ATACs®: a Unique New Mode of Action to Fight Cancer

EKF - 28th November 2022
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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Heidelberg Pharma – a Clinical Stage Company

**Our Company**
- ~110 employees
- Headquarters in Heidelberg area, Germany
- Listed on Frankfurt Stock Exchange: HPHA
- Clinical stage biotech
- Complete in-house research capabilities
- Cash reach until mid-2025
  (as of November 2022)

**Our Approach**
- Inhibition of RNA Polymerase II
- Targeted delivery via antibodies (ADC technology)
- Use Amanitin as toxic payload (ATAC® technology)

**Our Mission**
- Provide new options in cancer therapy
- Overcome resistance mechanisms
- Kill dormant tumor cells
- Develop biomarker for patient stratification
Management Team with Strong Pharma and R&D Experience

Dr. Jan Schmidt-Brand, CEO, CFO
@ Heidelberg Pharma since 2001
30 years experience in commercial and financial leadership positions in pharma and chemical companies, including BASF
LLD from the University of Mannheim

Prof. Dr. Andreas Pahl, CSO
@ Heidelberg Pharma since 2001
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

Dr. András Strassz, CMO
@ Heidelberg Pharma since 2020

Dr. George Badescu, CBO
@ Heidelberg Pharma since 2018

Dr. Mathias Locher, CDO
@ Heidelberg Pharma since 2021

Dr. Ulrike Grimm, interim COO
@ Heidelberg Pharma since 2021

Dr. Ulrike Grimm, interim COO
@ Heidelberg Pharma since 2021

Dr. Ulrike Grimm, interim COO
@ Heidelberg Pharma since 2021
## 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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<tbody>
<tr>
<td>HDP-101</td>
<td>BCMA</td>
<td>Multiple Myeloma (DBCL/CLL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Huadong (Asia)</td>
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<tr>
<td>HDP-102</td>
<td>CD37</td>
<td>NHL</td>
<td></td>
<td></td>
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<td>Huadong (Asia, option)</td>
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<tr>
<td>HDP-103</td>
<td>PSMA</td>
<td>Prostate cancer</td>
<td></td>
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<td></td>
<td>Huadong (Asia)</td>
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<tr>
<td>HDP-104</td>
<td>GCC</td>
<td>Gastrointestinal (e.g. CRC)</td>
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<td>Huadong (Asia, option)</td>
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<tr>
<td>HDP-XX</td>
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<td>Solid &amp; hematological malignancies</td>
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<td></td>
<td></td>
<td></td>
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<td>Proprietary</td>
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ATAC® pipeline

<table>
<thead>
<tr>
<th>Product</th>
<th>Target</th>
<th>Indication</th>
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<tbody>
<tr>
<td>MGTA-ATACs</td>
<td>CD117, CD45</td>
<td>HSCs, conditioning programs for blood cancers and genetic diseases</td>
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<tr>
<td>TAK-ATAC</td>
<td>n/a</td>
<td>Oncology</td>
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<tr>
<td>CHIOME-ATAC</td>
<td>CDCP1</td>
<td>Oncology</td>
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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>
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<tbody>
<tr>
<td>TLX250-CDx</td>
<td>CA-IX</td>
<td>Renal and urothelial carcinoma, TNBC</td>
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<td></td>
<td></td>
<td></td>
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<td>Telix</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>
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<tr>
<td>RHB-107</td>
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<td>Oncology/GI, Covid-19</td>
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<td>RedHill</td>
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<td>LH011</td>
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<td>Pancreatic</td>
<td></td>
<td></td>
<td></td>
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<td>Link Health</td>
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</table>
ATACs: ADCs with Amanitin as a Payload

Amanitin as Warhead
- Differentiated mechanism of action: inhibition of RNA Polymerase
  - 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
- Improved therapeutic index (TI)
- Excellent stability in circulation
The Payload Makes The Difference!

