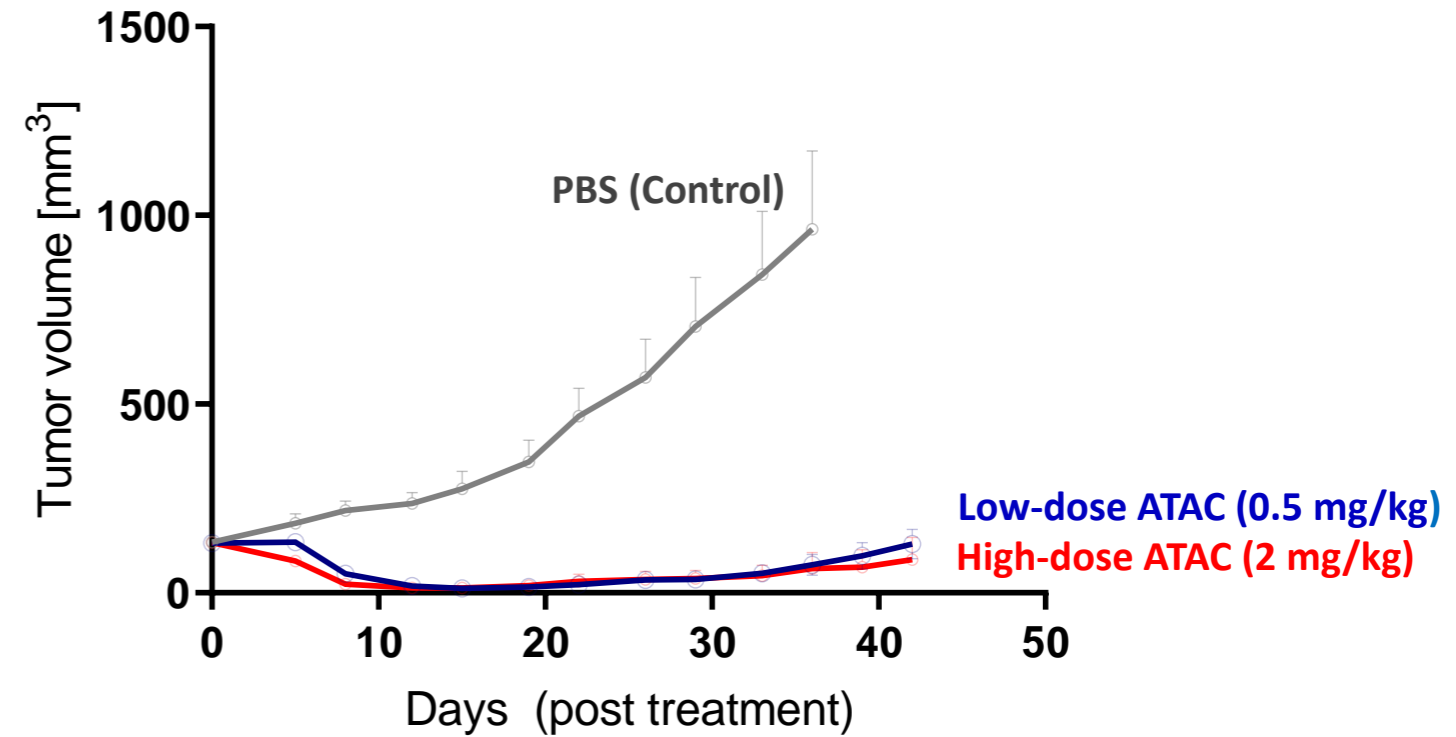
Del(17p): Potential platform-wide predictive biomarker

