ATACs: Unique new mode of action to fight cancer

German Equity Forum, Frankfurt
28th November 2023
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.

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This material is not intended as an offer or solicitation for the purchase or sale of shares of Heidelberg Pharma AG. This material may not be distributed within countries where it may violate applicable law.
Our mission is to create inspired medicines that matter to cancer patients based on our expertise and ADC technologies
Key achievements

Differentiated ADC Technology
- In Plug & Play mode
- 2 years from target to IND

GMP Manufacturing
- Fully synthetic process
- 5 GMP batches completed

Clinical Stage
- 1 Phase 1 ongoing
- 2 additional INDs in preparation

Strong IP
- Several IP families
- Monopoly in the Amanitin/MOA space

Strategic partnerships
- Huadong: China-focused partnership
- Takeda: ATAC technology partnership

Corporate & Finance
- Experienced leadership team
- Cash (runway): EUR 50.7m* (mid-2025)

* as per end of August (Q3 published results)
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

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

The Payload MOA is what makes the difference!

**Enhertu®**
Payload: deruxtecan (Topo 1 inhibitor)

**Kadcyla®**
Payload: emtansine (Tubulin inhibitor)

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

Amanitin: Novel payload with novel MoA to overcome resistance

<table>
<thead>
<tr>
<th></th>
<th>Tubulin inhibitors e.g. Maytansines &amp; Auristatines</th>
<th>DNA-damaging agents e.g. PBDs, PDDs, IGNs, Calicheamicin, Duocarmycins</th>
<th>Topoisomerase inhibitors e.g. Camptothecins, Deruxtecan, SN-38</th>
<th>RNA polymerase inhibitors</th>
<th>Amanitin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potency</td>
<td>High</td>
<td>Ultra-high</td>
<td>Low</td>
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<td>Medium</td>
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<tr>
<td>Hydrophilicity</td>
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<tr>
<td>Overcome resistance</td>
<td>✗</td>
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<td>✗</td>
<td></td>
<td>✓</td>
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<td>Active on non-dividing cells</td>
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</table>

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

Antibody
- Targeting tumor antigen

Site-specific conjugation
- Proprietary conjugation sites
- Reduced Fcγ-receptor binding for improved therapeutic index (TI)
- Excellent stability in circulation
- Drug-Antibody Ratio (DAR) = 2.0
ATACs overcome resistance to current ADCs

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

Trastuzumab ATAC leads to complete remission in resistant model after single-dose
Del(17p): Potential platform-wide predictive biomarker

- High incidence across cancer indications and tumor types
- More aggressive tumors resistant to SoC and poor prognosis
- Higher sensitivity to ATAC treatment

Her2 1+ patient-derived xenograft models

Less amanitin is required to kill del(17p) cells
Wider therapeutic index in patients with del(17p) tumors
ATACs address the limitations of current cancer therapies

<table>
<thead>
<tr>
<th>Cancer Diagnosis</th>
<th>Treatment</th>
<th>Long-Term Response</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>CSCs survive tumor bulk dimished</td>
<td>CSCs survive tumor regrows</td>
<td>Tumor relapse minimal survival increase</td>
</tr>
<tr>
<td>ATACs</td>
<td>CSCs killed tumor bulk dimished</td>
<td>Tumor eliminated</td>
<td>Tumor eradication cure?</td>
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</tbody>
</table>


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

• Four patient cohorts (20, 30, 60 and 80 µg/kg) completed, 12 patients in total
• Latest Safety Review Committee conclusions (September 2023):
  • Treatment is safe and well-tolerated in the four cohorts
  • Continue dose escalation
• Dose escalation continues with 100 µg/kg in the fifth cohort
HDP-101: It works in the clinic

- 1 patient from cohort 3 with SD for 13 cycles, on monotherapy for 10 months

Cohort 1 - 20µg/Kg
- 0101001
  - Start date - 14Feb2022
  - Stop date - 12Apr2022
  - Progressive Disease - Survival FU

