HOOKIPA PHARMA

Supercharging Immunotherapy

March 2022

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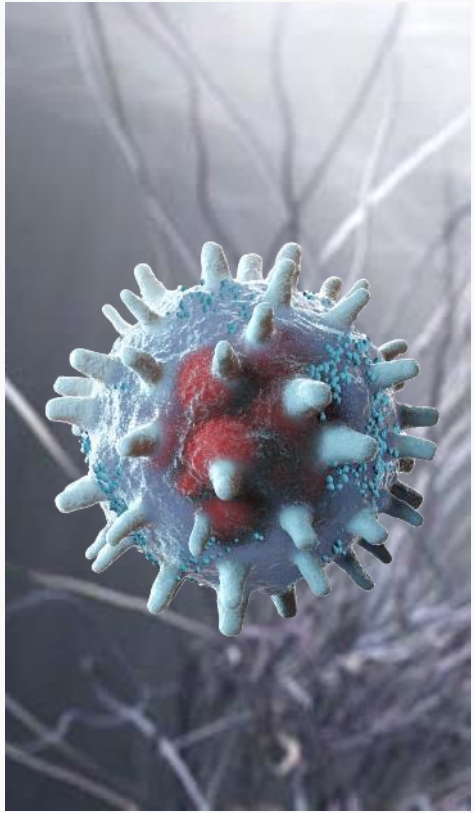
Directing the Power of the Immune System Against Serious Diseases



Vision A world in which cancers can be chronically managed or eradicated

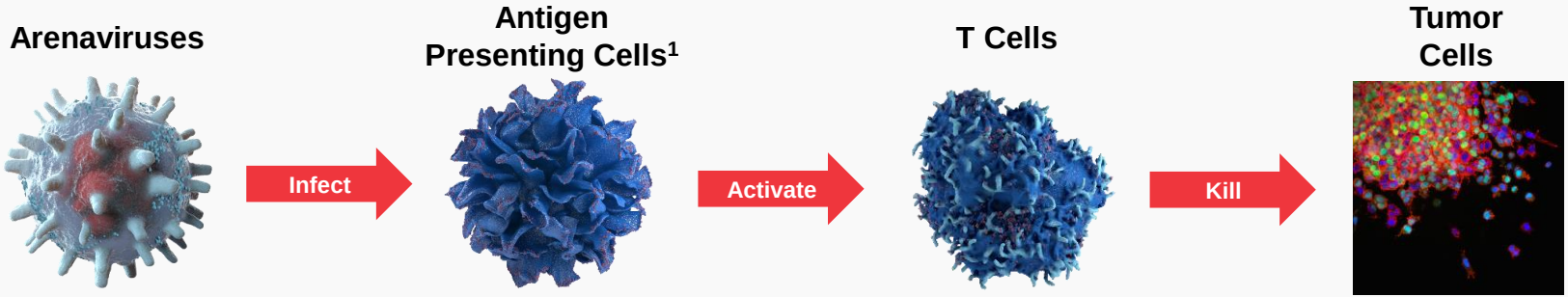
Mission Advancing the field of immunotherapy by using a novel, arenavirus-based antigen delivery system

Strategy Focus on **T cells**

- **Optimize** induction of T cells to achieve unprecedented levels of antigen-specific T cells
- **Mobilize** high numbers of functional antigen-specific T cells that efficiently infiltrate the tumor and kill malignant cells
- **Maximize** the potential benefits of our products through rational combination with other therapeutic modalities

Arenaviruses Naturally Target Immune Cells to Activate T Cells - Using This Mechanism to Direct T Cells to Specifically Kill Tumor Cells