Her2 1+ patient-derived xenograft models

Wildtype - normal RNA Pol II levels



Del(17p) - reduced RNA Pol II levels



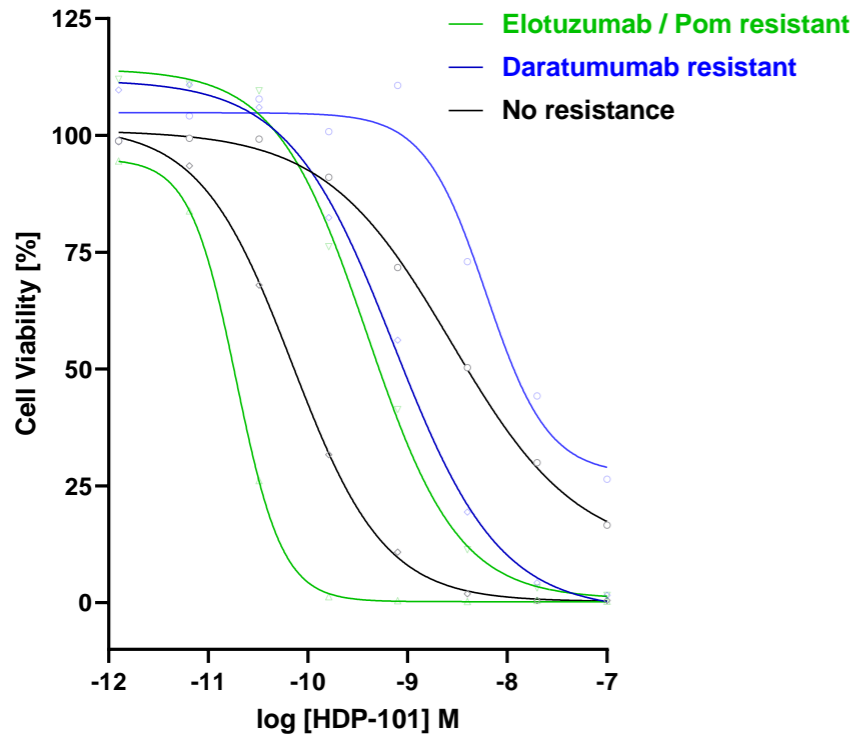
Less amanitin is required to kill del(17p) cells

