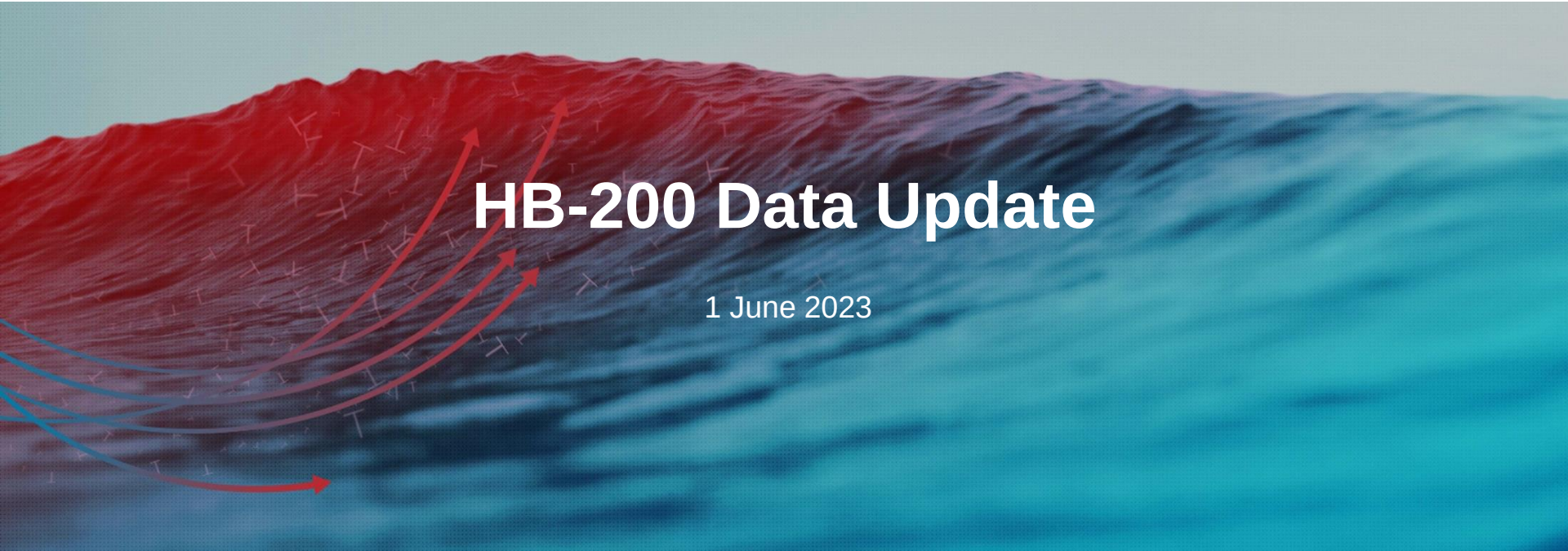

HB-200 Data Update

1 June 2023

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Today's presenting team

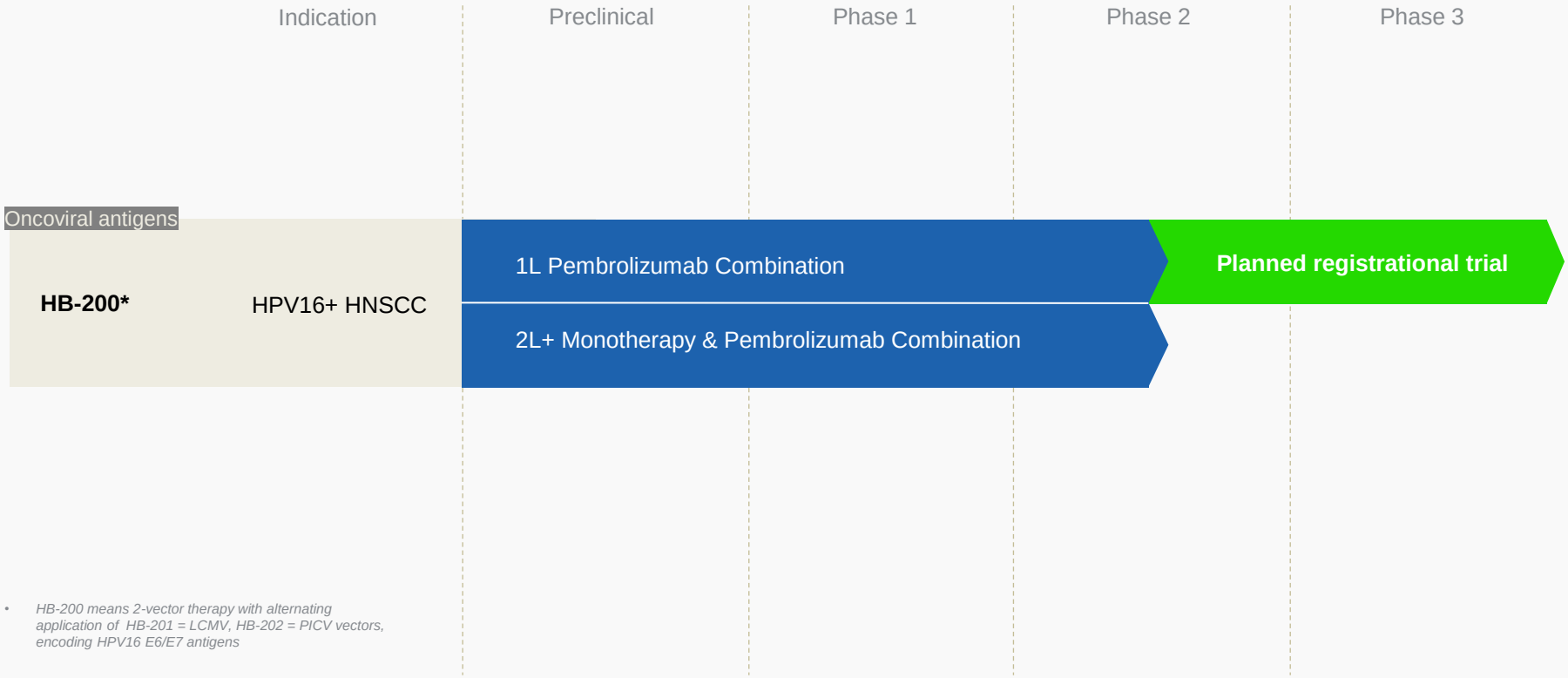
Joern Aldag
Chief Executive Officer

Katia Schlienger
Chief Medical Officer

Reinhard Kandera
Chief Financial Officer

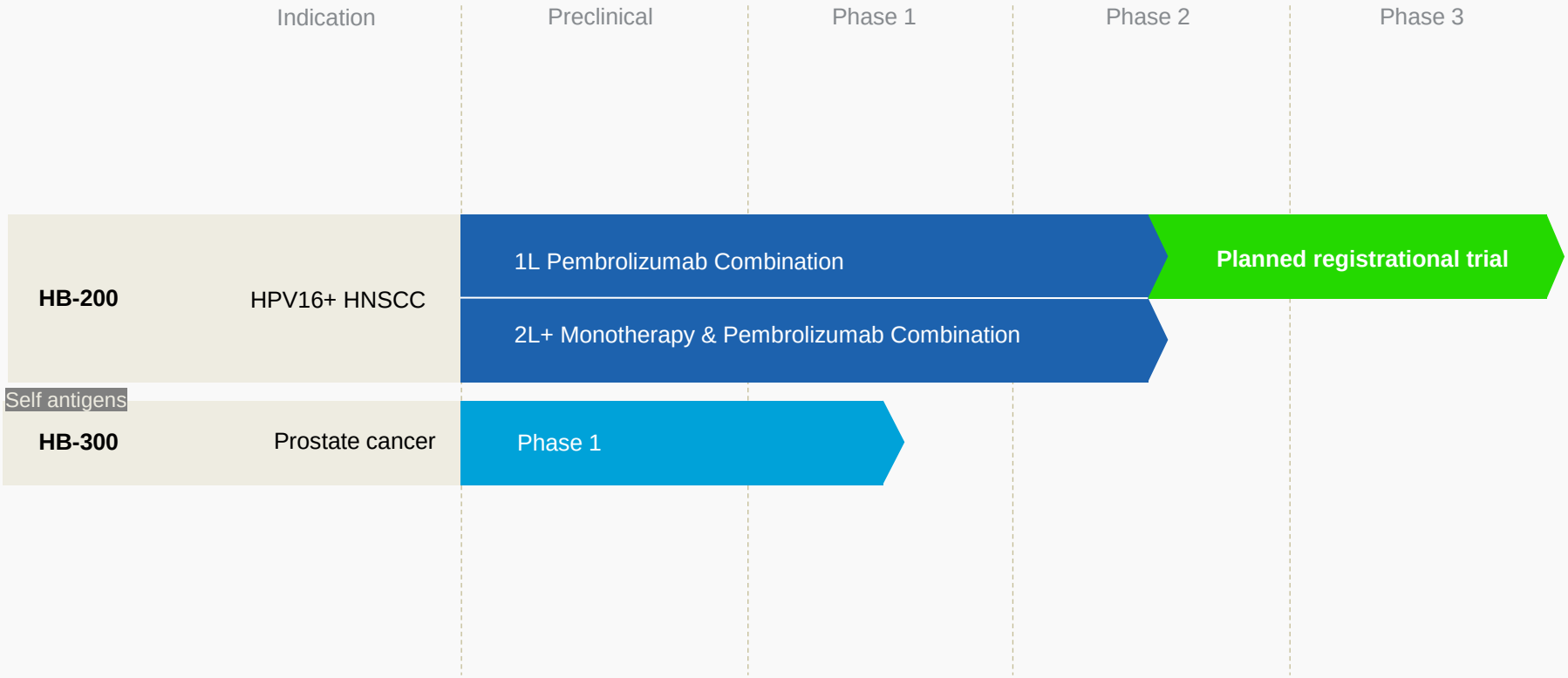
Klaus Orlinger