Arenavirus Vector Mode of Action



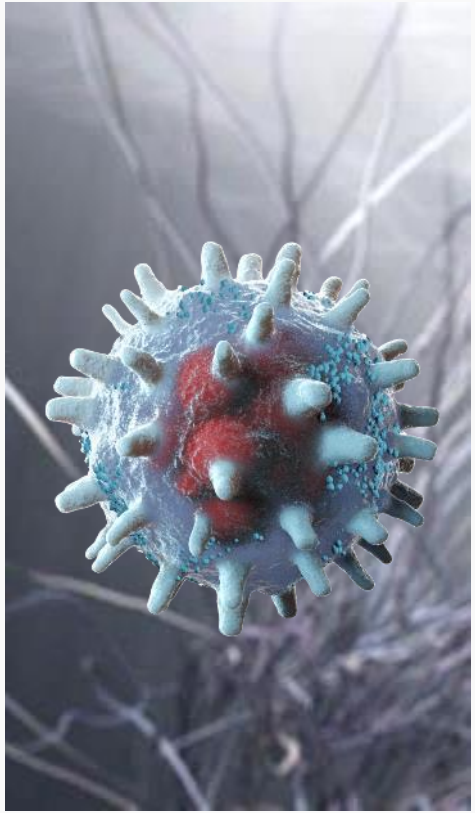
Potential to design drugs that are:

- Safe
- Off-the-shelf
- *In vivo* administration
- Repeat administration

[1]*Antigen Presenting Cells include dendritic cells and macrophages.*

Proof of Hookipa's T Cell Technology – Early Human Anti-Tumor Activity

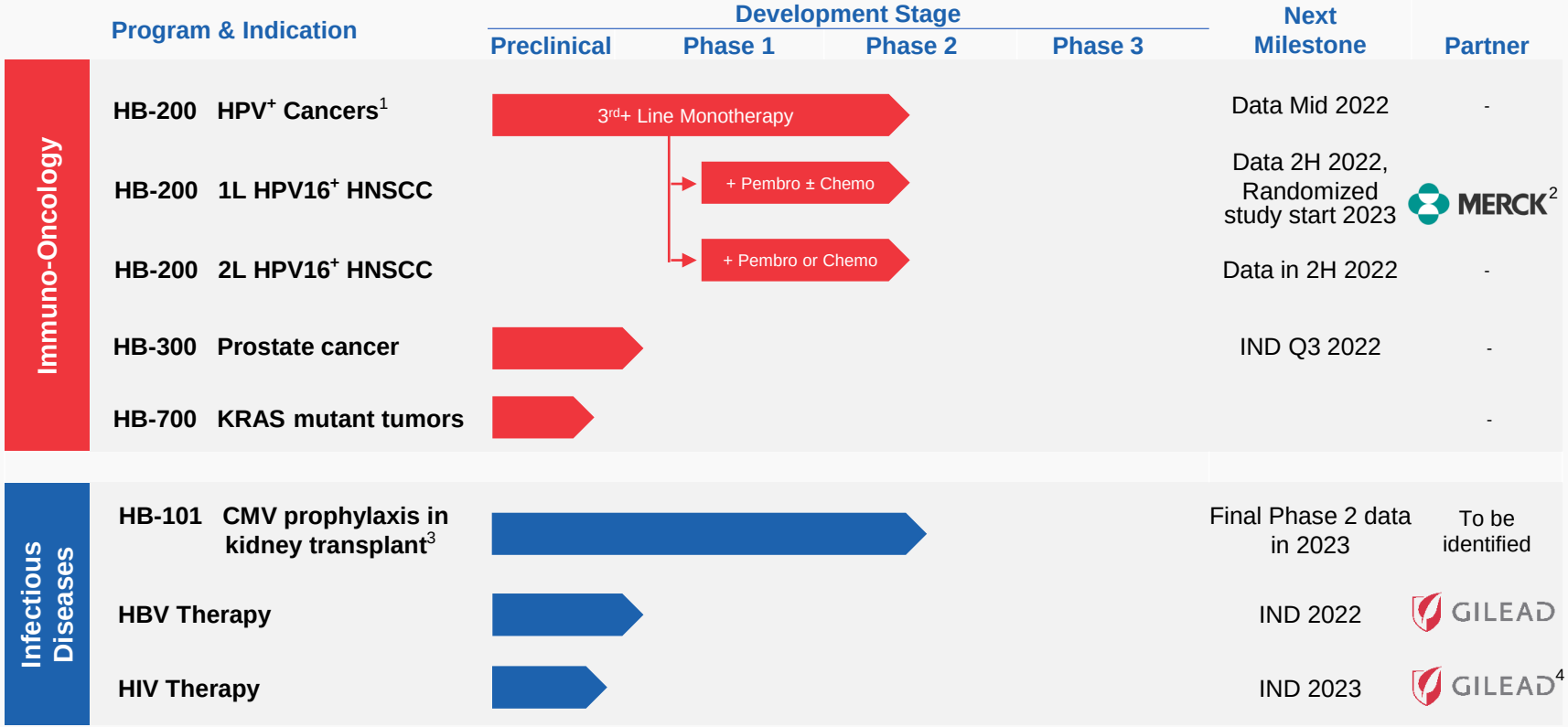
HB-200 For Recurrent/Metastatic Patients Progressed on Standard of Care (Median: 3 Prior Lines)