Wider therapeutic index in patients with del(17p) tumors

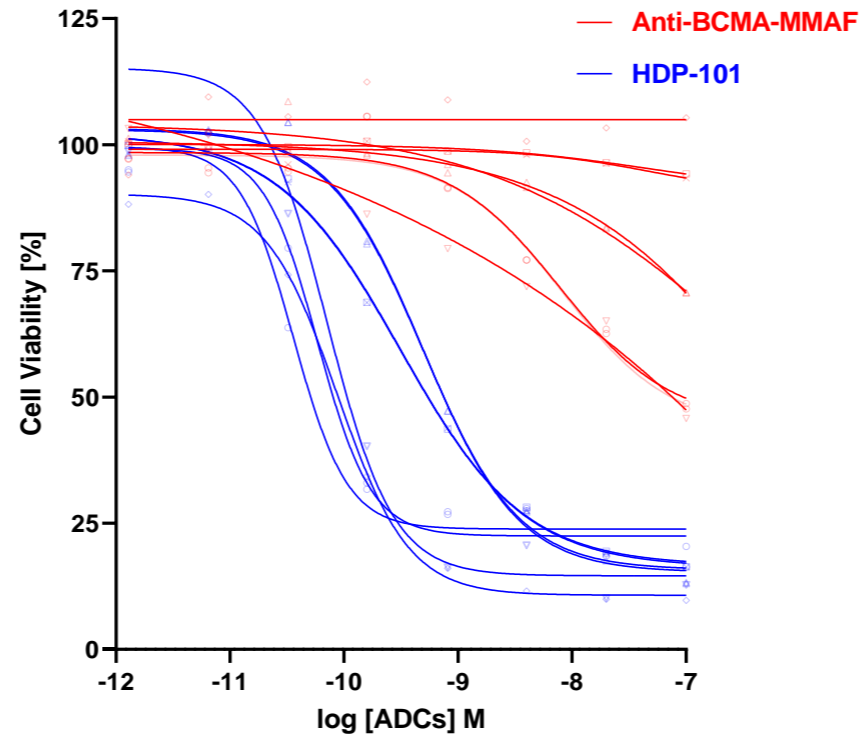
We know ATACs work

HDP-101 is highly efficacious in primary myeloma cells from patients

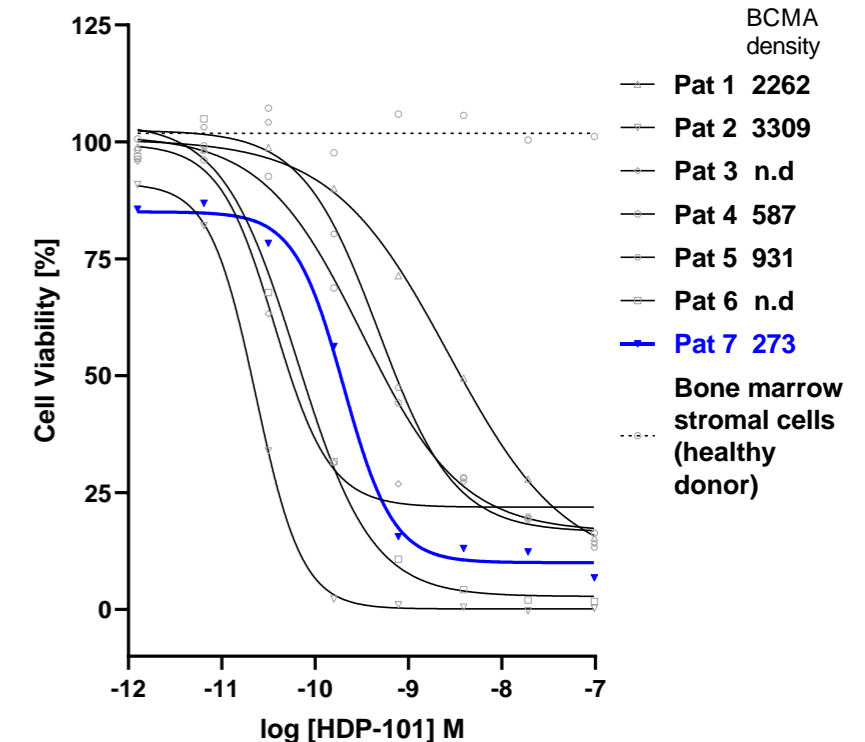
Overcomes resistance in patients refractory to SOC



More efficacious than other payloads by killing non-dividing tumor cells



Overcomes resistance through antigen escape by killing cells with ultra-low antigen expression



HDP-101 overcomes multiple types of resistance in patient cells

HDP-101 Phase I/IIa study in Multiple Myeloma patients

Multiple Myeloma (MM) is a type of blood cancer

- that develops from plasma cells in the bone marrow and can affect more than one part of the body
- In myeloma, the bone marrow makes lots of abnormal (cancerous) plasma cells.
- Worldwide incidence of multiple myeloma is currently 160,000 with a mortality of 106,000.

Phase I part is making good progress

- Five patient cohorts (20, 30, 60, 80 and 100 µg/kg) completed
 - 18 patients in total
 - Treatment was safe and well-tolerated in the first four cohorts
 - 1 patient in stable disease on monotherapy for > 1 year from cohort 3
- Cohort 5:
 - First efficacy: 3 objective responses at dose level 100 µg/kg,
 - 3 partial remissions out of 5 patients treated continuously with 100 µg/kg
 - Safety Review Committee recommended dose optimization to increase tolerability
 - Initial reduction of thrombocyte count addressed by planned modification and optimization of the medication regimen (protocol amendment) in Cohort 6