Cohort 2 - 30µg/Kg
- 0101002
  - Start date - 01Jun2022
  - Stop date - 18Jul2022
  - Progressive Disease - Survival FU

Cohort 3 - 60µg/Kg
- 0102002
  - Start date - 11Oct2022
  - Stop date - 18Jul2022
  - Progressive Disease - Survival FU
- 4904002
  - Start date - 13Jun2022
  - Stop date - 13Jul2022
  - Progressive Disease - Survival FU

- 0102003
  - Start date - 23Jan2023
  - Stable Disease
  - 13 cycles completed
  - No signs of toxicity, improving organ function

Cohort 4 - 80µg/Kg
- 4815003
  - Start date - 10Jul2023
  - Treatment discontinued/Progressive Disease

- 4815004
  - Start date - 17Jul2023
  - Treatment discontinued/Progressive Disease

- 3613001
  - Start date - 01Aug2023
  - Treatment discontinued/Progressive Disease

- 0102004
  - Start date - 02Aug2023
  - Treatment discontinued/Progressive Disease

Dose elevated to 80 µg/kg
First-in-human clinical trial with an ATAC ongoing
HDP-101: anti-BCMA-ATAC for multiple myeloma

2022/23
- FPI - Dose escalation in MM patients
- First clinical safety data

2024
- Expansion cohorts
- RP2D - Non-stratified MM patients

2025
- Asses accelerated approval option
- Del(17p) stratified

2026
- Registrational cohort
- BLA

High unmet medical need – overall survival of del(17)p patients is less than half vs. standard risk

Overall Survival:
- Standard Risk: 110 months
- Del(17p): 47 months
**ATACs promise significant clinical benefits**

**Unique preclinical features of ATACs**

- Efficacious against dormant tumor cells
- Efficacious in ultra-low target-expressing tumor cells
- Novel MoA to which all patients will be naïve
- No ocular toxicity seen for Amanitin or HDP-101
- Enhanced efficacy in high-risk del(17p) tumors

**Potential clinical benefit**

- Longer PFS and MRD negativity
- Deeper responses and higher ORR
- Overcome resistance
- Superior safety profile
- Breakthrough designation and accelerated approval

**ATACs have best-in-class potential**
Our Vision
Value creation through development of best-in-class ADC assets

Discovery & development engine

- Multiple targets
- Antibodies
- Development Expertise
- Toolbox of proprietary payloads

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
We are NOT Ab Discovery Company
Strong in-house R&D capabilities and expertise

Synthetic chemistry
Antibody generation & bioconjugation
Preclinical testing

CMC
Bioanalytical sciences
Clinical Development

We are able to generate the best ADC candidate in the shortest time
## Growing pipeline of proprietary and partnered programs

<table>
<thead>
<tr>
<th>Product</th>
<th>Target</th>
<th>Indication</th>
<th>Research</th>
<th>Preclinic</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Partner</th>
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<td><strong>ATAC pipeline</strong></td>
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<tr>
<td>HDP-101</td>
<td>BCMA</td>
<td>Multiple Myeloma</td>
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<td>Huadong (China+)</td>
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<tr>
<td>HDP-102</td>
<td>CD37</td>
<td>NHL (DLBCL/CLL)</td>
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<td>Huadong (option China+)</td>
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<tr>
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<td>Huadong (China+)</td>
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<td>Gastrointestinal (e.g., CRC)</td>
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<td><strong>Legacy assets</strong></td>
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<td>TLX250-CDx</td>
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<td>Renal Carcinoma</td>
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<tr>
<td>TLX250</td>
<td>CA-IX</td>
<td>Renal carcinoma</td>
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<td>RedHill</td>
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</table>
Risk balanced payload & indication portfolio

Clinically validated targets

- **HDP-101**
  - BCMA
  - Multiple Myeloma
  - Most advanced & validating ATAC.
  - Projected peak sales: $4.5B

- **HDP-102**
  - CD37
  - NHL
  - Low risk validating ATAC backup.
  - Projected peak sales: $1.2B

- **HDP-103**
  - PSMA
  - Prostate Cancer
  - First solid tumor ATAC.
  - Projected peak sales: $2.5B