- ✓ **Favorable safety & tolerability profile**
- ✓ **Strong translational data**
  - Tumor antigen specific $CD8^+$ T cell induction up to 40% in circulation
  - Polyfunctional, not exhausted
  - TILs in 50% of patients with paired biopsies (3/6 patients)
- ✓ **Anti-tumor activity**
  - 75% disease control rate
  - Tumor shrinkage in 53% of 28 evaluable patients
  - 3 PRs, 1 "near PR" (SD with -29% shrinkage) and 1 PR from a patient after pembro add-on
  - Qualitatively, responses with HB-202/HB-201 "better" than with HB-201 alone (2-vector candidate shrinks soft-tissue large lesions)
- ✓ **Phase 2 ongoing for HB-201 in combination with pembrolizumab**
  - First patient dosed in 1st line advanced/metastatic HNSCC in January 2022
  - FDA granted Fast Track Designation to combination of HB-200 + pembrolizumab for 1st line HNSCC

Clinical activity and safety data as of Nov. 1, 2021 cut-off; clinical translational data as of Sept. 1, 2021 cut-off.

Investing in a Diverse Oncology Pipeline, Partnering Infectious Disease Programs



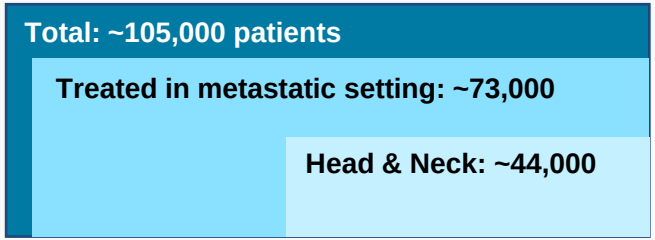
[1]ClinicalTrials.gov: NCT04180215; [2]Clinical supply agreement for Pembrolizumab; [3]ClinicalTrials.gov: NCT03629080.
[4]HIV Therapy: Upon completion of Phase 1b study, Gilead has exclusive right for further development.

HB-200 Program in HPV16^{+} Cancers

Large Unmet Medical Need in HPV16+-driven Cancers for Novel Arenavirus-based Approach with Product Candidate HB-200

The HPV+ Cancer Challenge

- Many head & neck (60%), cervical (99%), genitourinary cancers (70 – 88%) are HPV-driven
- Expected 2030 HPV+ squamous cell carcinoma incidence in G7:



- High unmet need with SOC (1L pembrolizumab and/or chemo: 17% ORR, mOS 13.6 months, mPFS 8 months)