Source: healthcare-in-europe.com

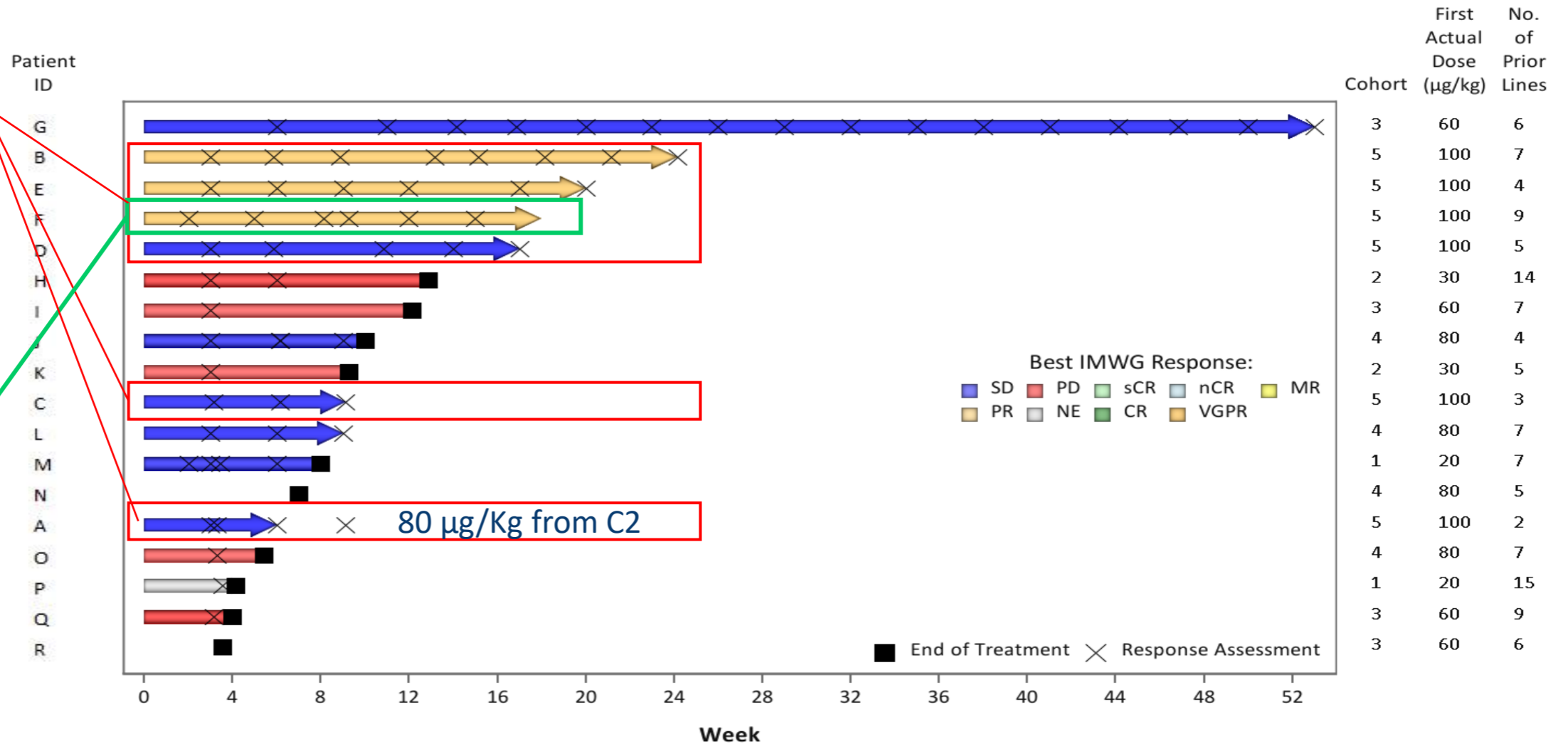


Source: Heidelberg Pharma

HDP-101-01 – Overview of efficacy data – Best responses

100 µg/Kg
3 of 6 responders
(one patient with PD had dose reduction after C1)

Prior exposure to BCMA and GPRC5D directed drug



Each bar represents one patient in the study. Right arrow cap indicates continued on study.
 Response criteria: IMWG for Multiple Myeloma (MM): SCR=Stringent Complete Response, CR=Complete Response, VGPR=Very Good Partial Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease, NE=Non-evaluable, ND=Not done.

Dose scheme adaptation

Dose escalation continues with amended dosing scheme in Cohort 6

Starting from cohort 6, cohort will have 3 arms:

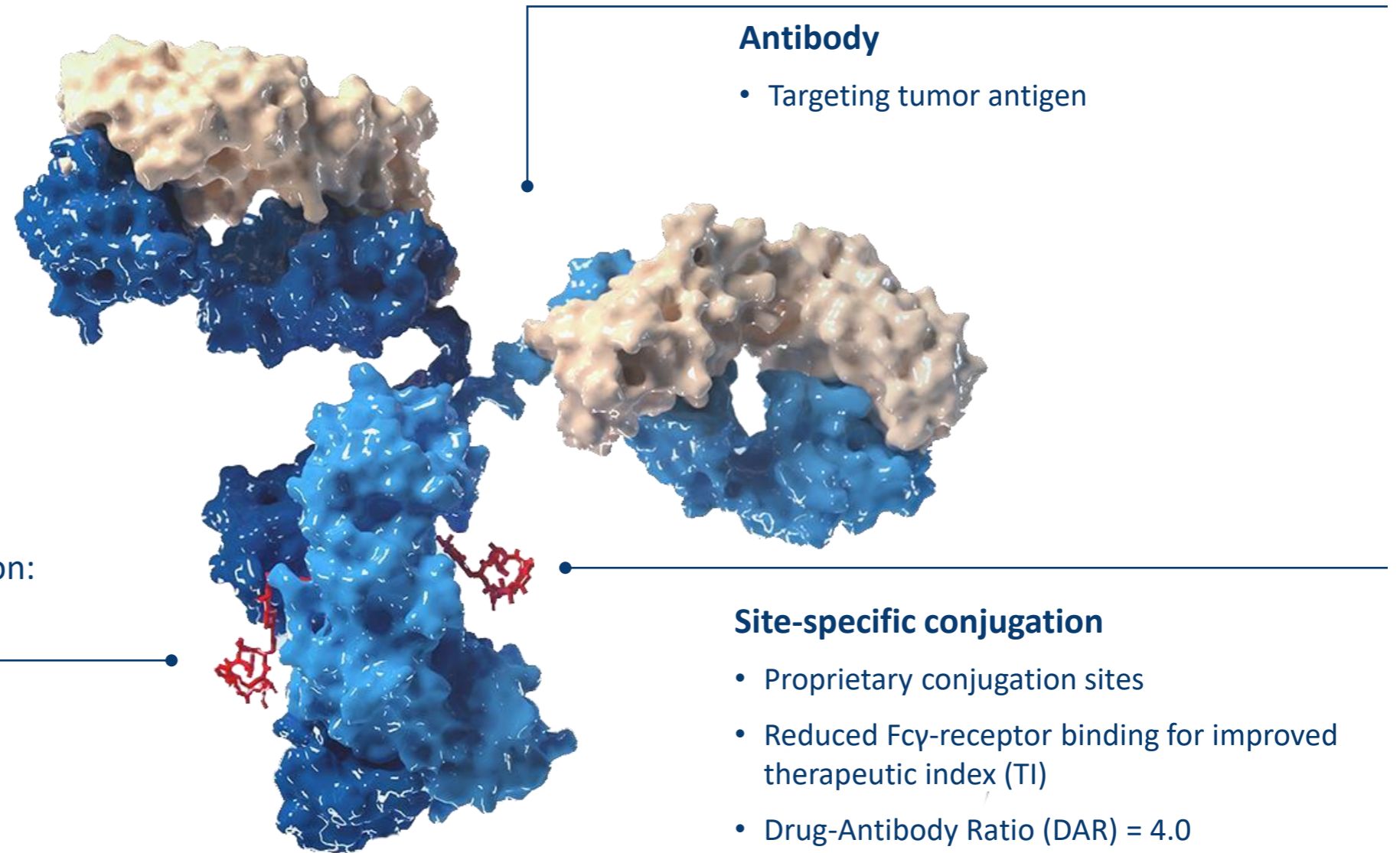
- Arm A: single dose of HDP-101 (after premedication) on day 1 of each 21-day cycle
- Arm B: split dose of HDP-101 on days 1, 8, and 15 of each cycle (weekly dosing)
- Arm C: split dose of HDP-101 on days 1 and 8 of cycle 1 followed by a single dose on day 1 of each subsequent cycle

