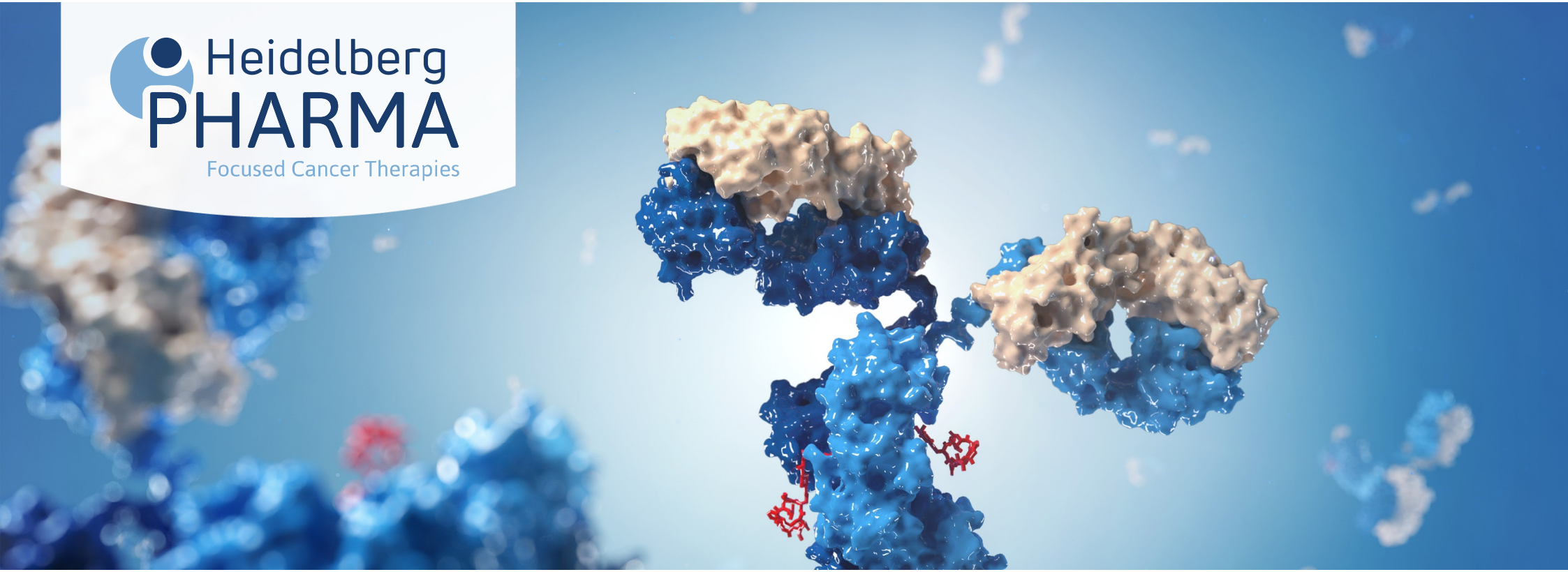
Heidelberg PHARMA
Focused Cancer Therapies



ATACs: a Unique New Mode of Action to Fight Cancer

September 2021

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, 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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Corporate Overview

Technology & Validation

Business model

Proprietary ATAC projects

Financials & Outlook

Heidelberg Pharma at a Glance

Developing new options to address major challenges in cancer therapy

Our Company

Listed as Heidelberg Pharma AG
Frankfurt Stock Exchange: HPHA

Shares outstanding: 34.17 million

Market cap: ~€230 million

Headquarters: Ladenburg, Germany

~ 90 employees

Our Mission

New option in cancer therapy with a unique mode of action

Overcome resistance mechanisms

Kill dormant tumor cells

Biomarker for patient stratification and expedited development

Our Approach

Inhibition of RNA Polymerase II

Amanitin as toxic payload

Targeted delivery via antibodies (ADC technology)

ATAC Technology

Business model: develop proprietary ATAC pipeline, partner ATAC technology platform and generate upside potential from legacy clinical portfolio

Highlights of ADC Deals and Approvals

ADCs are HOT!