Product Candidate HB-200's Potential Solution

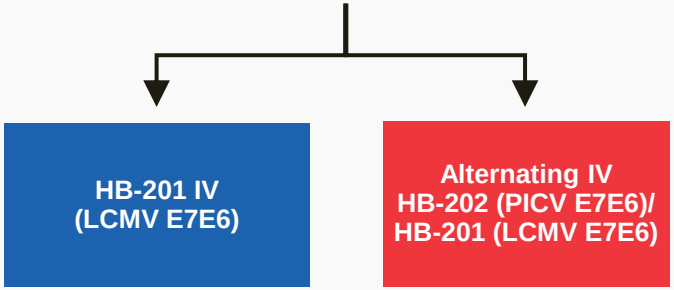
- Replicating arenaviral vectors encoding non-oncogenic HPV16+ E6/E7 fusion antigens
  - HB-201 = Lymphocytic Choreomeningitis Virus (LCMV)
  - HB-202 = Pichinde Virus (PICV)
- Clinical HB-201 testing ongoing; Recommended Phase 2 Dose (RP2D) selected
- Alternating 2-vector HB-202/HB-201 approaching RP2D
- Intravenous (IV) delivery

https://gco.iarc.fr/tomorrow/en/dataviz/tables?cancers=39&single_unit=500&years=2030&populations=840_276_250_380_724_826_392&group_populations=0&multiple_populations=1; https://seer.cancer.gov/statfacts/html/oralcav.html; https://www.cdc.gov/cancer/hpv/statistics/cases.htm; https://gynoncrp.biomedcentral.com/articles/10.1186/s40661-017-0047-8; https://pubmed.ncbi.nlm.nih.gov/22966247/; https://pubmed.ncbi.nlm.nih.gov/27838135/; https://touchoncology.com/wp-content/uploads/sites/2/2016/06/private_articles_22352_pdf_ Bevacizumab-in-the-Treatment-of-Cervical-Cancer-%E2%80%93-Current-Evidence-and-Next-Steps_0.pdf; https://clincancerres.aacrjournals.org/content/clincanres/early/2020/01/28/1078-0432.CCR-19-2962.full.pdf

HB-200 Phase 1 Trial in Late-Stage Patients Achieved Study Objectives in Head & Neck Squamous Cell Carcinoma (HNSCC)

Phase 1 (2nd/3rd+ Line HNSCC)

Dose escalation, route of administration, tumor type selection, schedule determination



Phase 1 trial explored other cohorts that did not meet criteria to continue forward: initial intra-tumoral (IT) administration; dosing every 2 weeks (Q2W). Various other HPV16+ tumors are still being explored in Phase 1.

HNSCC, head and neck squamous cell carcinoma; LCMV, Lymphocytic Choriomeningitis Virus; PICV, Pichinde Virus.

Phase 1 monotherapy dose escalation study
(NCT04180215)

Study population:

- **Locally advanced/recurrent/metastatic HPV16+ solid tumors**
- Progressing on standard of care

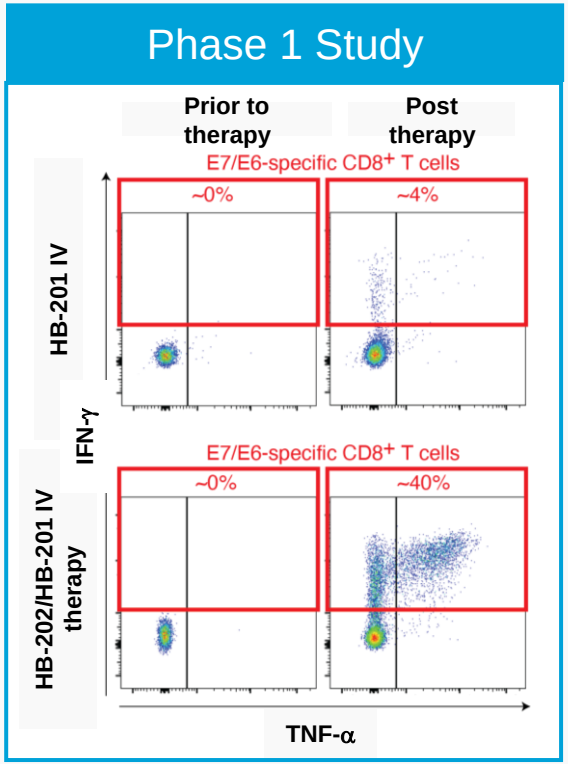
Study objectives:

- ✓ Primary: Recommended Phase 2 dose
- ✓ Secondary: Safety and tolerability, antitumor activity
- ✓ Exploratory: T cell activation, pharmacodynamic biomarkers

Principal Investigator:
David Pfister, MD
Chief, Head & Neck Oncology Service at Memorial Sloan Kettering Cancer Center

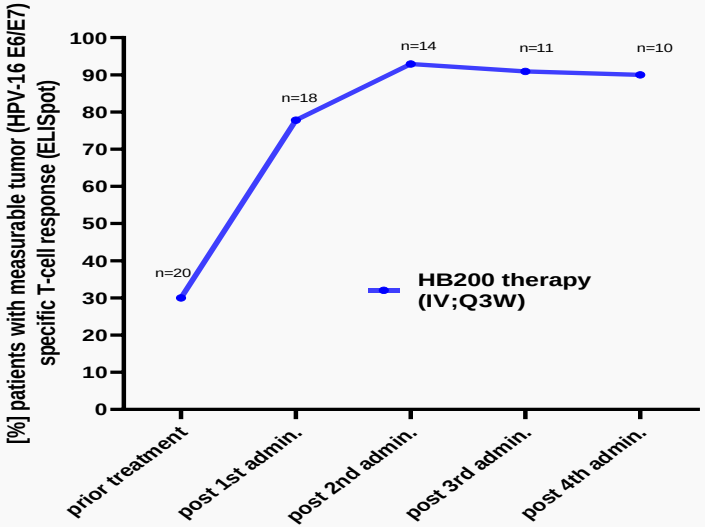
HB-200 Shows Robust E7/E6-specific CD8+ T Cell Responses

- Up to **40% of E7/E6-specific circulating CD8+ T cells**
- TNF-α and/or IFN-γ producing, polyfunctional, non-exhausted

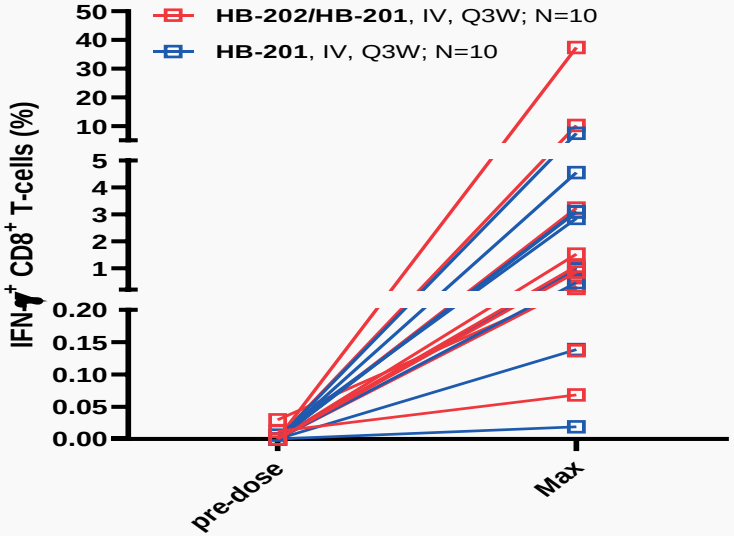


HB-200 Demonstrates Fast Tumor-specific T Cell Induction

Fast induction of active tumor-specific T cell responses[1] in nearly all patients
(ELISpot: HPV16+ E6/E7 specific responses)