At least 3 patients per arm to be included

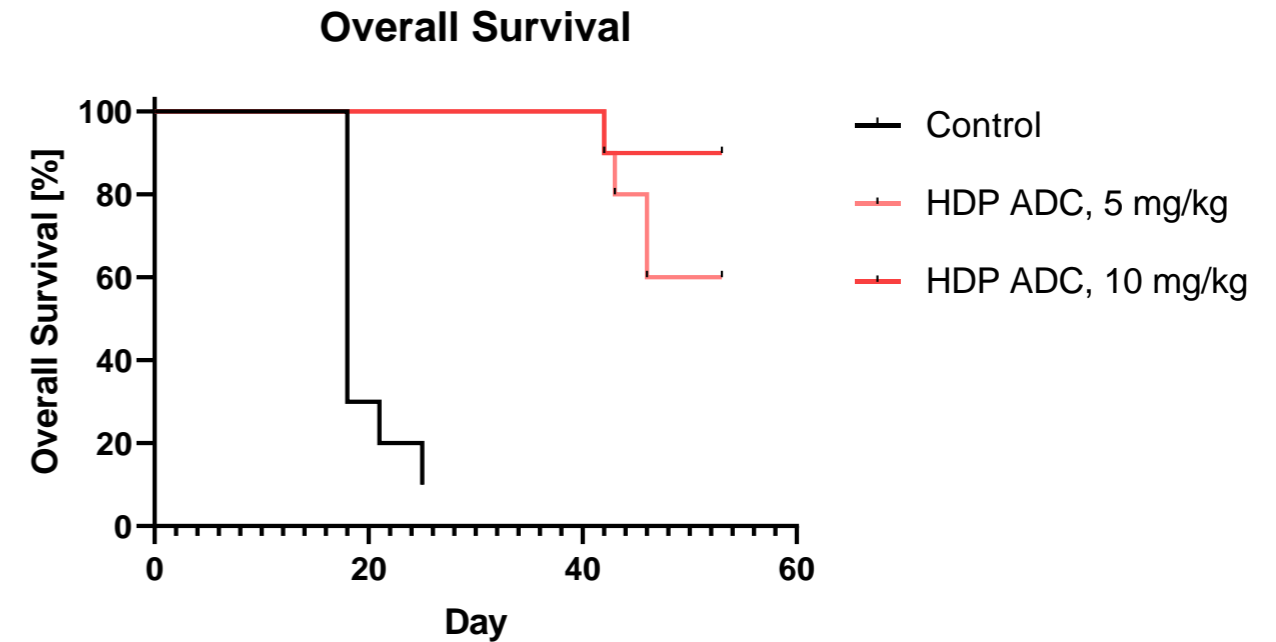
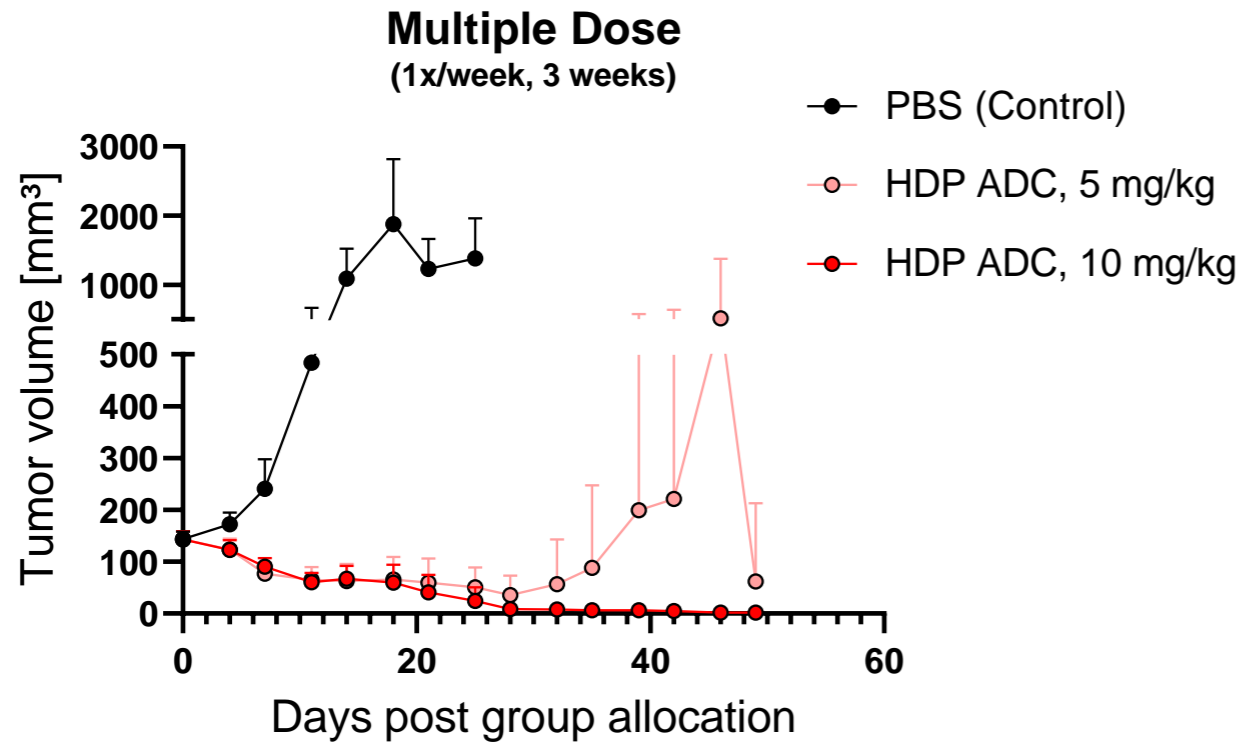
After Cohort 6, potential next cohorts will be continued with promising regimes only