- **HDP-201**
  - XXX
  - Solid tumors
  - Topo 1 inhibitor: Validated MoA payload.
  - Diversified payload risk
  - Projected peak sales: $3B

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Huge hype around ADCs due to approvals and deals

ADC market size is expected to grow from $8.6 B in 2023 to $25 B by 2028
Partner Projects & Next Steps
Partner Projects

Strategic partnership with Huadong Medicine (February/September 2022)

Exclusive licensing agreement for Asia*
• Exclusive license for HDP-101 and HDP-103; deal value: up to USD 469 m + royalties
• Exclusive option for HDP-102 and HDP-104; deal value: up to USD 461 m + royalties

Investment Agreement
• Equity investment of € 105 m in Heidelberg Pharma

ATAC Technology Collaborations

License agreement for an ATAC with Takeda (September 2022):
• Worldwide exclusive license for an ATAC against an undisclosed target.

* 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
Highlights Legacy Portfolio: TELIX

TLX250-CDx is Progressing towards Market Approval

TLX250-CDx ($^{89}$Zr-girentuximab) (imaging) enables accurate diagnosis of clear cell renal cell carcinoma (ccRCC)

Pivotal Phase III study (ZIRCON) reported positive results in November 2022
- Global multicenter phase III trial with 300 patients with renal masses - completed
- Pivotal trial met all endpoints

Next steps:
- Filing for regulatory approval with the FDA and other agencies
- Planned approval and launch in ccRCC in 2024
- Estimated peak annual revenue for Heidelberg Pharma from US alone: > $ 100 m*

Indication expansion:
- Ongoing phase II studies in bladder cancer and in triple-negative breast cancer

TLX250 ($^{177}$Lu-girentuximab) (therapy) – ongoing phase II studies in kidney cancer

*Based on estimated initial addressable market in the US, published by Telix
Financials & Outlook
Financials and shareholdings (August 31st, 2023)

<table>
<thead>
<tr>
<th>in € m</th>
<th>9M 2023</th>
<th>6M 2023</th>
<th>Actual 2022</th>
<th>Guidance 2023</th>
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<tbody>
<tr>
<td>Sales revenue and other income</td>
<td>13.9</td>
<td>4.7</td>
<td>19.9</td>
<td>7.0 to 10.0</td>
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<tr>
<td>Operating expenses</td>
<td>30.8</td>
<td>20.7</td>
<td>37.0</td>
<td>37.0 to 41.0</td>
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<tr>
<td>Operating result (EBIT)</td>
<td>(16.9)</td>
<td>(16.0)</td>
<td>(17.2)</td>
<td>(28.5) to (32.5)</td>
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<tr>
<td>Funds required for operations, capex</td>
<td>27.4</td>
<td>18.9</td>
<td>8.9</td>
<td>32.5 to 36.5</td>
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<tr>
<td>Funds required per month</td>
<td>3.0</td>
<td>3.2</td>
<td>0.7</td>
<td>2.7 to 3.1</td>
</tr>
</tbody>
</table>

- **Average cash usage per month** was €3.0 m compared to average cash requirement of €3.2 m in H1 2023, excluding financing activities.
- Including cash effects from financing activities, the **average cash usage per month** was €3.4 m compared to average cash requirement of €4.0 m in H1 2023.
- **Cash** of €50.7 m below the year-end figure of €81.3 m due to ongoing operational costs and partial loan repayment.
- **Cash reach** is unchanged expected until mid-2025 based on current planning.
Solid cash runway until mid 2025 supports execution of ongoing programs and clinical validation of ATACs

- Additional financing required to reach multiple value inflection points across our portfolio until end of 2026
- (Bridge-) Financing until non-dilutive funding becomes available through licensing income and royalties
- Develop portfolio potential in full and without delay
- Accelerate business transformation from R&D to market focused company
- Flexible financing structure possible
Outlook

• We are a clinical-stage company with the goal of becoming a leading global ADC player

• Multiple inflection points over the next 36 months with potential to many-fold increase of company valuation