ADCs have become one of the most validated and sought-after therapeutic modalities

2019

Mar
AstraZeneca inks $6bn deal with Daiichi Sankyo for HER2 ADC

Jun
POLIVY polatuzumab vedotin-piiq
CD79B
Genentech

Dec
PADCEV enfortumab vedotin-ejfv
Nectin-4
Astellas Pharma

2020

Dec
ENHERTU fam-trastuzumab deruxtecan-nxki
Her2
AZ/Daiichi Sankyo

Apr
TRODELVY sacituzumab govitecan-hziy
TROP2
Immunomedics
Accelerated approval

Jul
AstraZeneca $6bn deal with Daiichi Sankyo for TROP2 ADC

Aug
BLENREP belantamab mafodotin-blmf
BCMA
GSK0

Sep
Gilead acquires Immunomedics for $21bn

Sep
Merck inks $4.5bn deal with SeaGen

Nov
Merck acquires VelosBio for $2.8bn for ROR1 ADC

Dec
Boehringer acquires NBE-Therapeutics for $1.4bn

2021

Apr
Zynlonta loncastuximab tesirine-lpyl
CD19
ADC Therapeutics

May
Daiichi Sankyo invests $13.8bn in 3 ADC programs

May
Zydus Cadila markets Ujvira®, the first ADC biosimilar of Roche's (Kadcyla®)

Aug
BMS acquires anti-FOLR1 ADC for $650m from Elsai

Seagen signs deal for up to $2.6 bn with RemeGen for HER2 ADC

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ATACs Fill the Gap
Missing MoA of Cancer Chemotherapeutics

Amanitin – novel mode of action for cancer therapy

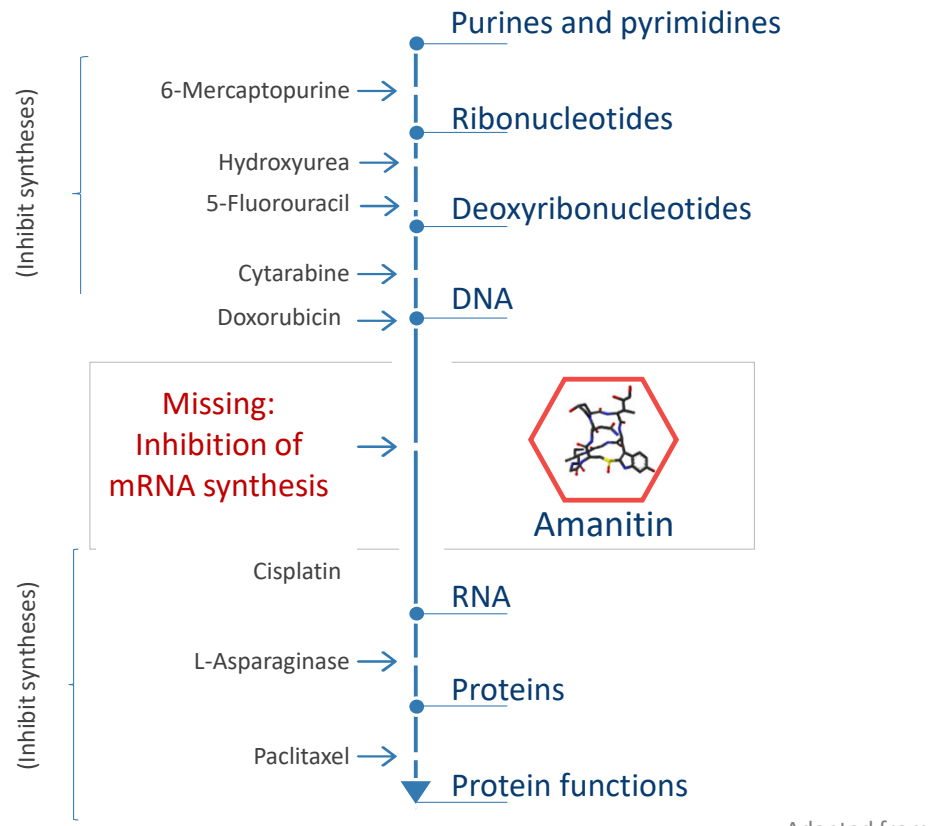
Amanitin specifically binds and inhibits RNA polymerase II – the only currently known inhibitor of RNA polymerase II

Amanitin kills dividing AND quiescent tumor cells by inhibiting mRNA synthesis

→ **Potential clinical benefits by**

- **Strong efficacy** in *in vivo* and *in vitro* models
- Ability to **overcome resistance**
- **Kill dormant tumor cells** causing metastasis & tumor relapse, independent of cell proliferation

Heidelberg Pharma's technology platform makes highly toxic Amanitin accessible for cancer therapy



Adapted from
http://chemistry.elmhurst.edu/vchembook/655cancer2.html

Antibody Targeted Amanitin Conjugates (ATACs)
Combining the Best of Two Therapeutic Modalities

ADCs with Amanitin as toxic payload = **ATACs** (**A**ntibody **T**argeted **A**manitin **C**onjugates)