ADCs with TOPO I inhibitor as a payload



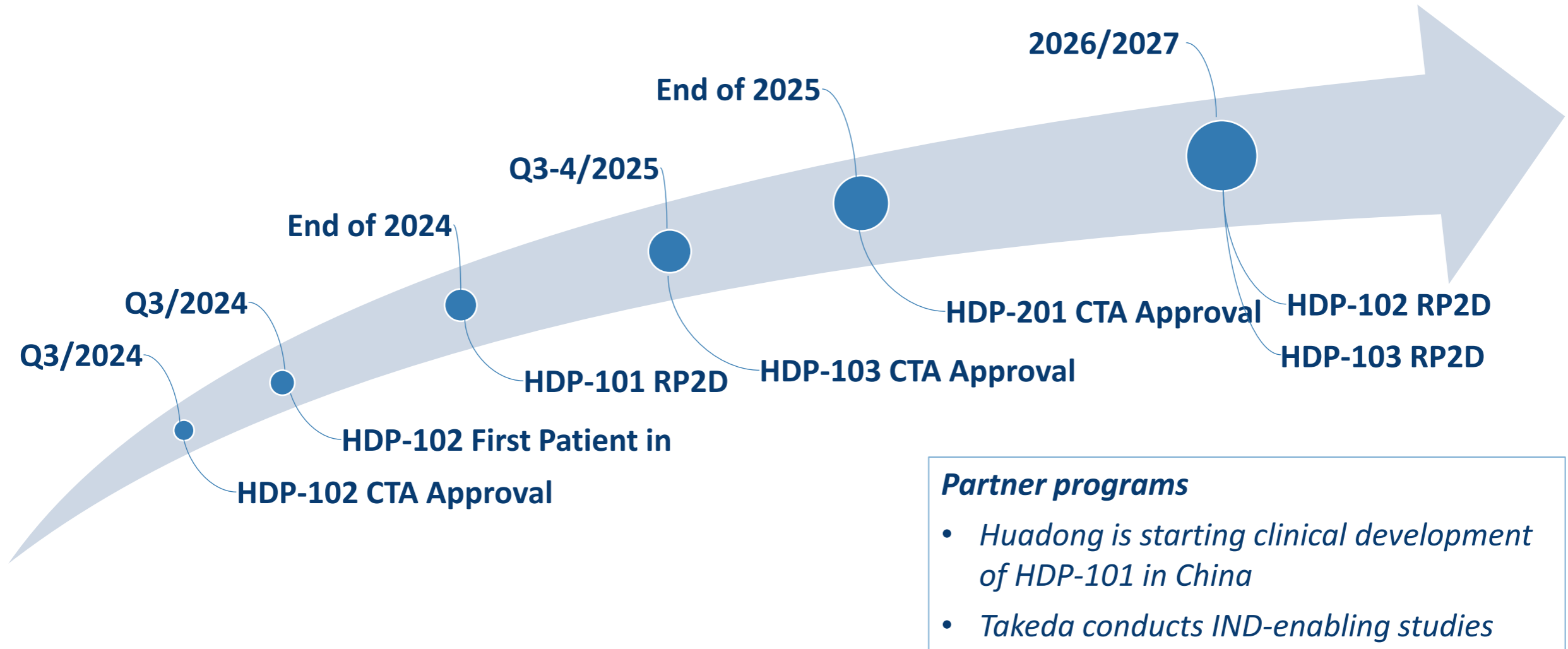
Strong efficacy of TOPO I ADC upon multiple dose treatment

