JUNE 2024

Supercharging Immunotherapy

HOOKIPA PHARMA

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Today's Presenters

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Chief Executive Officer

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Innovative pipeline of novel arenaviral therapies

The platform is scalable across disease areas and multiple antigen classes

	Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status
Oncoviral Antigens	**HB-200**	**HPV16+ OPSCC**					• Pivotal 1L Ph. 2/3 expected to start Q4 2024
Neo Antigens	**HB-700**	**KRAS$_{mut}$ tumors**					• IND Cleared Q2 2024
Infectious Disease	**HB-400**	**Hepatitis B**	GILEAD				• Gilead-led Ph. 1 ongoing
	HB-500	**HIV**	GILEAD				• Ph. 1 start in Q2 2024

Our advantage: Consistent data and a clear path to registration for HB-200

Targeted immunotherapy treatment option to address significant unmet need in HPV+ head and neck cancers

Targeted approach to HPV16+ cancers:

- HPV-driven cancers represent a distinct disease, yet there are no disease-specific therapies
- Patient-centric strategy with IO / IO combination with potential to deliver improved survival benefit

Best-in-class HPV16+ Phase 2 clinical data[1]:

- 53% ORR for target patient population
- 18% complete response rate highlights depth of response
- Promising preliminary durability data

Potential for first-to-market in HPV16+:

- Pivotal Phase 2/3 trial expected to begin Q4 2024
- FDA aligned on pivotal Phase 2/3 design & protocol
- EMA PRIME designation

[1] Harrington Updated Data KEYNOTE-048 JCO 2023
ORR: Objective response rate; SOC: Standard of care, pembro monotherapy

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Unmet medical need in HPV16+ head and neck squamous cell carcinoma

- **HPV infection has been linked to the increasing incidence of HNSCC in the US[1]**
  - 70% of OPC cases are related to HPV infection, with the most prominent subtype, HPV16, causing ~90% of OPC cases[2]
- **Pembrolizumab created a shift in the management of metastatic/recurrent HNSCC, but improvements are needed**
  - Only ~19% of patients with PD-L1 CPS ≥1 treated with pembrolizumab monotherapy have an objective response, with approximately 23% ORR and ~8% CR rate in the PD-L1 CPS ≥20 sub-population and ~15% ORR and ~3% CR rate in the PD-L1 CPS 1-19 sub-population[3,4]
  - In the PD-L1 CPS ≥20 sub-population receiving pembrolizumab monotherapy, mPFS and mOS were 3.4 months and 14.9 months, respectively, and 12 months OS rate was ~56%[3,4]
  - Pembrolizumab + chemotherapy and Cetuximab improves response rates, with increased toxicity and shorter duration of response[5,6]
- **HPV-positive disease is mediated via distinct biological drivers compared to HPV-negative HNSCC[7]**
  - **Opportunity to improve existing therapy in HNSCC by developing immunotherapy tailored to HPV biology**

CPS, combined positive score; ORR, objective response rate; CR, complete response; HNSCC, head and neck squamous cell carcinoma; HPV16, human papillomaviiologrus 16; OS, overall survival; mPFS, median progression free survival; mOS, median overall survival; OPC, oropharynx cancer.

1. Tota J, et al. J Clin Oncol. 2019;37:1538. 2. Chaturvedi A, et al. J Clin Oncol. 2011;29:4294. 3. Harrington et al. J Clin Oncol. 2023;41(4);790-802. 4. Burtness B, et al. J Clin Oncol 2022;40:2321-2332; 5. Burtness B, et al. Lancet. 2019;394:1915. 6. Sacco AG, et al. Lancet Oncol 2021; 22: 883–92; 7. Powell SF, et al. Cancers (Basel). 2021;13(20):5206.

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HB-200 Therapy: Activating HPV16+ Specific T Cell Response