Highly effective payload

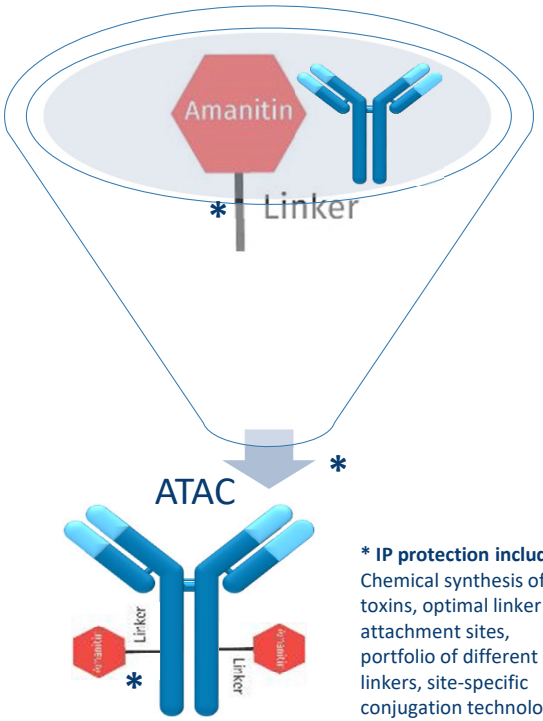
Death cap mushroom

From nature to the lab

Chemical synthesis *

Amanitin

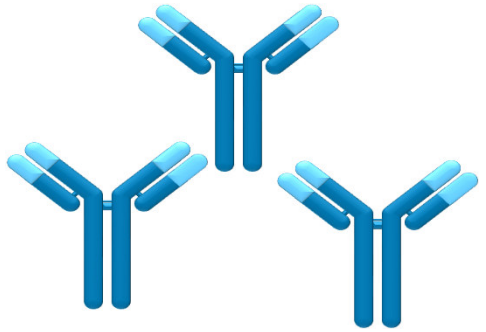
ATAC technology



*** IP protection includes** Chemical synthesis of toxins, optimal linker attachment sites, portfolio of different linkers, site-specific conjugation technology

Highly specific antibody

- Antibodies for **different tumor targets**
- Targets determine indications
- Tumor specific delivery
- Internalization of target
- Access to antibodies through licensing or partnering



Source: pilz-ratgeber.de

ATACs Overcome Resistance
Early and Explorative Model for Breast Cancer

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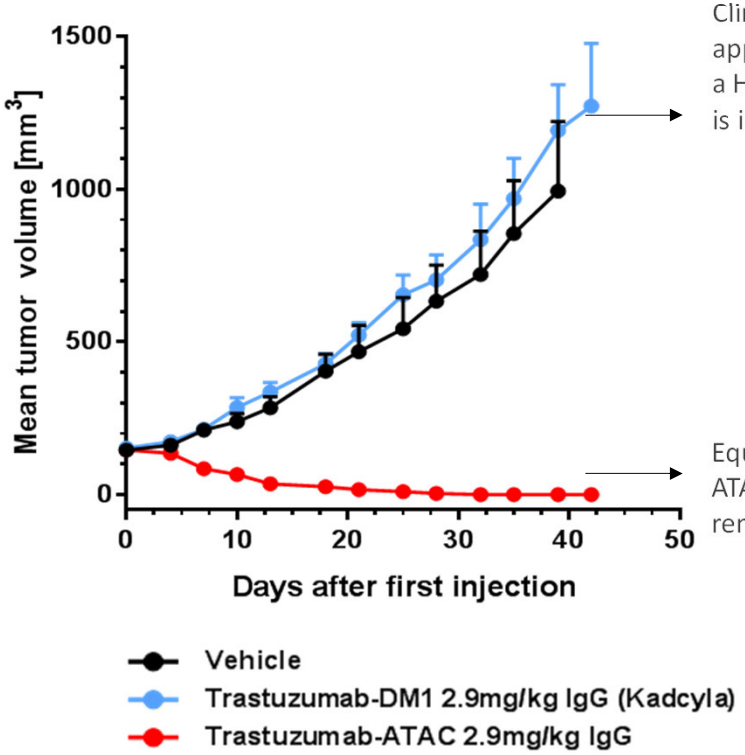
Complete remission of a breast cancer xenograft model after single-dose application of HER2-ATAC

JIMT-1 Xenograft



Clinical dose of FDA-approved Kadcyla®, a HER2-DM1-ADC, is ineffective

Equivalent dose of HER2-ATAC shows complete remission

→ **ATACs** are **highly potent & superior** to existing payloads

→ **ATACs** can **overcome resistance** in *in vivo* models

ATACs Kill Dormant Tumor Cells
Lead Candidate HDP-101 ex-vivo Model

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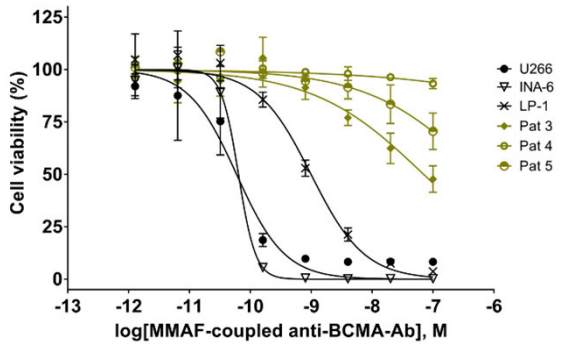
Anti-BCMA-ATAC (HDP-101) is able to kill non-dividing primary tumor cells