>50% of patients break single digit % threshold of tumor specific systemic CD8+ T cells[2]
(HPV16+ E6/E7 specific CD8+ responses)

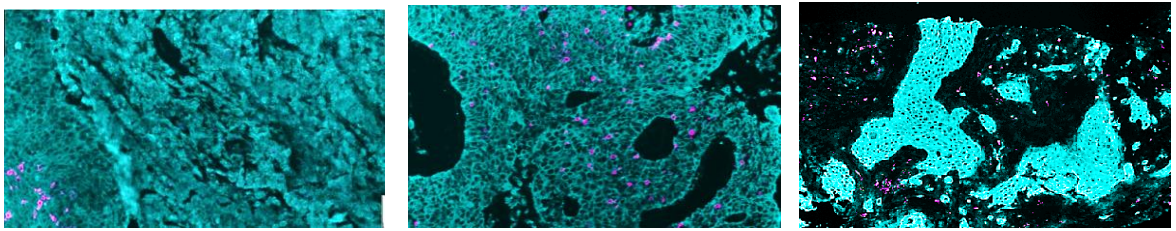


[1]*Direct measurement without prior in vitro expansion of cells; data from HB-201 and HB-202/HB-201 combined.*
[2]*Direct measurement without prior in vitro expansion of cells; majority of patients show peak responses 2-3 weeks post first administration.*

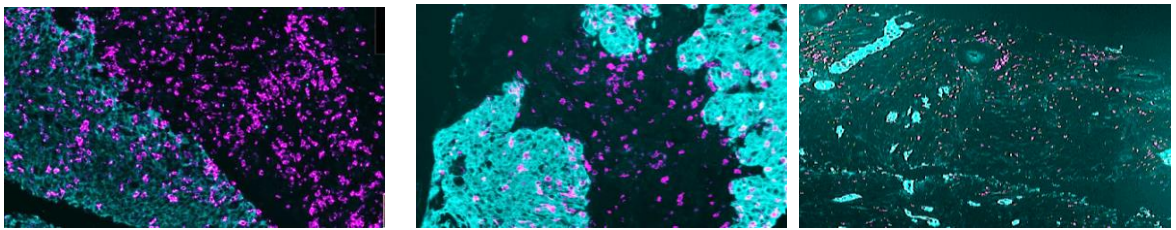
HB-200 T Cells Become Tumor Infiltrating Lymphocytes (TILs): CD8⁺ T Cells Penetrate Tumors

- 50% of biopsied patients show TILs[1] (i.e. CD8⁺ T cells infiltrating tumors)

Prior to therapy



HB-200 treated



Staining Legend:
CD8⁺ T cells | **Tumor**

[1]Analysis of all available paired (pre- and post treatment) tumor biopsies from patients treated with HB-201 or HB-202/HB-201 IV Q3W interval (N=6).

HB-200 Exhibits a Favorable Tolerability Profile

All groups all cohorts (N=62)	Treatment Related AEs	All AEs
Any event	41 (66%)	56 (90%)
Grade ≥3	5 (8%)	26 (42%)
Serious	2 (3%)	17 (27%)
Leading to dose reduction	1 (2%)	1 (2%)
Leading to discontinuation	2 (3%)	6 (10%)
Deaths	0	3 (5%)

Grade ≥3 events noted as related to study drug:

- Grade 3
  - Anemia (HB-202, also related to baseline anemia)
  - Arthritis (HB-201, also related to baseline arthritis)
  - Rash (HB-201, leading to dose reduction)
- Grade 4
  - Encephalopathy* (HB-201, also reported as serious, dose discontinuation)
  - AST increase* and Grade 3 febrile neutropenia (HB-202, also reported as serious, dose discontinuation)