Chief Scientific Officer

Building a Pipeline for the Novel Arenaviral Vector Technology Platform: Pioneer product HB-200 nearing registrational trial as a combination-therapy



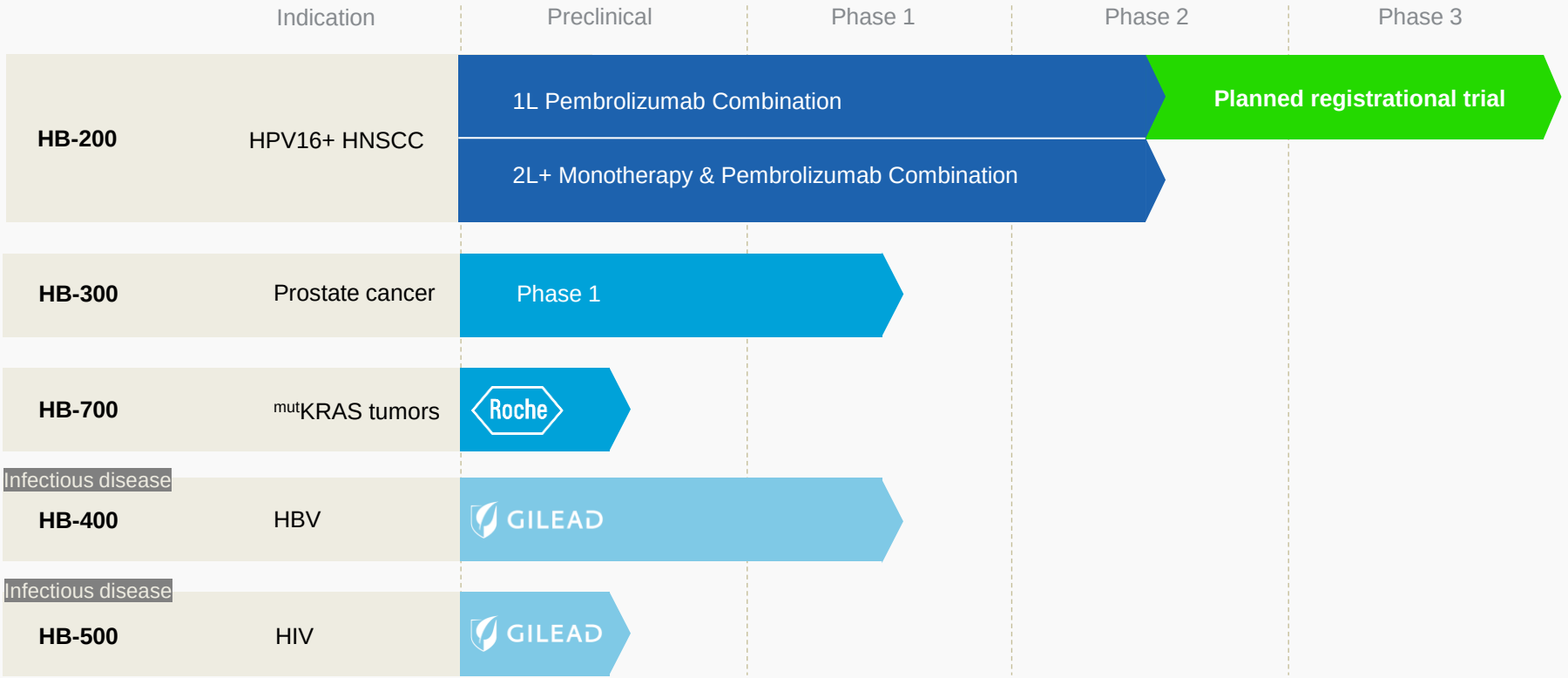
- *HB-200 means 2-vector therapy with alternating application of HB-201 = LCMV, HB-202 = PICV vectors, encoding HPV16 E6/E7 antigens*