**Amatoxins – a novel mode of action in oncology**

Group of toxins from the poisonous green death cap mushroom (Amanita phalloides)

**Amanita phalloides**

**Amanitin is a specific inhibitor of RNA polymerase II activity:**
- The only currently known inhibitor of RNA polymerase II:
  - A new mode of action in oncology
  - All tumors are naïve to it
  - Cell-cycle independent mechanism of action
  - Low intracellular target copies, 1:1 binding

### Murine breast cancer xenograft model

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

**Graph:**
- PBS (Control) (10mL/kg) i.v.
- Enhertu, 20 mg/kg, i.v.
- Trastuzumab-ATAC, 2.5mg/kg, i.v.

Drawing: Tamara Clark; tamaracleark.com
ATACs promise higher efficacy in certain aggressive tumors

**del(17p) as a potential biomarker for higher ATAC sensitivity**

- Chromosomal deletion that eliminates p53 (higher-risk tumor) and frequently POL2RA gene: lower RNA polymerase II level
- Less amanitin is required to kill these cells: larger therapeutic window

**Clinical relevance:**
- Broad prevalence (ca. 25-60%) across most tumors
- Increased prevalence in advanced and metastatic disease
- Associated with aggressive disease, poor outcomes

**Significance:**
- Higher ATAC efficacy in aggressive tumors with del(17p)
- Use as clinical biomarker in development for patient stratification

**Collaboration with MD Anderson:**

Higher ATAC® sensitivity of del(17p) myeloma cells

Orlowski et al. MD Anderson ASH 2019
First-in-Human Clinical Trial with an ATAC
HDP-101: anti-BCMA-ATAC for multiple myeloma

Clinical trial designed to determine safe dose and assess preliminary efficacy

Two-part, Open-label, Multicenter Phase I/IIa Study

2022

- FPI

Dose escalation in MM patients: up to 36 patients

2023

- RP2D

First clinical safety data

2024

- Expansion cohorts

- Assess accelerated approval option

- BCMA naïve MM Del(17p) stratified

- Post BCMA Tx MM Del(17p) stratified

2025

- AA

- Registrational cohort

- Additional indications / Combinations

- BLA

Trial sites active and enrolling*:

- MD Anderson, Houston
- Emory University, Atlanta
- Mount Sinai Hospital, New York
- University Hospital Heidelberg
- University Hospital Mainz
- University Hospital Kiel

*Further US and European sites currently being opened
## ATACs Promise Significant Clinical Benefits

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

**ATACs® have best-in-class potential**
Strategic partnership with Huadong
Strategic Partnership With Huadong Medicine

Building a robust ADC product pipeline with best-in-class potential

Investment 105 m EUR  
Proceeds 80 m EUR  
Shareholding 35%  
2 seats in Supervisory Board

Commercial Agreements

• Exclusive development and commercialization rights for HDP-101 and HDP-103,
  • Deal value: up to 469 m USD + royalties
• Exclusive option for HDP-102 and HDP-104;
  • Deal value: up to 461 m USD + royalties
• Next 2 ATAC® candidates: Right of first negotiation (ROFN)
• Territory: Asia*

* 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
A Transformative Deal with a Strong Partner: Supporting our Strategy to Become a Global ADC Player

Immediate strengthening of cash position
Dedicated, long-term investor
Accelerated development and broadening of pipeline
Potential expansion of the collaboration

Success-based milestones and royalties offer long-term cash infusion
Efficient resource sharing via co-development
Secures market access in large parts of Asia
Partner Projects & Next steps
Targeted conditioning programs with ATACs®:
selectively eliminate stem cells and/or immune cells from a patient
prior to transplant or gene therapy.