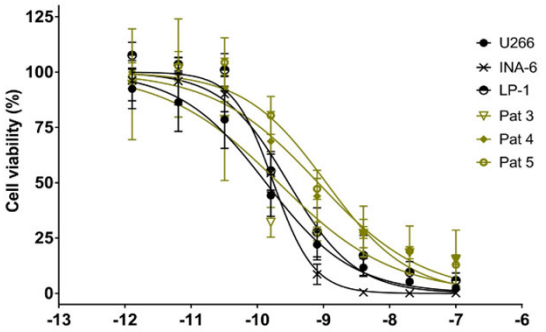
Comparison with MMAF (Auristatin Conjugate as used by GSK) on MM Patient Cells

- Non-dividing (quiescent) cells isolated from multiple myeloma patients bone marrow biopsies
- Dividing tumor cells from lab cell lines

Anti-BCMA-Ab coupled with GSK payload MMAF



HDP-101 (anti-BCMA-Ab coupled with payload Amanitin)

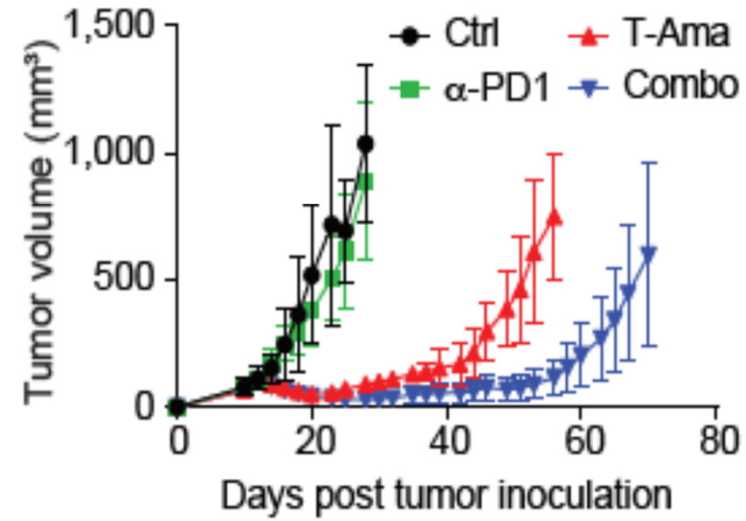


ATACs can kill non-dividing primary tumor cells and may eliminate dormant tumor stem cells

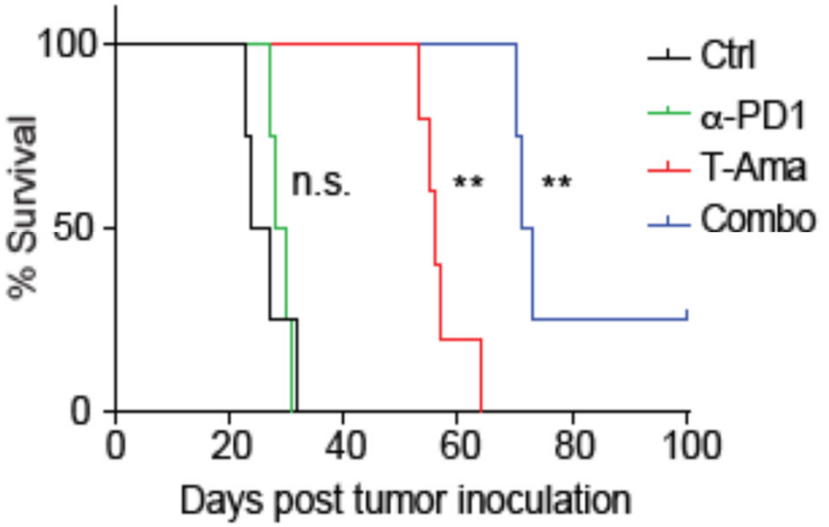
ATACs Exhibit Synergy with Immune Checkpoint Inhibitors

C57BL76-Tg(WapHER2) mice orthotopically implanted with HER2-low EO771 cells with 11B loss

Tumor growth curve



Survival analysis

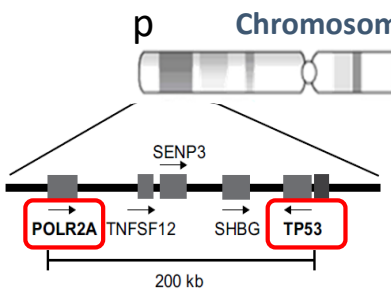


Sci. Transl. Med. **13** (2021)

HER2-ATAC potentiates immune checkpoint blockade therapy in treating HER2-low Breast Cancer.

