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.

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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 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
• Listed @Frankfurt Stock Exchange Prime Standard
• Experienced leadership team
• Cash (runway): $60.8m* (mid-2025)

* as per end of May (Q2 published results)
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
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
The journey of many cancer patients

Before Treatment

Treatment

The journey of many cancer patients

Before Treatment

Treatment

Resistance & Relapse

Wagke, N. et al., J Clin Oncol. 2011; 29(22): 3085–3096
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>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>
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<td>High</td>
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<td>Low</td>
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<td>Overcome resistance</td>
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<tr>
<td>Active on non-dividing cells</td>
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<td>✓</td>
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<td>Biomarker</td>
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<td>Target Exclusivity / Single player / IP monopoly</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

**Site-specific conjugation**
- Proprietary conjugation sites
- Reduced Fc-y-receptor binding for improved therapeutic index (TI)
- Excellent stability in circulation
- Drug-Antibody Ratio (DAR) = 2.0

**Antibody**
- Targeting tumor antigen
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
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

Nature vol. 520,7549 (2015): 697-701
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
Only ATACs kill dividing and non-dividing cells equipotently

Anti-CD19 ADCs cytotoxicity on dividing and non-dividing primary human B cells

ATACs kill non-dividing (dormant) tumor cells that are typically resistant to SOC, drive tumor relapse and metastasis
ATACs address the limitations of current cancer therapies

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

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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
• Ahead of Schedule, 3 patients already dosed
HDP-101: It works in the clinic

- 1 patient from cohort 3 with SD for 12 cycles, on monotherapy for 9 months
- 2 patients from cohort 4 are still on treatment
First-in-human clinical trial with an ATAC ongoing
HDP-101: anti-BCMA-ATAC for multiple myeloma

- **2022/23**: Dose escalation in MM patients
- **2024**: Expansion cohorts
- **2025**: Assess accelerated approval option
- **2026**: Registrational cohort

**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(17)p: 47 months
### ATACs Promise significant clinical benefits

<table>
<thead>
<tr>
<th>Unique preclinical features of ATACs</th>
<th>Potential clinical benefit</th>
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<tbody>
<tr>
<td>Efficacious against dormant tumor cells</td>
<td>Longer PFS and MRD negativity</td>
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<td>Efficacious in ultra-low target-expressing tumor cells</td>
<td>Deeper responses and higher ORR</td>
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<td>Novel MoA to which all patients will be naïve</td>
<td>Overcome resistance</td>
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<tr>
<td>Neither hematologic nor ocular toxicity seen for Amanitin or HDP-101</td>
<td>Superior safety profile</td>
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<tr>
<td>Enhanced efficacy in high-risk del(17p) tumors</td>
<td>Breakthrough designation and accelerated approval</td>
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**ATACs have best-in-class potential**
# Growing pipeline of proprietary and partnered programs

<table>
<thead>
<tr>
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<th>Target</th>
<th>Indication</th>
<th>Research</th>
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HDP-102: Targeting CD37 in NHL

- Survival of animals for the whole observation period after single dose treatment of HDP-102.
- Complete remission after single-dose application of HDP-102 in PDX Model.
HDP-103 : PSMA-ATAC for prostate cancer

Efficacy in s.c. LNCaP model

Pharmacometric modelling predicts favourable TI

Target product profile for metastatic Castration Resistant Prostate Carcinoma (mCRPC).

• High prevalence of del(17p): 60% of mCRPC patients;
• Potential for breakthrough designation and accelerated approval.
Subcutaneous ATAC® dosing improves therapeutic index

- Subcutaneous administration changes the pharmacokinetic profile and reduces $C_{max}$.
- The potent anti-tumor efficacy of ATAC®-based ADCs is maintained after s.c. administration.
- S.c. administration of ATAC® in Cynomolgus monkeys reduces $C_{max}$ and improves tolerability.
Repeated HDP-103 dosing improves tolerability & efficacy

• First dose induced tolerability to subsequent dosing in repeated-dose NHP studies.

• **Repeated dosing** in s.c. LNCaP CDX mice leads to improved efficacy.
Value creation through development of best-in-class ADC assets

Discovery & development engine

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

Targets
Scouting, Partnering, In-licensing
Antibodies

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 efficacy of HDP’s Topo 1 ADC

- Efficacy of HDP’s Topo 1 ADC similar to a control Deruxtecan ADC
- Only half the amount of payload (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
Thank You For Your Attention