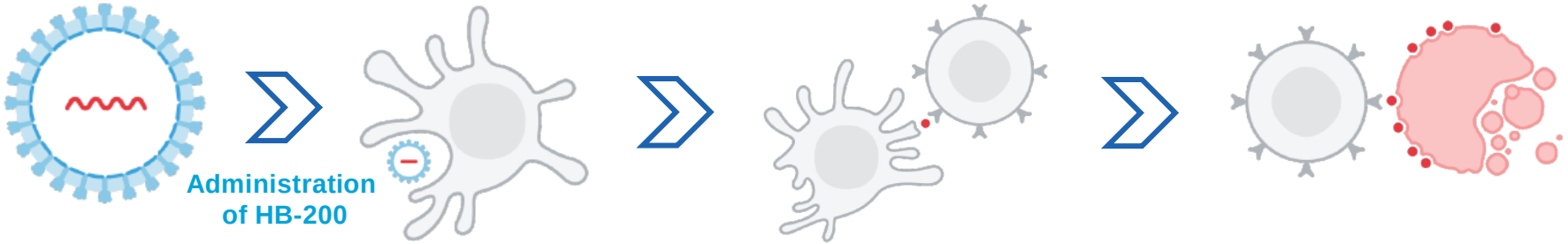
Engineered arenavirus supercharges natural action of immune system

1 Modification
of arenavirus with target antigen

2 Infection
of dendritic cells or macrophages

3 Activation
of antigen-specific T cells

4 Elimination
of tumor cells



HB-200 is an alternating treatment of replicating arenavirus vectors expressing a non-oncogenic HPV16 E7/E6 fusion protein[1]

As a monotherapy, HB-200 robustly induced antigen-specific circulating T cells in patients with HPV16+ cancers, with tumor shrinkage observed[2,3]

HPV16, human papillomavirus 16.
1. Lauterbach H, et al. Front Oncol. 2021;11:732166. 2. Fu S, et al. ASCO 2022. Abstract 2517.
3. Ho A, et al. SITC 2023. Abstract 679.

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Overview: Phase 1/2 study of HB-200 in recurrent/metastatic HPV16+ HNSCC

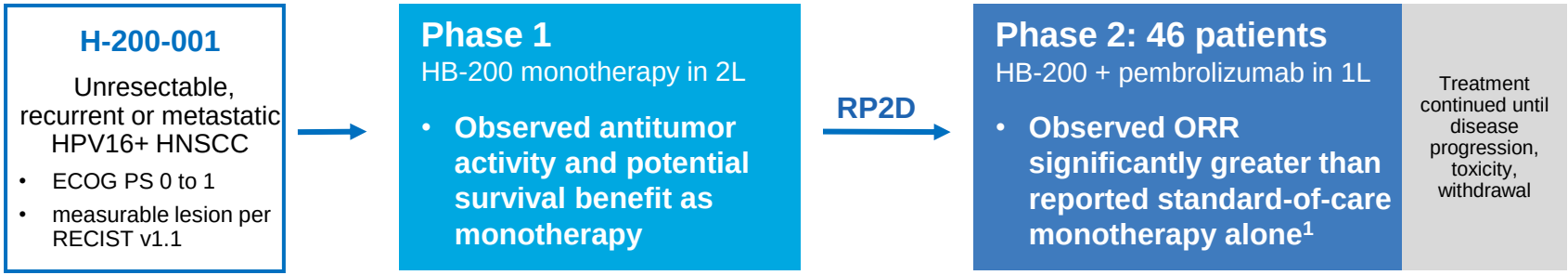
Open label, multi-center Phase 1/2 study

Phase 1 monotherapy objectives and endpoints:

- ✓ Primary: RP2D of HB-200 monotherapy alternating two-vector therapy
- ✓ Secondary: safety, preliminary antitumor activity
- ✓ Exploratory: immunogenicity, biomarkers

Phase 2 combination therapy objectives and endpoints:

- ✓ Primary: ORR by RECIST v1.1
- ✓ Secondary: safety, duration of response by RECIST v1.1 or iRECIST (OS, PFS, DCR, DOR)
- ✓ Exploratory: immunogenicity, biomarkers



[1] Harrington Updated Data KEYNOTE-048 JCO 2023

HPV: human papilloma virus; PD-L1: programmed-death ligand 1; CPS: combined positive score; OPSCC: oropharyngeal squamous cell carcinoma; ORR: Objective response rate; OS: overall survival; DOR: duration of response; DCR: disease control rate; PFS: progression free survival; RECIST v.1.1 = Response Evaluation Criteria in Solid Tumors version 1.1; RP2D: recommended for Phase 2 dose

HB-200 + pembrolizumab: Favorable safety profile

All Participants (N = 46)	Treatment-Emergent AEs, n (%)	Treatment-Related AEs, n (%)
Any event	44 (95.7)	39 (84.8)
Grade ≥3	18 (39.1)	7 (15.2)
Serious	11 (23.9)	2 (4.3)
Leading to discontinuation of HB-200	3 (6.5)	2 (4.3)[a]
Leading to discontinuation of pembrolizumab	4 (8.7)	3 (6.5)[b]
Deaths	2 (4.3)	0

a. One patient with grade 3 checkpoint inhibitor pneumonitis (noted as related to pembrolizumab), 1 patient with grade 1 cytopenia (noted as related to all treatment) along with unrelated events of grade 3 transaminitis and grade 2 abdominal pain (noted as progression related).

b. Aforementioned AEs and a grade 3 event of worsening pruritis (noted as related to pembrolizumab) leading to discontinuation of pembrolizumab but continuation of HB-200.