Platform Wide Del(17p) Biomarker to Enable Accelerated Approval

del(17p) tumors have higher sensitivity to ATACs



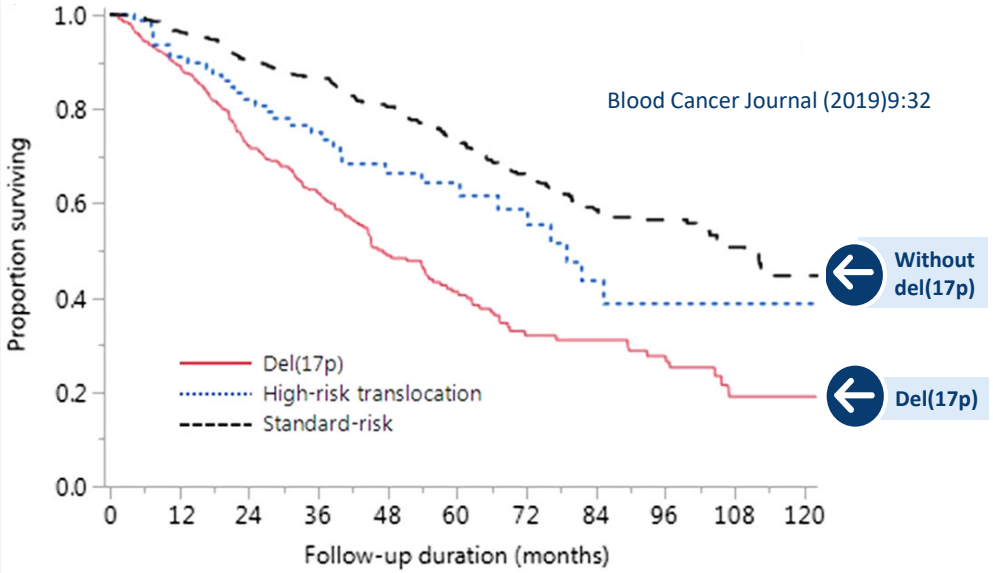
del(17p) co-deletion of:

- Tumor Suppressor (TP53)
- RNA Polymerase II (POLR2A)

- ATACs delivers Amanitin to tumor cells, where it binds to and inhibits RNA Polymerase II.
- Tumor cells with del(17p) have reduced RNA Polymerase II, leading to higher sensitivity to treatment with ATACs.
- Further, del(17p) identifies **high-risk patients** with unmet medical need.

Poor prognosis for MM patients with del(17p)

Lower survival for **del(17p)** compared to **Standard Risk**:
47.3 vs. **109.8** months



17p deletion is a potential biomarker to increase therapeutic window and identify high-risk patients

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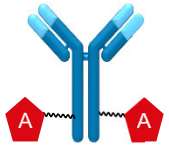
Strategic Cornerstones

Build proprietary ATAC pipeline

HDP-101 – ATAC targeted against BCMA (multiple myeloma)



ATACs for additional oncology indications (HDP-102 & HDP-103)

Antibody discovery for further targets

ATAC collaborations

Licensing collaborations with pharma and biotech

Takeda ONCOLOGY

magenta THERAPEUTICS

Various research partnerships based on Material Transfer Agreements

Licensed legacy assets (non-ATACs)

Additional upside potential from clinical programs

TLX250-CDx – diagnostic imaging agent (REDECTANE®)

TELIX PHARMACEUTICALS

RHB-107 – serine protease inhibitor (upamostat / MESUPRON®)

RedHill Biopharma

HG 领晟医疗 LINK HEALTH GROUP

GMP supply with Amanitin

Growing Pipeline of Proprietary and Partnered Programs

Product	Target	Indication	Research	Preclinic	Clinic			Partner
					I	II	III	
Proprietary ATAC pipeline								
HDP-101	BCMA	Multiple myeloma (DLBCL/CLL)						Proprietary
HDP-102	CD37	NHL						Proprietary
HDP-103	PSMA	Prostate cancer						Proprietary
CDXX-ATACs	n/a	Solid / Hematological tumors						Proprietary
ATAC collaborations								
MGTA-ATACs	CD117, CD45	HSCs, Conditioning programs for blood cancers and genetic diseases						Magenta
TAK-ATACs	n/a	Oncology						Takeda/ Millenium
Licensed legacy assets (non-ATACs)								
TLX250-CDx	CA-IX	Renal Ca						Telix
TLX250	CA-IX	Renal Ca						Telix
RHB-107		Oncology/GI						RedHill
RHB-107		Covid-19						RedHill
LH011		Pancreatic cancer						Link Health