Pipeline for the Novel Arenaviral Vector Technology Platform:
The platform is scalable in oncology space across multiple antigen classes



Pipeline for the Novel Arenaviral Vector Technology Platform:
In partnership with Roche the platform is targeted to neo-antigens for mutKRAS

Pipeline for the Novel Arenaviral Vector Technology Platform:
In partnership with Gilead, HOOKIPA is advancing functional cures for HBV and HIV



HB-200 Development Program:
Fundamental questions answered positively, unlocking potential of platform

HB-200 + Pembrolizumab is potentially more effective than Pembro alone	• **HB-200 + pembrolizumab combination doubles ORR in 1st line** • **ORR 43% vs. pembrolizumab 19%***
HB-200 is clinically active alone	• **Clinical responses in monotherapy in CPI resistant patients** • **Monotherapy shows preliminary mOS 14.2 mo. (ITT pop.)**
HB-200 is driving expected T cell biology	• **Unprecedented tumor-specific CD8+ T cells** • **HB-200 induced T cell infiltration in tumors associated with clinical benefit**
HB-200 shows favorable safety profile	• **Favorable safety profile from over 130 patients** • **In monotherapy and in combination**

** Harrington Updated Data KEYNOTE-048 JCO 2023*

HB-200 Development Program:
The totality of the data support progression into a pivotal study

- HB-200 + Pembrolizumab is potentially more effective than Pembro alone
- HB-200 is clinically active alone
- HB-200 is driving expected T cell biology
- HB-200 shows favorable safety profile

Preparations for Pivotal 1st Line HNSCC Trial

Evaluation of additional development opportunities

HB-200 Phase 1/2:
132 patients enrolled as of March 31, 2023

Phase 1 Monotherapy HPV16+ HNSCC Dose Escalation & RP2D Confirmation N=93	**2L-6L** **2-vector therapy** 11 patients at optimal dose Follow-up data	2L and later lines 2-vector therapy 18 patients added Data developing	2L and later lines 2-vector therapy 12 patients at other doses	2L and later lines 1-vector therapy 20 patients	Non-HNSCC HPV+ tumors 1/2-vector therapy 32 patients
Phase 2 Pembrolizumab Combination HPV16+ HNSCC N=39	1L Safety run-in 1-vector therapy 3 patients	**1L** **2-vector therapy** **14 patients evaluable** 20 treated	2L+ Safety run-in 1-vector therapy 1 patient	**2L-7L** **2-vector therapy** **5 patients evaluable** 15 treated	**1L and later lines** **2-vector therapy** 2 treated*

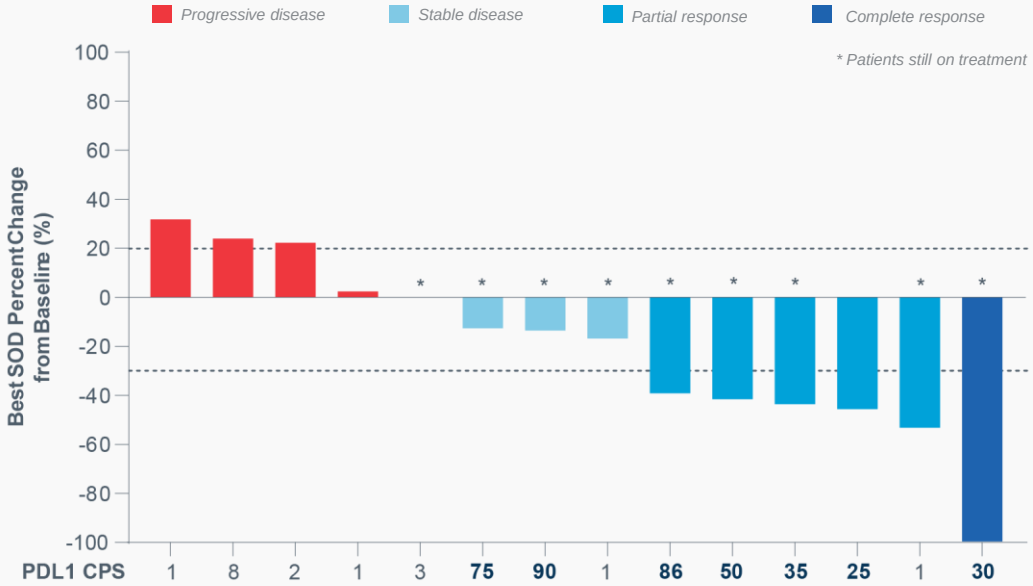
Data reported today

- *Preliminary Data: Includes unmonitored and unverified data based on current EDC data or data provided by Investigators. Data is subject to change.*
- *H 200-001 (NCT04180215)*

- **HB-200 + Pembrolizumab combination doubles ORR of Pembrolizumab in 1st line**