- Safety profile is in line with HB-200[1] or pembrolizumab monotherapy[2]
- No treatment-related AE leading to death and low rate of discontinuation
- Most patients experienced low-grade flu-like symptoms limited to Cycle 1

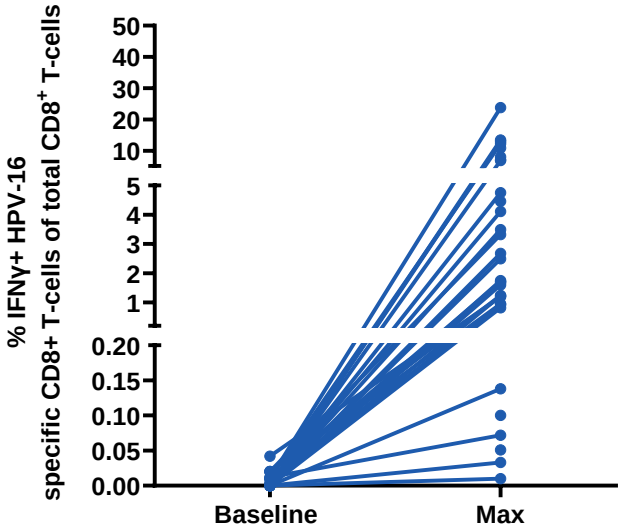
AEs, adverse events.

1. Fu S, et al. ASCO 2022. Abstract 2517. 2. Burtness B, et al. Lancet. 2019;394:1915-1928.

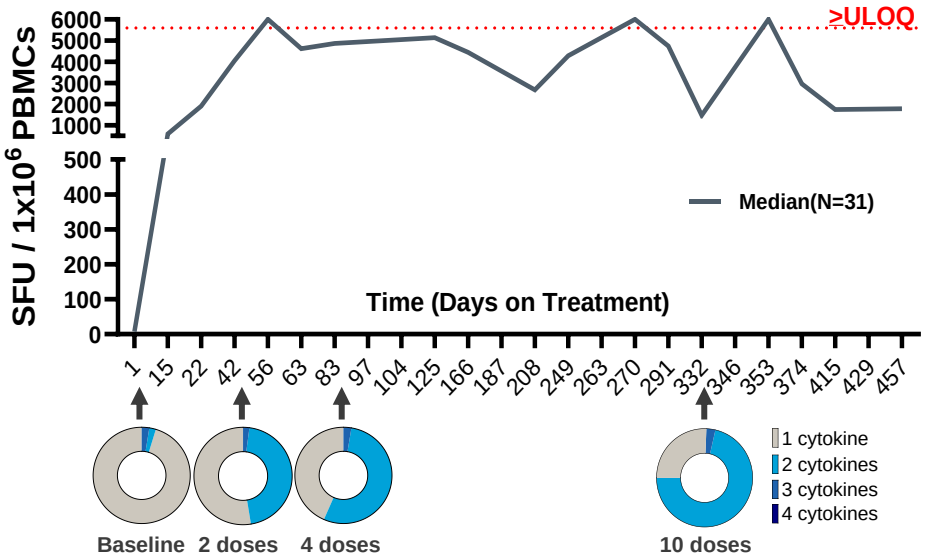
HB-200 + pembrolizumab: Unprecedented antigen-specific T cell activation