**MGTA-117**: Depletion of hematopoietic stem and progenitor cells
• Phase I/II trial in AML or MDS started in Q1 2022

**Next steps**: Initial clinical data expected at ASH 2022,
further data in Q1 2023

**CD45-ATAC**: Immune reset in various transplant and autoimmune
disease models
• IND-enabling activities ongoing

License agreement for an ATAC®:
Worldwide exclusive license for an ATAC targeting a previously
selected target molecule (not disclosed)

Research and option agreement for an ATAC®:
Couple amanitin to an antibody that targets CDCP1,
expressed on many solid tumors

HDP is entitled to clinical development, regulatory and sales-related milestone payments for each ATAC candidate
Partner Telix: Progressing towards Filing for Market Approval

Pivotal Phase III ZIRCON reported Positive topline results with imaging agent TLX250-CDx in November 2022

Accurate diagnosis of clear cell renal cell carcinoma (ccRCC) with TLX250-CDx (89Zr-DFO-girentuximab)

- Global multicenter Ph III trial with 284 evaluable patients with renal cancer
- Imaging compared to histology of surgically obtained tissue (standard of truth)
- All endpoints met: 86% sensitivity, 87% specificity and 93% positive predictive value
- Next steps: Filing for regulatory approval with the FDA and other agencies
- Indication expansion: Ongoing Ph I and II studies in bladder cancer and in triple-negative breast cancer
## Financials and Shareholdings

### Rights issue completed in September 2022

- Proceeds of €80 m
- Huadong to become 2\textsuperscript{nd} largest shareholder, dievini remains largest shareholder
- Two new members of the Supervisory Board representing Huadong
- Cash reach is secured until mid-2025 based on current budget planning

### Financials

<table>
<thead>
<tr>
<th>in € m</th>
<th>FY 2021</th>
<th>Guidance 03/2022</th>
<th>9M 2022</th>
<th>Rev. guidance 10/2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales revenue and other income</td>
<td>2.3</td>
<td>7 to 9.5</td>
<td>16.8</td>
<td>18.5 to 20.5</td>
</tr>
<tr>
<td>Operating expenses</td>
<td>27.9</td>
<td>41.0 to 45.0</td>
<td>27.6</td>
<td>35.0 to 39.0</td>
</tr>
<tr>
<td>Operating result (EBIT)</td>
<td>(25.6)</td>
<td>(32.5) to (36.5)</td>
<td>(10.8)</td>
<td>(16.0) to (20.0)</td>
</tr>
<tr>
<td>Funds income / funds required</td>
<td>28.1</td>
<td>33.0 to 37.0</td>
<td>0.6</td>
<td>8.0 to 11.0</td>
</tr>
<tr>
<td>Funds income / funds required per month</td>
<td>2.3</td>
<td>2.8 to 3.1</td>
<td>0.1</td>
<td>0.6 to 0.9</td>
</tr>
</tbody>
</table>

### Shareholdings

- Dietmar Hopp and affiliated companies: 46%
- Huadong Medicine: 35%
- Freefloat: 14%
- Corporate bodies: 5%
- Huadong: 35%
- Dietmar Hopp and affiliated companies: 46%
# Next Steps Proprietary ATAC Pipeline

<table>
<thead>
<tr>
<th><strong>HDP-101</strong></th>
<th><strong>HDP-102</strong></th>
<th><strong>HDP-103</strong></th>
<th><strong>HDP-104</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase I/IIa study in RRMM</strong></td>
<td><strong>CD37-ATAC for NHL</strong></td>
<td><strong>PSMA-ATAC for prostate cancer</strong></td>
<td><strong>Guanylyl cyclase C (GCC)-ATAC for colorectal cancer</strong></td>
</tr>
<tr>
<td>• Dose escalation ongoing</td>
<td>• On track to IND 2024</td>
<td>• On track to IND 2023</td>
<td>• Preclinical development ongoing</td>
</tr>
<tr>
<td>• First safety data expected 2022</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Phase I completion in 2023</td>
<td></td>
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Investment Summary

A clinical-stage company with the goal of becoming a global ADC player

- **Disruptive first-in-humans** mode of action provides **high efficacy** and **potential for unique clinical advantages**

- **Clinical lead program** with **best-in-class potential** for indication with high medical need

- **Increased efficacy against certain aggressive tumors** based on **biomarker**

- **Validated by international high-quality partnerships**

- **Strategic partnership for Asia**, fastest growing pharmaceutical market

**High value potential with growing ATAC® pipeline and attractive ADC environment**