HB-200 + Pembrolizumab as 1L Treatment Shows 43% ORR

All responses confirmed under RECIST 1.1



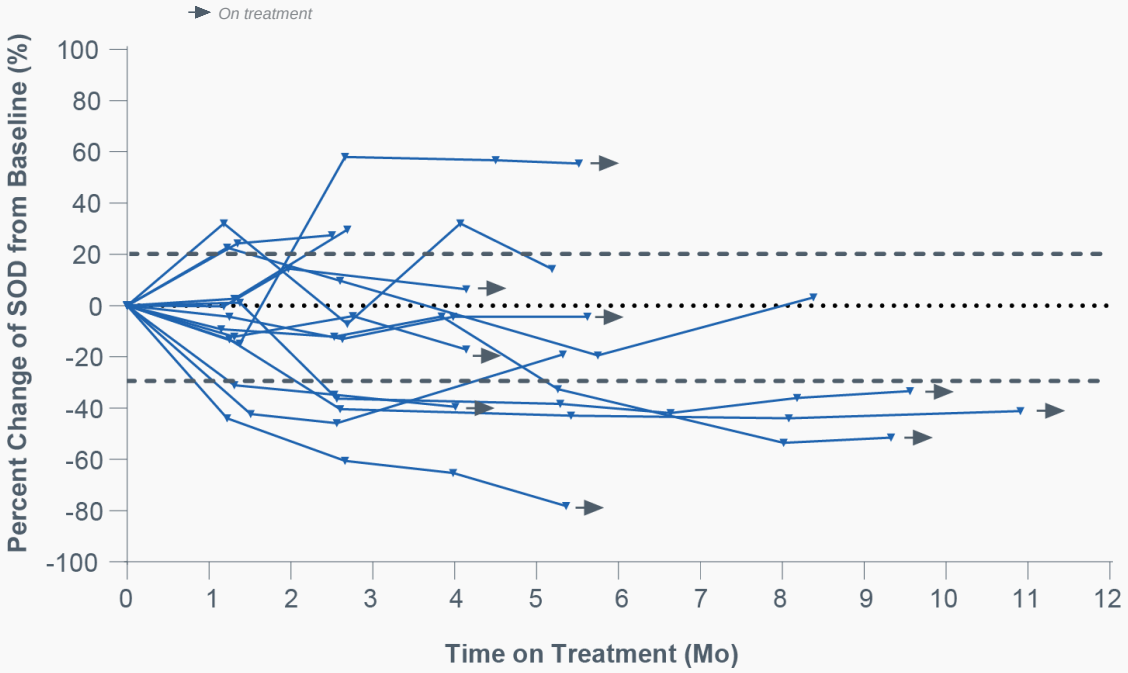
- **Objective Response Rate is 43% (6/14)**
  - **1 confirmed CR**
  - **5 confirmed PR**
- **Disease Control Rate is 71% (10/14)**
  (DCR = SD+PR+CR)

Data cut-off 31-Mar-2023; 14 oropharynx cancer patients evaluable from 15 with at least 3 mo. follow up (≥ 2 scans); median follow-up 5.6 mo
Responses assessed by RECIST v1.1 per investigator assessment; RECIST: Response Evaluation Criteria in Solid Tumors; SOD: Sum of diameters of target lesions
Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.
ORR= Objective Response Rate; DCR= Disease Control Rate; CR=Complete Response; PR=Patrial Response; SD=Stable Disease; PD=Progressive Disease

Pembrolizumab 1L:
ORR: 19 % DCR: 47 %[1]

1 Harrington Updated Data KEYNOTE-048 JCO 2023

HB-200 + Pembrolizumab 1st Line
Sustained responses in majority of patients



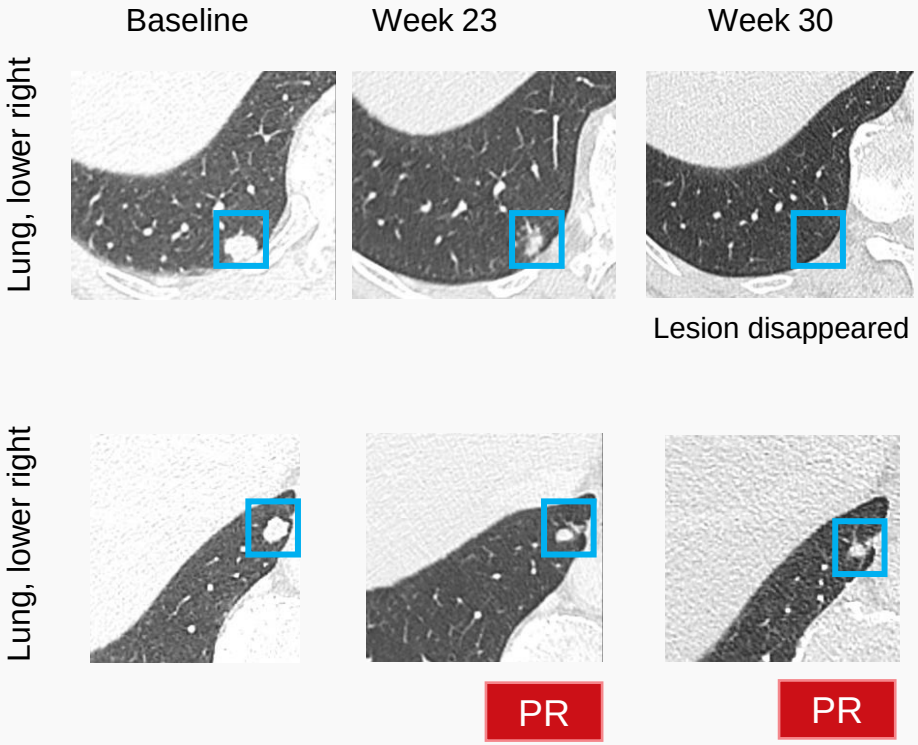
- **Shows Trends toward Durable Responses and Prolonged Disease Control**
- **mPFS not reached**
- **mOS not reached**

Data cut-off 31-Mar-2023; 14 oropharynx cancer patients /20 treated with HB-202/HB-201 + pembrolizumab in the 1L setting evaluable for efficacy *(at least ≥ 2 scans); median follow-up 5.6 mo*
Responses assessed by RECIST v1.1 / iRECIST per investigator assessment; RECIST: Response Evaluation Criteria in Solid Tumors, iRECIST: immune RECIST; SOD: Sum of diameters of target lesions
Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.