Robust & sustained induction of polyfunctional HPV16+ tumor-specific T cells

Meaningful antigen-specific T cell reactivity



Long-lasting, healthy T cells with growing polyfunctionality over time



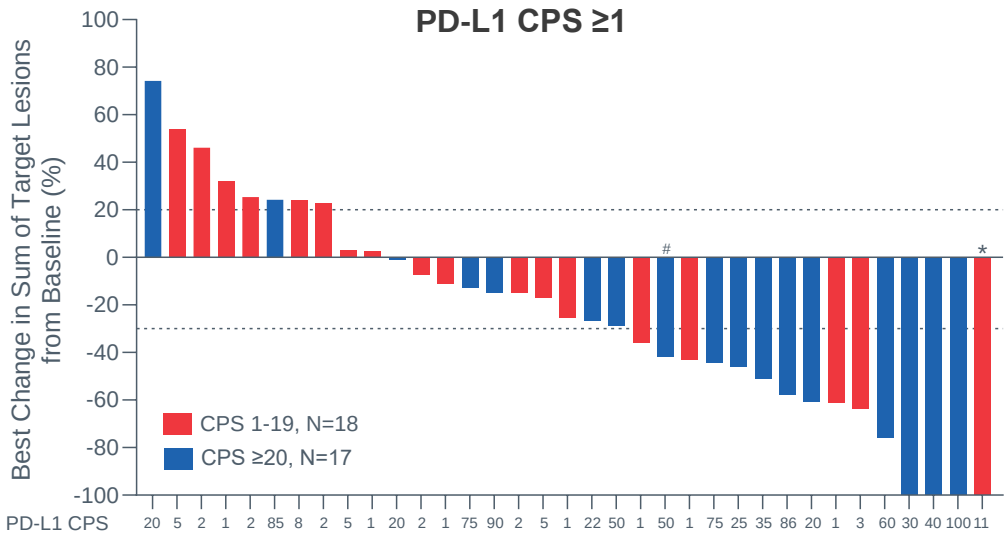
1 T cell immunogenicity data for 31 out of 38 patients available;
Graph: Systemic T cell kinetics per HPV-16 E6/E7 specific ELISPOT (N = 31pt) and analysis of polyfunctionality of E6 / E7 specific CD8+ T cells by intracellular cytokine staining; cytokines analyzed were IFN-γ, TNF, IL-2; CD107a
HPV16, human papillomavirus 16; PBMCs, peripheral blood mononuclear cells; SFU, spot-forming unit; ULOQ, upper limit of quantitation.

HB-200 + pembrolizumab: Consistent & meaningful anti-tumor activity

38 patients in efficacy population with minimum of 4.5 months on study or discontinued early during this period

PD-L1 CPS ≥1 Evaluable Population	Confirmed Responses (RECIST v1.1)	ORR	CR Rate	DCR (CR+PR+SD)
N = 35	13	37.1%	11.4%	68.6%

Excludes three patients who did not have a post-baseline tumor evaluation on trial: One patient had a sudden death on Study Day 2; One patient had a grade 5 COVID pneumonia event on Study Day 27; One patient withdrew consent prior to the first scan



* Confirmed PR at data cutoff, confirmed CR after data cutoff date

\# PD per RECIST v1.1, iPR per iRECIST

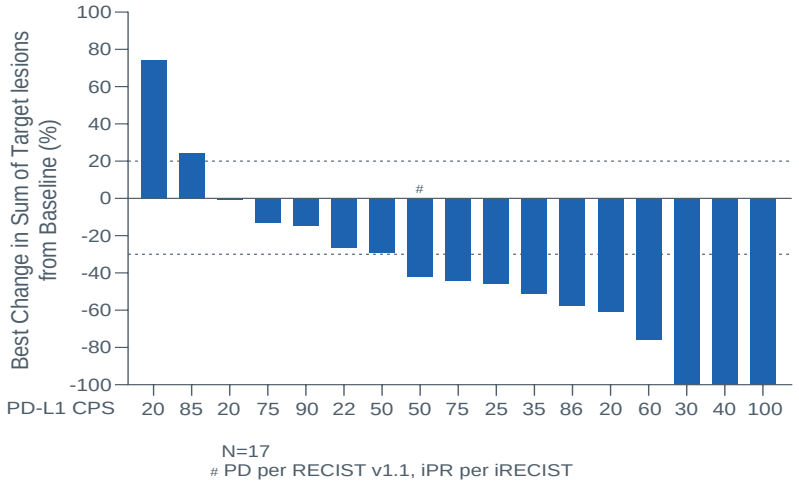
Data as of 29-Mar-2024. Efficacy dataset includes 38 patients with minimum 4.5 months of follow-up time after first dose as of data cutoff or discontinued early during this period.