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Proprietary ATAC Candidates: HDP-101, HDP-102 and HDP-103

HDP-101: anti-BCMA-ATAC

- BCMA (B-cell maturation antigen) overexpression and activation are associated with multiple myeloma
- Multiple myeloma:
  - 70,000 deaths due to MM annually;
  - Characterized by the proliferation of single clone of plasma cells derived from B-cells
  - Median survival ~47-110 months
- MM patients with 17p deletions have a particularly high medical need for new treatment options
- Potential for biomarker-based stratification
- Potential improvement on ocular toxicity risk seen in approved and marketed anti-BCMA ADC Blenrep from GSK
- IND granted

HDP-102: anti-CD37-ATAC

- CD37 is overexpressed on B-cell lymphoma cells
- Specific indication of non-Hodgkin lymphoma (NHL)
- High prevalence of 17p deletion in NHL

HDP-103: anti-PSMA-ATAC

- PSMA is overexpressed in nearly all cases of prostate cancer; limited expression in normal tissue
- Target indication is Metastatic Castration-Resistant Prostate Cancer (mCRPC)
- Prevalence of 17p deletion in mCRPC is 60%
- 17p biomarker has been validated preclinically for prostate cancer (Nature Commun. 2018 22:4394)

HDP-101 has best-in-class potential for relapsed / refractory multiple myeloma (RRMM)

Potential IND application for both preclinical candidates 2022/23

HDP-101: Anti-BCMA-ATAC with Unique Properties

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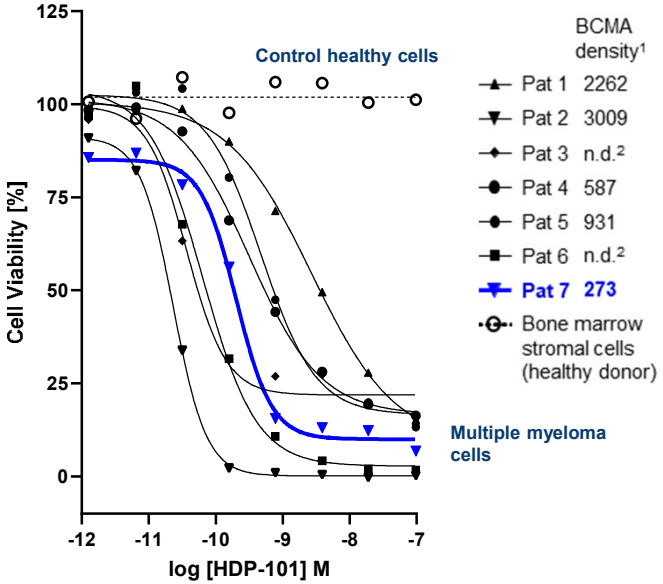
Cytotoxicity data in primary tumor cells from multiple myeloma patients

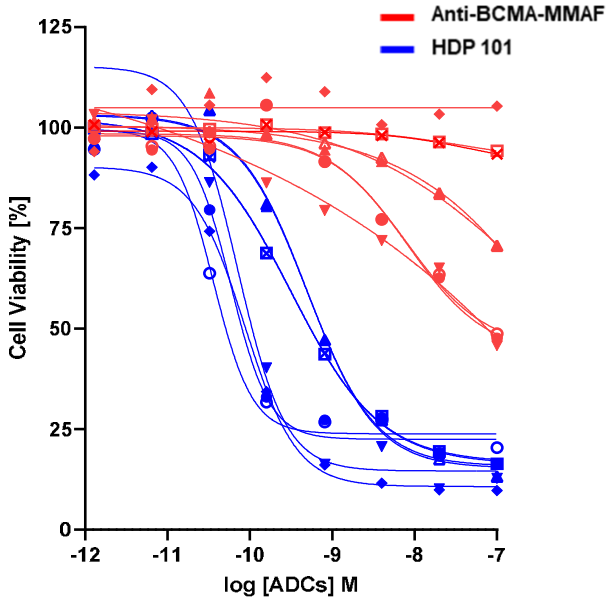
Efficacious in ultra-low BCMA cells



HDP-101 is efficacious in dormant tumor cells that express BCMA at very low levels, e.g. multiple myeloma patient 7.

No toxicity in control bone marrow stromal cells from healthy donor.