HB-200 + Pembrolizumab Demonstrate Durable Response and Tumor Reduction in Lung Lesions – Patient 1

Patient 1:

- 67-year-old male
- HPV16+ oropharynx cancer (CPS 1)
- Refractory to platinum-based chemoradiation (< 3 months)
- **Response**: PR in lung metastases at 5 months
- **Status**: Ongoing treatment at 10 months

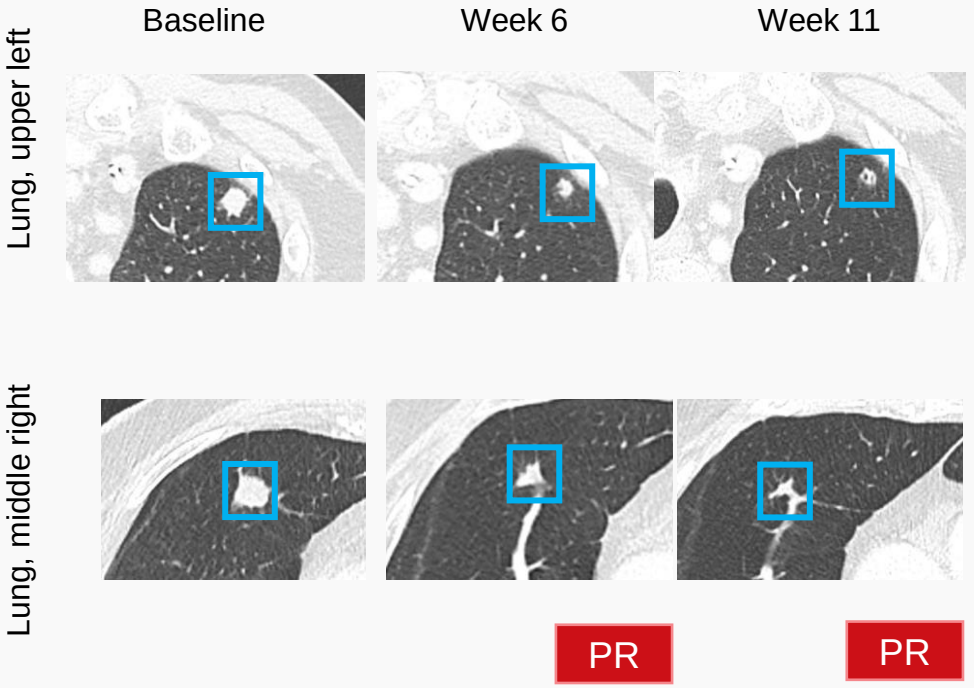


Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.

HB-200 + Pembrolizumab Demonstrate Durable Response and Tumor Reduction in Lung Lesions – Patient 2

Patient 2:

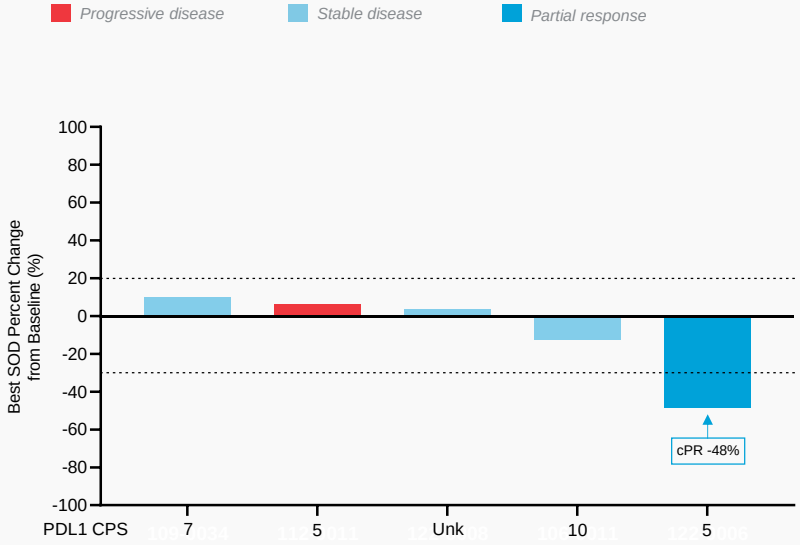
- 75-year-old male
- HPV16+ oropharynx cancer (CPS 86)
- 1L setting
- **Response**: rapid response in lung metastases since Week 6
- **Status**: Ongoing treatment at 4.5 months



Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.

- HB-200 + Pembrolizumab combination doubles ORR of Pembrolizumab in 1st line
- **Activity in 2nd Line+ (combination and monotherapy)**

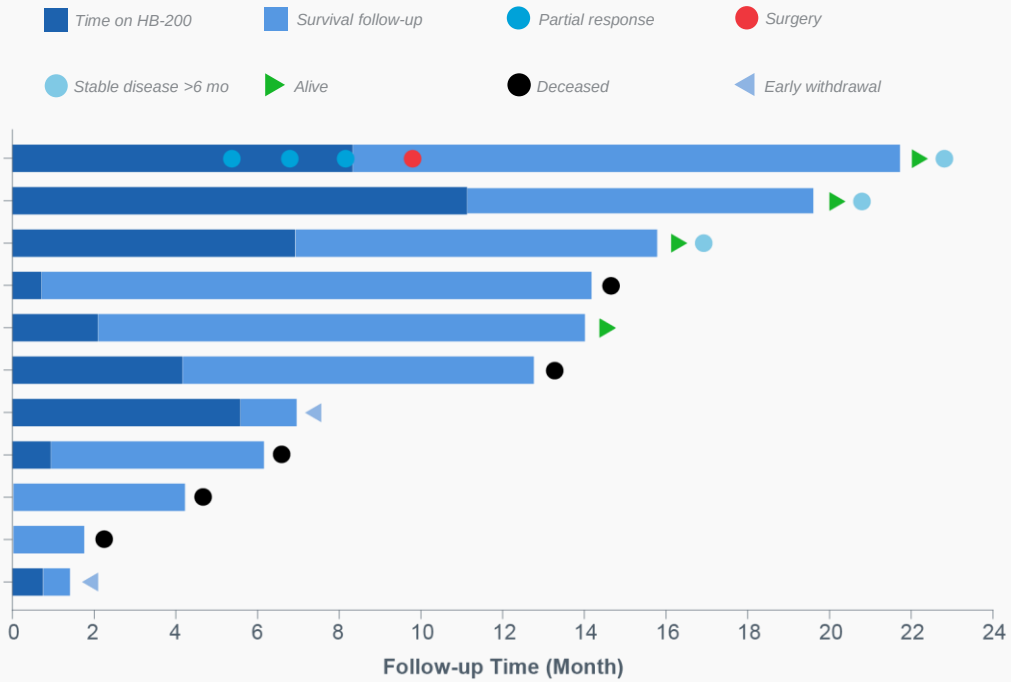
HB-200 Activity in 2nd Line+ in Combination with Pembrolizumab