1L, first-line; CPS, combined positive score; CR, complete response; DCR, disease control rate; iPR, immune partial response; iRECIST, immune Response Evaluation Criteria in Solid Tumors; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

HB-200 + pembrolizumab: Meaningful anti-tumor activity in 1L patients

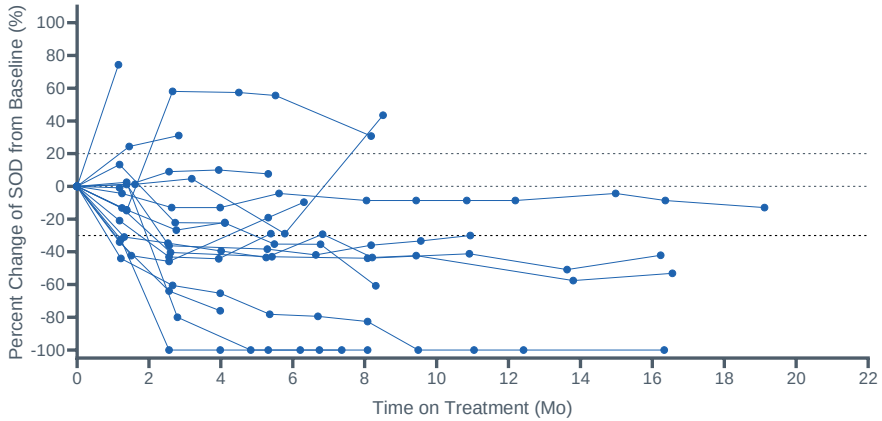
PD-L1 CPS ≥20 population identified to benefit most from HB-200 + pembrolizumab combination therapy

Deepening of responses observed over time; 67% of responders ongoing



N=17

PD per RECIST v1.1, iPR per iRECIST



PD-L1 CPS ≥20 Evaluable Population	Confirmed Responses (RECIST v1.1)	ORR	CR Rate	DCR (CR+PR+SD)
N = 17	**9**	**52.9%**	**17.6%**	**82.4%**

Excludes 2 patients who did not have a post-baseline tumor evaluation on trial. 1 patient had a grade 5 COVID pneumonia event on Study Day 27; 1 patient withdrew consent prior to the first scan.

- 8.4 months follow up time
- Median duration of response not yet mature

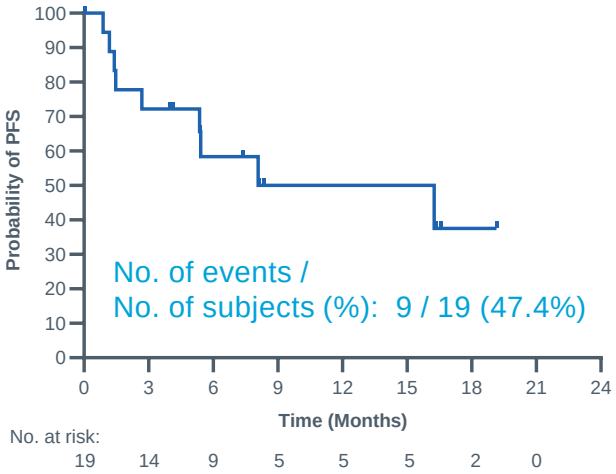
Data as of 29-Mar-2024. Efficacy dataset includes 38 patients with minimum 4.5 months of follow-up time after first dose as of data cutoff or discontinued early during this period.

HB-200 + pembrolizumab: Promising preliminary PFS and OS

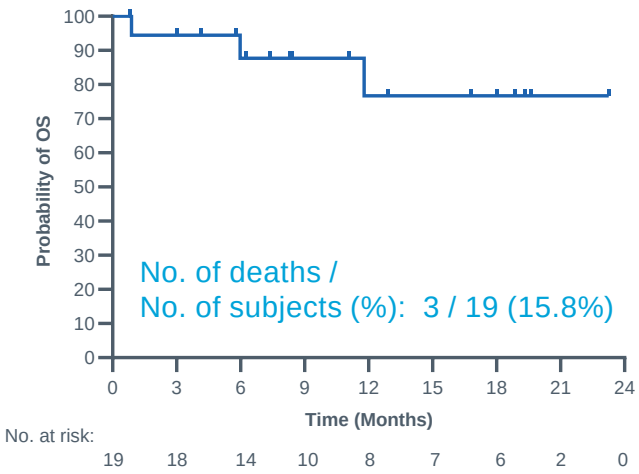
PD-L1 CPS ≥20 population identified to benefit most from HB-200 + pembrolizumab combination therapy