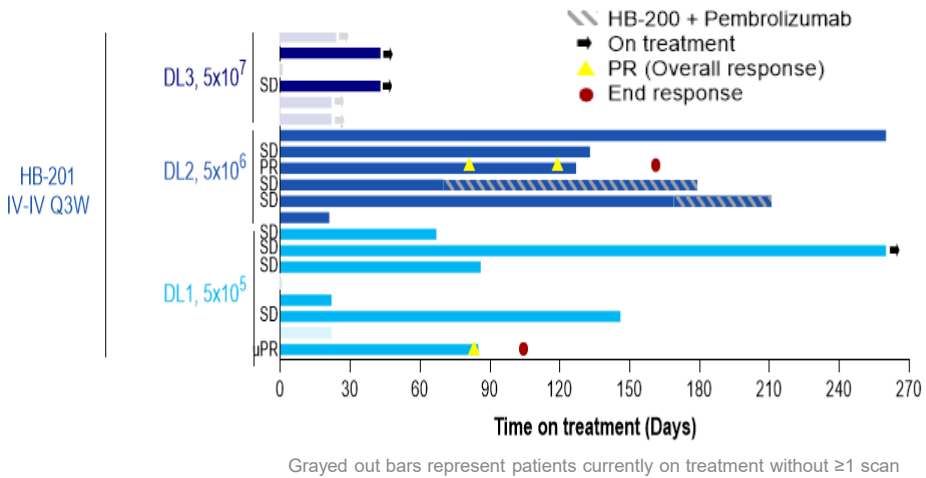
***No additional grade* ≥3 AEs have been observed to date**

No deaths reported as related to study drug

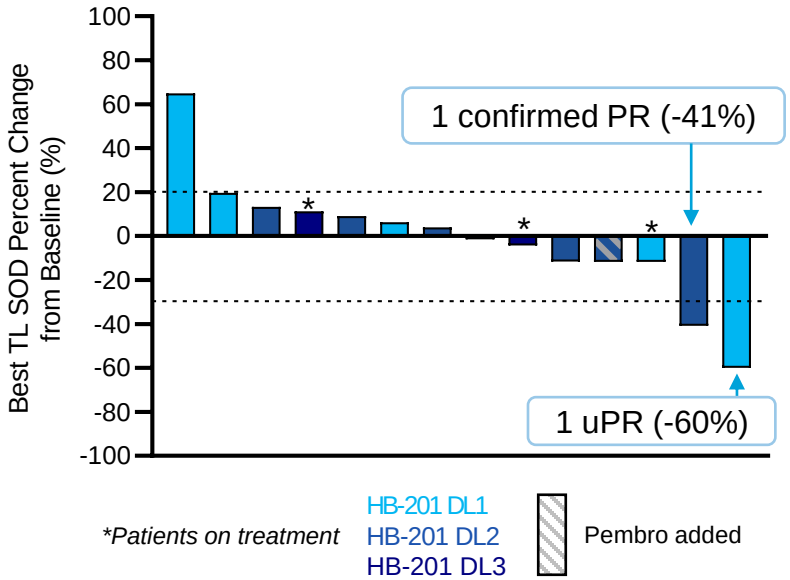
Data as of 1 Nov 2021.
Preliminary Data: Includes unmonitored and unverified data based on current EDC data or data provided by Investigators. Data is subject to change.

**Events of Grade 4 encephalopathy and Grade 4 AST increase have been considered dose-limiting toxicities, leading to treatment discontinuation.*