- **15 patients heavily pre-treated (2L – 7L), 5 patients evaluable**
- **ORR:**
  - **1/5 patients with cPR**
  - **3/5 patients with SD**
- **Preliminary mPFS: 5.3 months**

Data cut-off 31-Mar-2023; 5/14 oropharynx cancer patients treated with HB-200 + pembrolizumab in the 2L and later line setting evaluable for efficacy *(at least ≥ 2 scans); median follow-up 4.2 mo*
Responses assessed by RECIST v1.1 : Response Evaluation Criteria in Solid Tumors; SOD: Sum of diameters of target lesions
Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.

HB-200 Phase 1 Monotherapy Follow-up in 2nd Line+ Preliminary mOS: 14.2 Months

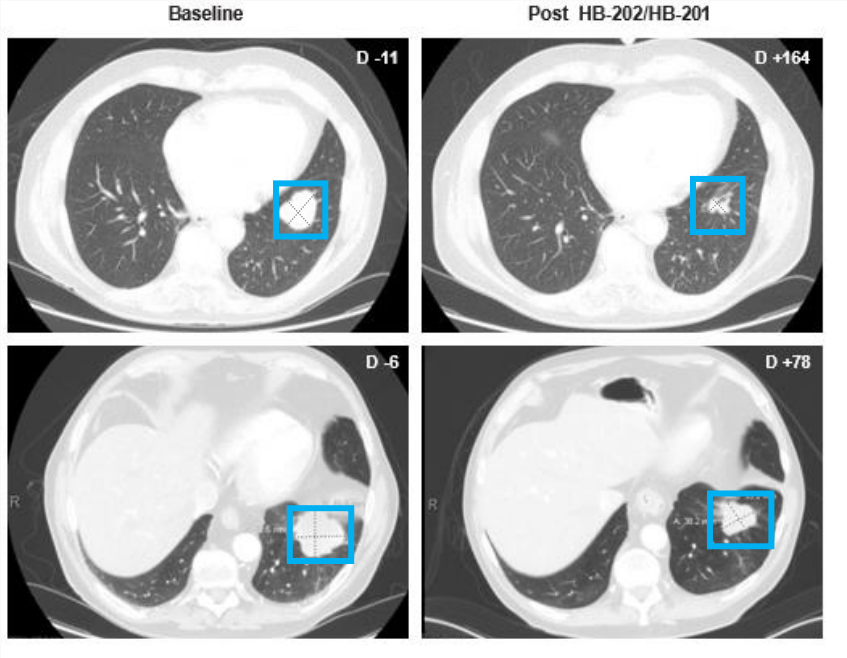


- **Monotherapy activity supports HB-200 potential in combinations**
- **mOS not reached in evaluable patients**
- **Preliminary Median Overall Survival (mOS): 14.2 Months**

Update on Initial Cohort of HB-200 in Monotherapy

Data cut off 31 Mar 2023. Survival follow-up for 11 ITT (intent-to-treat) patients who received HB200 monotherapy at the same doses moved forward to Phase 2. Median follow-up: 12.8 mo (range 1.4-21.7 mo).
Preliminary Data: includes unmonitored and unverified data based on current EDC data. Data is subject to change.

HB-200 Monotherapy: 2 Case Studies



Case 1:

- 65-year-old male with HPV16+ oropharynx cancer
- **Prior treatment:** pembrolizumab + lenvatinib
- **Response**: PR -33% in lung lesion 5 months into treatment
- **Status**: Discontinued treatment at 8 months, surgical resection of lung lesion at 10 months. No residual tumor. Ongoing long-term follow-up at 22 months

Case 2:

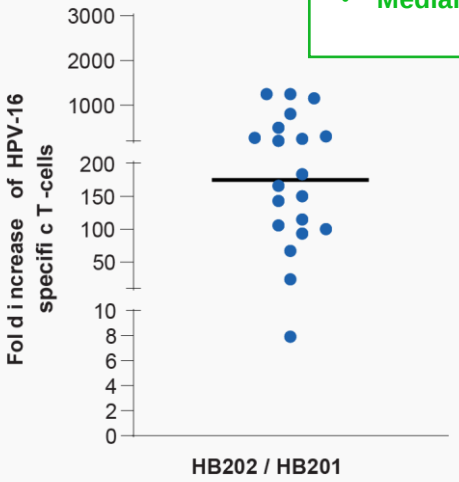
- 75-year-old male with HPV16+ oropharynx cancer
- **Prior treatment:** 4 lines of therapy, incl. Chemo and CPI
- **Response**: near PR -29% in lung metastases after 2.6 months
- **Status**: Continued on HB-200 monotherapy until progression after over 11 months of therapy; added pembrolizumab per protocol and remains on study at 20 months.

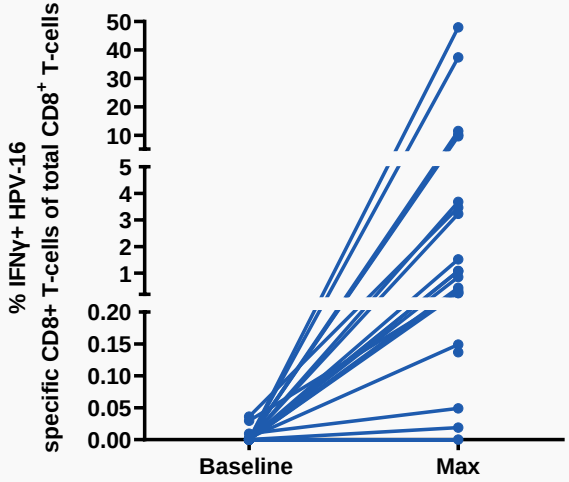
Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.