Preliminary progression-free survival and overall survival are promising

Progression-Free Survival: 16.3 months



Median Overall Survival: Unreached



Data as of 29-Mar-2024. Efficacy dataset includes 38 patients with minimum 4.5 months of follow-up time after first dose as of data cutoff or discontinued early during this period.
1L, first line; CI, confidence interval; CPS, combined positive score; CR, compete response; DCR, disease control rate; Mo, month; mPFS, median progression-free survival; mOS, median overall survival; n.c., not calculable; No, number; ORR, objective response rate

HB-200 + pembrolizumab: Seamless and adaptive pivotal Phase 2/3 trial

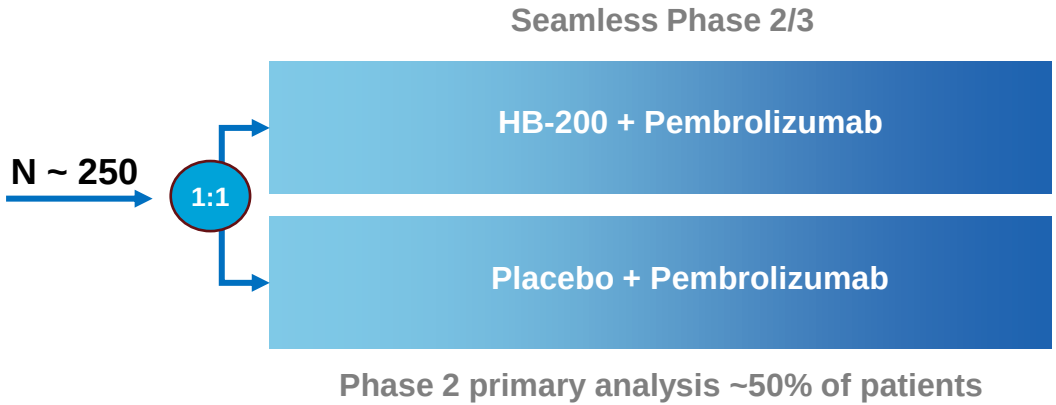
Primary Ph2 read-out expected in 2026, potential submission for Accelerated Approval, FDA-aligned trial design and protocol

Key eligibility criteria

Unresectable, recurrent or metastatic HPV16+ oropharyngeal cancer

PD-L1+

CPS ≥20



Treatment schedule:

- **HB-200 IV:** Q3w for first 5 doses; Q6w later
- **Pembrolizumab IV**: 200 mg first 5 doses followed by 400 mg
- **Duration:** up to 20 cycles

Expected Milestones & study endpoints:

Study start: Q4 2024
Phase 2 primary analysis: 2026, potential submission for AA
Phase 3 primary analysis: 2028

Primary endpoints:

- Phase 2: ORR
- Phase 3: OS

Secondary endpoints (Phase 2/3):

- Safety/tolerability
- PFS, ORR, DOR, DCR, PFS2
- Patient reported outcomes

PD-L1: programmed-death ligand 1; CPS: combined positive score; ORR: Objective response rate; OS: overall survival; DOR: duration of response; DCR: disease control rate; PFS: progression free survival; PFS2: progression free survival on second-line therapy; AA, accelerated approval

Additional applications of HB-200: Neoadjuvant & adjuvant settings

HB-200 plus chemotherapy followed by response-stratified de-intensification in HPV16+ oropharyngeal cancer

Neoadjuvant setting: HB-200 + chemotherapy

- **Trial sponsor:** University of Chicago Medicine
- Presented by Dr. Ari Rosenberg at ASCO 2024, abstract: 6017
- Early efficacy signal with deep response rate of 81% (17 of 21) vs ~70% historical rate for neoadjuvant chemotherapy alone
- Expansion of HPV16-specific T-cell responses and reduction in ctHPV-DNA was observed
- HB-200 plus chemotherapy is safe and feasible

Adjuvant setting: HB-200 monotherapy

- **Trial sponsor:** Memorial Sloan Kettering Cancer Center
- Patients with detectable tumor-tissue modified viral (TTMV) DNA after definitive treatment
- Randomized study HB-200 vs placebo with goal to eliminate TTMV-HPV DNA to delay or eradicate recurrent cancer in patients
- **Enrollment to begin imminently**