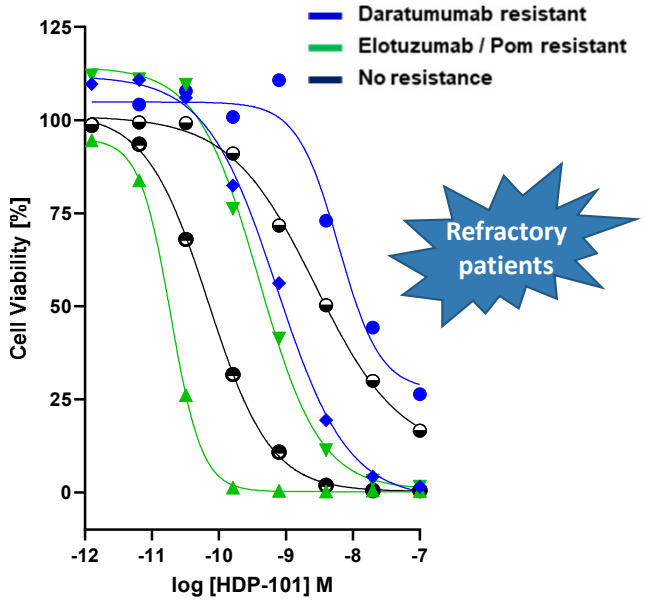
More efficacious than MMAF-BCMA ADC



HDP-101 is highly efficacious in dormant tumor cells from MM patients, while an MMAF-BCMA ADC[3] shows very poor activity in these patient cells.

GSK's BLENREP is an MMAF-containing anti-BCMA ADC.

Overcomes resistance mechanisms



HDP-101 is efficacious in tumor cells resistant to daratumumab and elotuzumab / pomalidomide.

[1] *BCMA density expressed as antibody binding sites per cell* [2] *n.d. = not determined* [3] *MMAF conjugated to HDP's anti-BCMA Ab (DAR=4) as a surrogate for Blenrep*

HDP-101: Differentiated Profile Predicts Clinical Benefit

Unique preclinical features of HDP-101	Potential clinical benefit
Efficacious on dormant tumor cells	Longer PFS and MRD negativity
Efficacious in ultra-low BCMA tumor cells	Deeper responses and higher ORR
Novel MoA to which all patients will be naïve	Overcome resistance
Ocular toxicity not seen for Amanitin or HDP-101	Superior safety profile
Enhanced efficacy in high-risk del(17p) tumors	Breakthrough designation and accelerated approval

HDP-101 has best-in-class potential for relapsed / refractory multiple myeloma (RRMM)

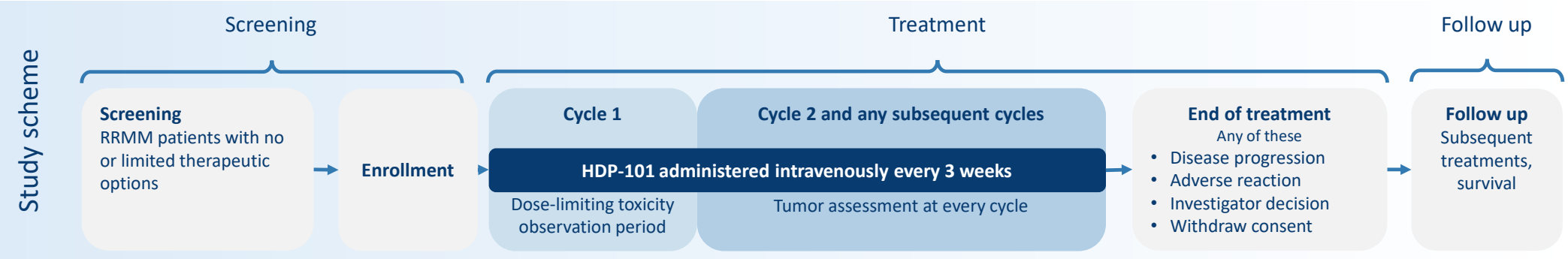
HDP-101-01 Clinical Trial for Multiple Myeloma
Two-part, Open-label, Multicenter Phase I/IIa Study