- HB-200 + Pembrolizumab combination doubles ORR of Pembrolizumab in 1st line
- Activity in 2nd Line+ (combination and monotherapy)
- **Highly functional T cell response associated with clinical benefit**

HB-200 Monotherapy: Unprecedented CD8+ T cell Response

- **Increase of tumor specific T cells[1]: up to 1250 fold**
- **Median: 174 fold**



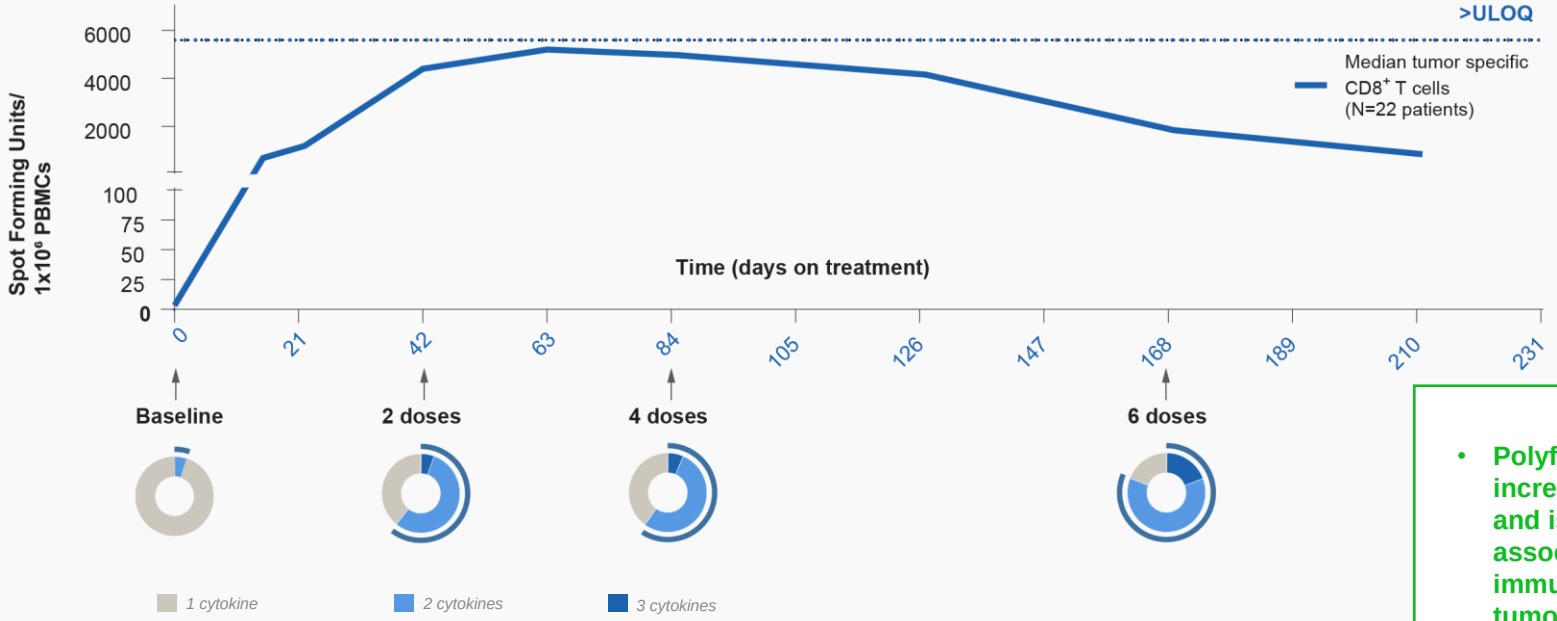


- **Conversion to functional tumor-specific CD8+ T cells[2]: up to: 48%**
- **57% of patients break 1% threshold**

Direct measurement of T cells without prior in vitro expansion of cells (all HNSCC patients treated with 2 vector therapy Q3W)

[1]HB200 two vector therapy mediated fold increase (max response on treatment vs before treatment) of systemic HPV-16 E7 and E6 specific T cells measured by ELISPOT;
[2]HPV-16 E6 and E7 specific CD8+ (killer) T cells out of total CD8+ T cells measured by intracellular cytokine staining;

HB-200 Monotherapy:
T cell longevity and polyfunctionality



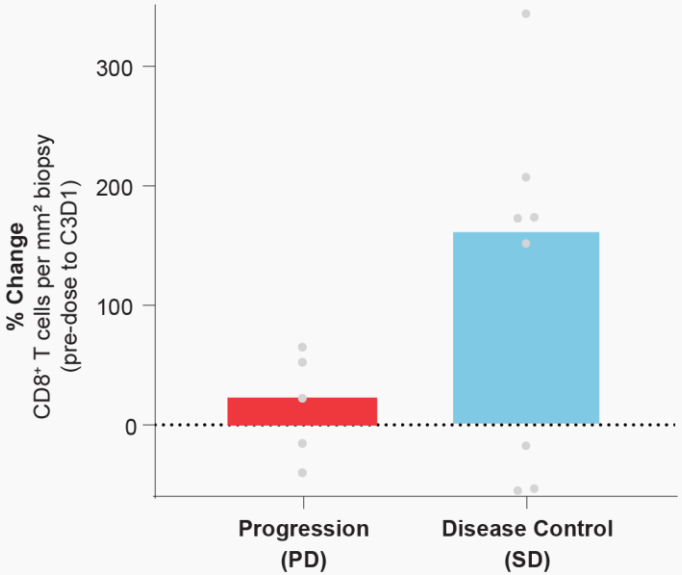
- **Polyfunctionality[1] increases over time and is known to be associated with immune control of tumors**

T cell kinetics by ELISPOT & analysis of IFN-g, IL-2, TNF-a and CD107a cytokine expression by intracellular cytokine staining at indicated timepoints

Pie charts indicate the percentage of tumor specific T cells expressing various numbers of cytokines (mean of all patients at indicated timepoints)

1 Polyfunctionality is the ability of T cells to carry out multiple functions simultaneously at the single cell level; The appearance of polyfunctional CD8+ effector cytotoxic T cells in vivo has been demonstrated to be a critical determinant of the success of immunological control of tumors (Imai N et al 2009, Yuan J et al 2008);