Presented by Ari J. Rosenberg, MD, University of Chicago Cancer Center, at ASCO 2024 Annual Meeting
Abstract: 6017; Neoadjuvant HPV16-specific arenavirus-based immunotherapy HB-200 plus chemotherapy followed by response-stratified de-intensification in HPV16+ oropharyngeal cancer: TARGET-HPV

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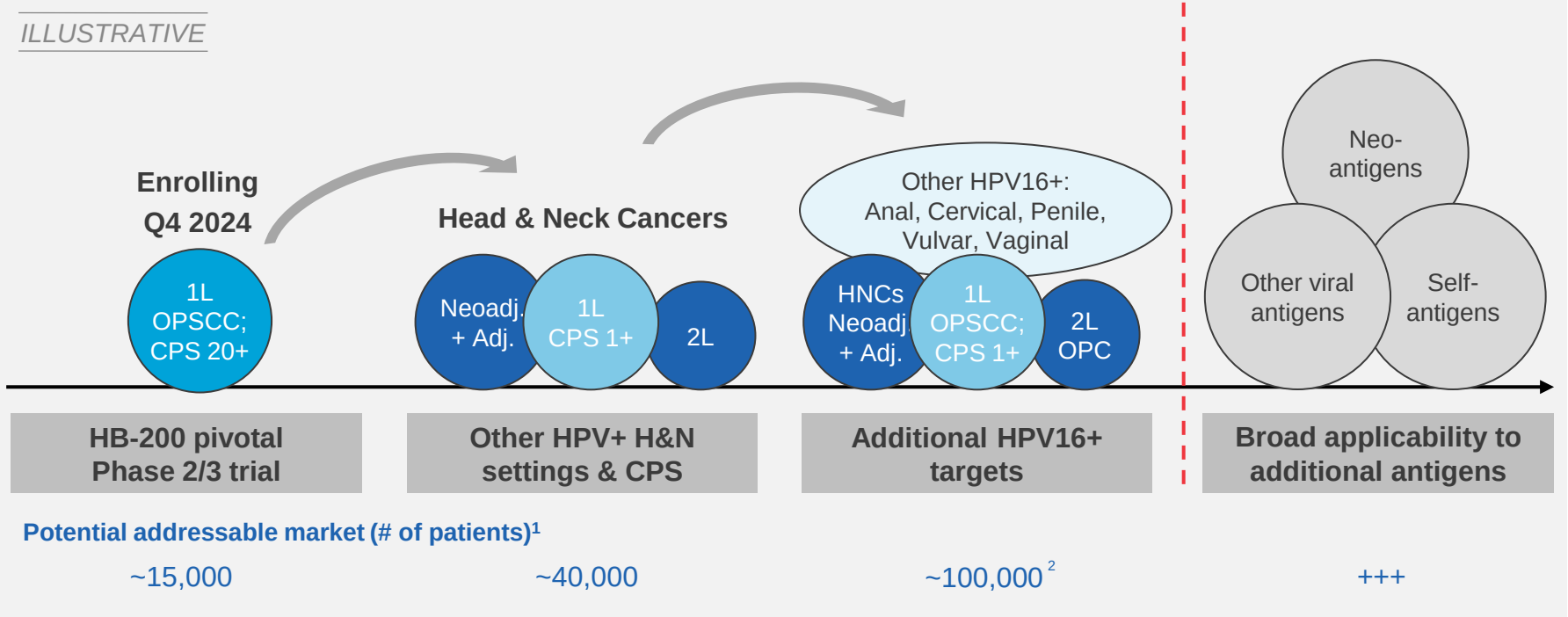
Patient-centric oncology strategy starts with HB-200 in head and neck cancer

Arenavirus platform offers a strategy designed to address the significant unmet need in HPV16+ tumors and beyond



[1] Source: SEER; GLOBOCAN 2022; Clinical Trials.gov; NCCN Guidelines; ClearView Analysis.
[2] Systemic therapy patients only, assumes non-resectable or partially resectable only
Neoadj. = Neoadjuvant; Adj. = Adjuvant

HB-200 + pembrolizumab: HPV16+ specific immunotherapy treatment option

- **Best-in-class targeted HPV16+ immunotherapy combination**
- **Encouraging response rates & promising preliminary durability**
- **Potential to be first-in-class: FDA-alignment on registrational trial**

Expect to initiate registrational Phase 2/3 trial in Q4 2024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