ATACs: Unique new mode of action to fight cancer
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.

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.
Key achievements

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

**GMP Manufacturing**
- Fully synthetic process for Amanitin
- 5 GMP batches completed

**Clinical Stage**
- 1 ATAC in ongoing Phase I
- 2 additional ATAC INDs within the next year

**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 2023
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

- 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
Payload Toolbox – Multiple MOAs

ATAC-Technology
RNA-Polymerase II Inhibitor
Amanitin-based

TOPO1-Technology
Topoisomerase I Inhibitor
Exatecan-based

IM-Technology
TLR7 agonist
## 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>
</tr>
</thead>
<tbody>
<tr>
<td>HDP-101</td>
<td>BCMA</td>
<td>Multiple Myeloma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Huadong (China+)</td>
</tr>
<tr>
<td>HDP-102</td>
<td>CD37</td>
<td>NHL (DLBCL/CLL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Huadong (option China+)</td>
</tr>
<tr>
<td>HDP-103</td>
<td>PSMA</td>
<td>Prostate cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Huadong (China+)</td>
</tr>
<tr>
<td>HDP-104</td>
<td>GCC</td>
<td>Gastrointestinal (e.g., CRC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Huadong (option China+)</td>
</tr>
<tr>
<td>HDP-201</td>
<td>n/a</td>
<td>Solid tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Proprietary</td>
</tr>
</tbody>
</table>

### ATAC partners

<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>
</tr>
</thead>
<tbody>
<tr>
<td>TAK-ATAC</td>
<td>n/a</td>
<td>Oncology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Takeda</td>
</tr>
</tbody>
</table>

### ATAC pipeline

<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>
</tr>
</thead>
<tbody>
<tr>
<td>TLX250-CDx</td>
<td>CA-IX</td>
<td>Renal Carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Telix</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urothelial Carcinoma, TNBC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLX250</td>
<td>CA-IX</td>
<td>Renal carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Telix</td>
</tr>
<tr>
<td>RHB-107</td>
<td></td>
<td>Oncology/GI, Covid-19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RedHill</td>
</tr>
</tbody>
</table>
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

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
Novel payloads 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>
<td>Medium</td>
<td>✓</td>
</tr>
<tr>
<td>Hydrophilicity</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Overcome resistance</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Active on non-dividing cells</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Biomarker</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Target Exclusivity / Single player / IP monopoly</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</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)
• Drug-Antibody Ratio (DAR) = 2.0
Breast cancer model (JIMT-1 Xenograft) is resistant to Kadcyla® 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

Cancer Diagnosis

Treatment

Long-Term Response

Outcome

Cancer Stem Cell (CSC)

Cancer Cells

CSCs survive
Tumor bulk diminished

CSCs killed
Tumor bulk diminished

CSCs survive
Tumor Regrows

Tumor Eliminated

Tumor Relapse Minimal Survival Increase

Tumor Eradication Cure?

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

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 14 cycles, on monotherapy for 11 months
ADCs with TOPOI inhibitor as a payload

TOPOI inhibitor as warhead

• Clinically validated mechanism of action: *inhibition of Topoisomerase I*

Site-specific conjugation

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

Antibody

• Targeting tumor antigen
Strong efficacy of HDP’s Topo 1 ADC upon multiple dose treatment

- Efficacy of HDP ADC similar to Deruxtecan ADC
- Only half the amount of toxin (DAR 4 vs DAR 8-10)
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