Heidelberg PHARMA

Clinical trial designed to determine safe dose and assess preliminary efficacy

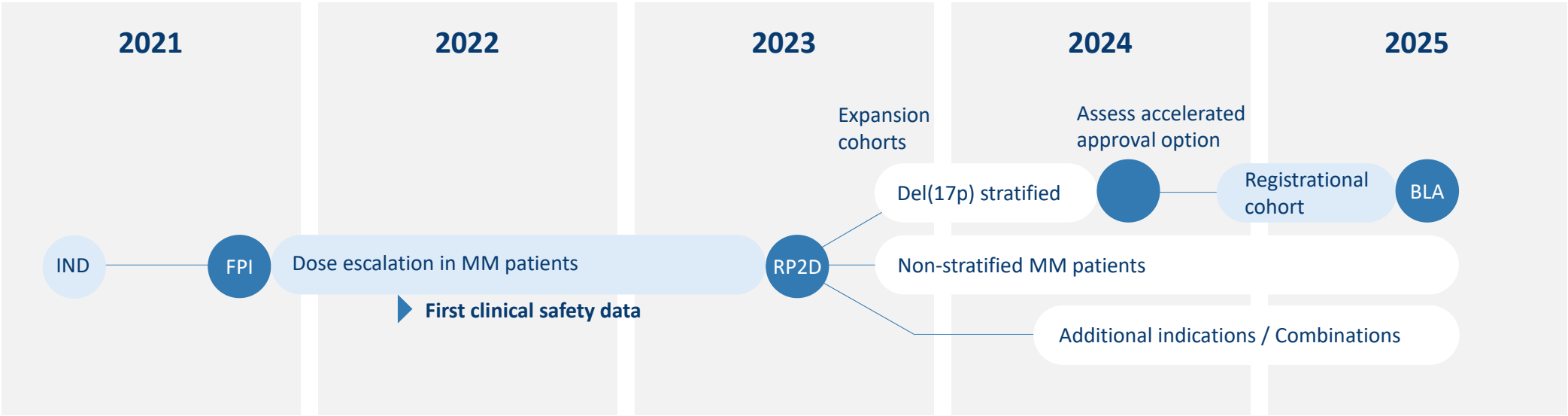
Phase I:
- Up to 36 patients with relapsed / refractory multiple myeloma (RRMM)
- Dose-escalation of HDP-101
- Retrospective biomarker evaluation
- **Establish optimal and safe dose for Phase IIa part**

Phase IIa:
- Up to 30 patients with RRMM
- Biomarker stratification based on 17p deletion status
- **Preliminary anti-tumor activity of HDP-101 and clinical relevance of the 17p deletion**



- Adaptive study design applied using Bayesian Logistic Regression Model to guide dose escalation and select the best dose for the phase II part
- Robust safety features to ensure early detection of possible toxicities especially liver and kidney damage

HDP-101: Clinical Development Plan for Multiple Myeloma



Status

- Contract with MD Anderson Cancer Center signed; further US and German sites to follow
- MD Anderson site initiation planned for second half of September
- Treatment of the first patient this year

HDP-101 has best-in-class potential in **all RRMM** patients.

Additionally, HDP-101 has potential for accelerated approval in **high-risk myeloma patients** with **del(17p).**

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Financials

in € m	FY 2020	H1 2021	Guidance FY 2021
Sales revenue and other income	9.6	1.1	5.5 – 7.5
Operating expenses	**27.9**	**14.0**	36.0 – 40.0
Cost of sales	5.6	2.0	
R&D costs	18.3	10.1	
Administrative costs	3.6	1.7	
Other expenses	0.4	0.2	
Operating result (EBIT)	**18.3**	**12.9**	30.0 – 34.0
Net loss for the period	**18.4**	**13.1**	

Shares

Shares outstanding: 34,173,009

Shareholders:

- 75% Dietmar Hopp and affiliated companies*
- 3% UCB
- 22% Freefloat and Corporate Bodies

Analysts

- Stifel 07/21: target € 8.94
- Pareto 07/21: target € 9.30
- Bryan, Garnier 07/21: target € 12.00
- EQUI.TS 02/21: target € 8.15

Financing

- Cash as of 31 May 2021: €0.9 m
- €20 m gross proceeds from private placement in June 2021 with select institutional investors and dievini, using €12.5 m from dievini financing commitment
- Remaining financing commitment from dievini: €5 m loan + €17.5 m
- Cash reach is secured until mid-2022 based on current budget planning

Investment Summary

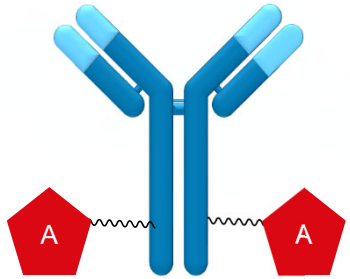
Disruptive first-in-humans mode of action provides **high efficacy** and **potential for unique clinical advantages,** including treatment of dormant tumor cells

Increased efficacy against 17p deleted and aggressive tumor cells based on **biomarker**

Validated by **high quality collaborations** (early validation and cash)

On the verge of becoming a **clinical-stage company**

High value potential with growing proprietary portfolio and attractive **ADC environment**



Contact Us

Upcoming conferences & events	Venue	Date
H.C. Wainwright 23rd Annual Global Investment Conference	Virtual	13 – 15 September 2021
Q3 – Interim Results on the first nine months of 2021		7 October 2021
World ADC	Virtual	11 – 14 October 2021
BioEurope	Virtual	25 – 28 October 2021
PEGS Europe	Barcelona	9 – 12 November 2021
German Equity Forum	Virtual	22 – 24 November 2021

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Reuters:	HPHA.DE
Bloomberg:	HPHA.GY