HB-200 Monotherapy – Association between T cell Induction and Clinical Outcome



- **Association Between HB-200 Induced CD8+ T Cells in Tumors and Clinical Benefit In Patients**
- **Greater CD8+ T cell infiltration observed in those with stable disease**

Analysis of all available paired tumor biopsies from Phase I monotherapy study; Bars represent median increase (% change) of tumor infiltrating CD8+ T cells during therapy
(i.e. 1 & 2 vector therapy, different administration (IV & IT), different tumor sites (Oropharyngeal; anal, cervical))
SD: Stable disease; PD: Progressive disease; C3D1: day 1 of third administration cycle

- HB-200 + Pembrolizumab combination doubles ORR of Pembrolizumab in 1st line
- Activity in 2nd Line+ (combination and monotherapy)
- Highly functional T cell response associated with clinical benefit
- **Favorable safety profile from over 130 patients**

HB-200 Monotherapy and Combination
Favorable safety profile across 132 patients in all settings

- Serious adverse events related to treatment: 7% of patients
- Treatment related-adverse events leading to dose reduction or discontinuation: 2% of patients
- No death related to treatment
- Data suggest that **Arenaviral therapies can safely be added** to any other immuno-therapy requiring more antigen-specific T cells

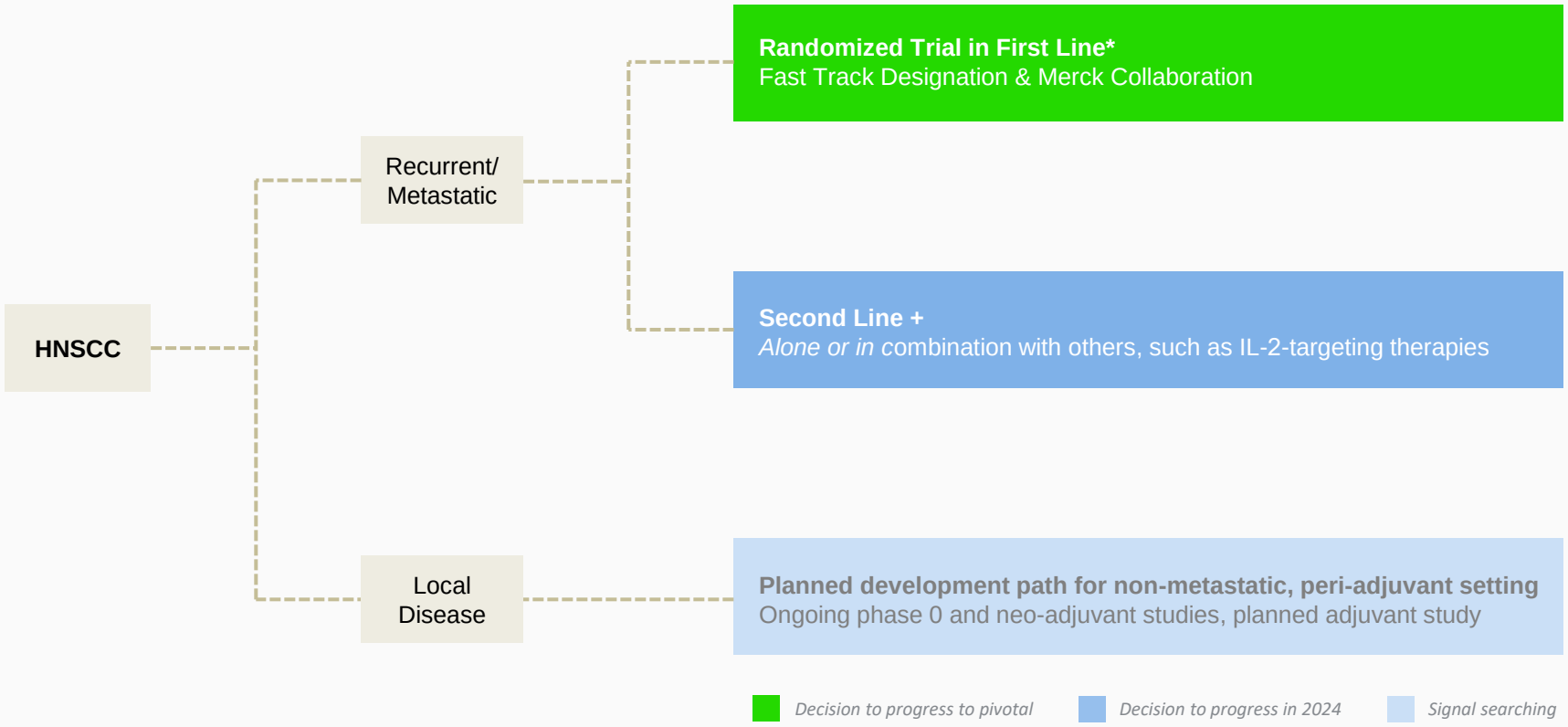
All participants (N=132)	Treatment related adverse events*	All adverse events
Any event	HB-201 73 (55%) HB-202 68 (52%) Pembrolizumab 25 (64%)	125 (95%)
Grade ≥3	17 (13%)	59 (45%)
Serious	9 (7%)	43 (33%)
Leading to dose reduction	2 (2%)	2 (2%)
Leading to discontinuation	3 (2%)	16 (12%)
Deaths	**0**	7 (5%)

Data as of 31-Mar-23
Preliminary Data: Includes unmonitored and unverified data based on current EDC data. Data is subject to change.

- *HB-200 means 2-vector therapy with alternating application of HB-201 = LCMV, HB-202 = PICV vectors, encoding HPV16 E6/E7 antigens*

- HB-200 + Pembrolizumab combination doubles ORR of Pembrolizumab in 1st line
- Activity in 2nd Line+ (combination and monotherapy)
- Highly functional T cell response associated with clinical benefit
- Favorable safety profile from over 130 patients
- **Preparing randomized trial with registrational intent**

Development Opportunities For HB-200 in HPV+ HNSCC



HB-200 Development Program:
The totality of the data support progression into a pivotal study

- **HB-200 + Pembrolizumab is potentially more effective than Pembro alone**
- **HB-200 is clinically active alone**
- **HB-200 is driving expected T cell biology**
- **HB-200 shows favorable safety profile**

Preparations for Pivotal 1st Line HNSCC Trial

Evaluation of additional development opportunities

HOOKIPA
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