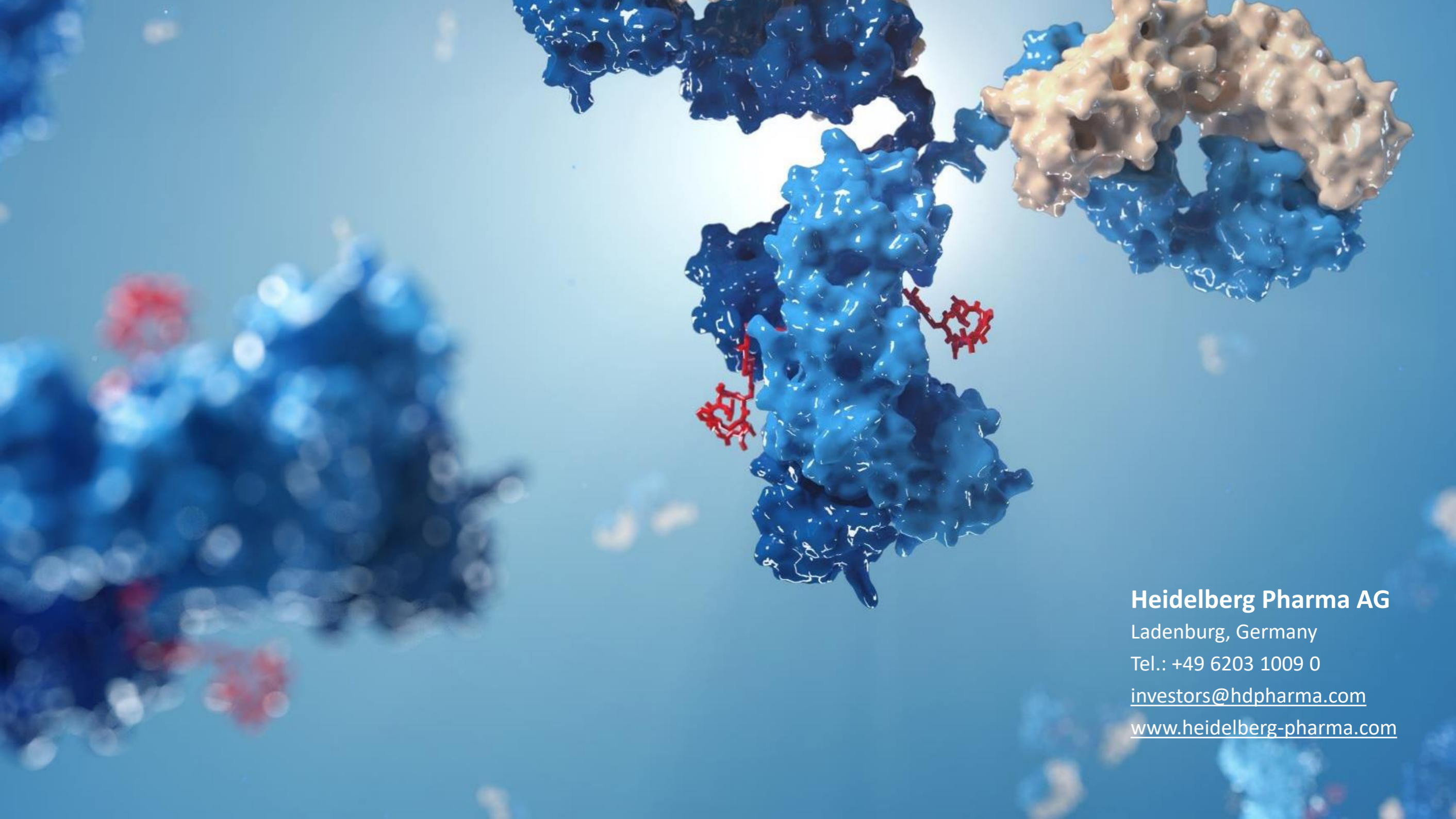


- Efficacy of Heidelberg Pharma's ADC similar to Deruxtecan ADC
- Only half the amount of toxin (DAR 4 vs DAR 8-10)

Our upcoming catalysts to become a leading global ADC player

Multiple inflection points with potential to increase company valuation significantly





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