HB-201 Single Vector:
71% Disease Control Rate and 50% Tumor Shrinkage

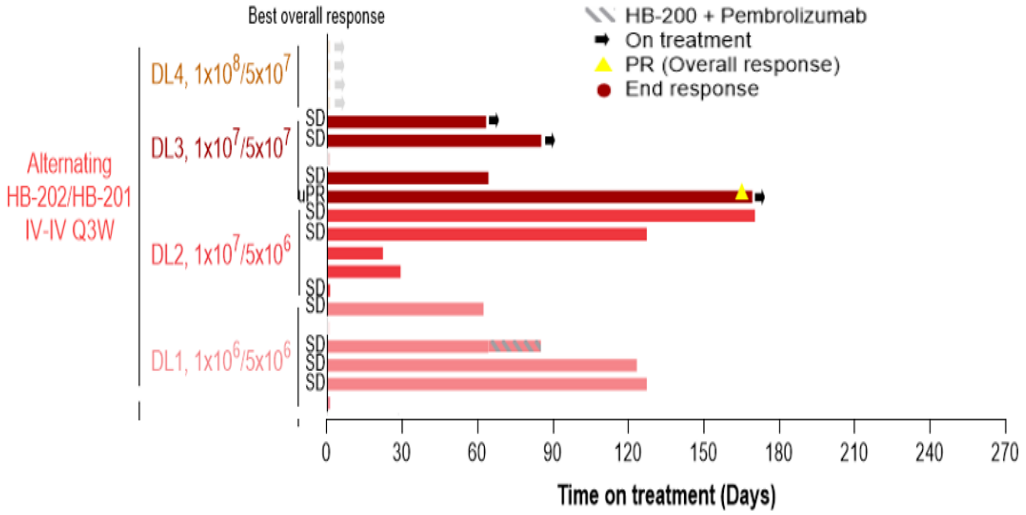


Grayed out bars represent patients currently on treatment without ≥1 scan

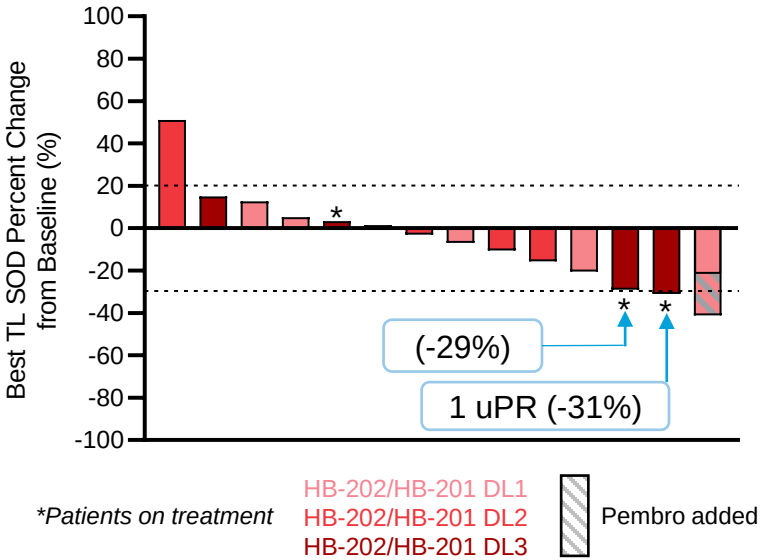


Data cut-off: 01 Nov 2021. Slide excludes patients without an evaluable anti-tumor activity scan. Time on treatment = Last treatment/death date – first dose date + 1. Best overall response indicates the patients who have a RECIST v1.1 determined stable disease or partial response.. Pembrolizumab was added to the HB-200 therapy in 3 patients by investigators. Back slashes represents time on pembrolizumab plus HB-200 therapy. Unconfirmed PR patient with 60% decrease was lymph node <1cm and therefore an unconfirmed complete response of target lesion. DL, dose level; IV, intravenous; PR, partial response; Q3W, every 3 weeks; SD, stable disease; SOD, sum of diameters; TL, target lesion; uPR, unconfirmed partial response.

HB-202/HB-201 Alternating Vector: 78% Disease Control Rate and 57% Tumor Shrinkage



Grayed out bars represent patients currently on treatment without ≥1 scan



Data cut-off: 01 Nov 2021. Slide excludes patients without an evaluable anti-tumor activity scan. Time on treatment = Last treatment/death date – first dose date + 1. Best overall response indicates the patients who have a RECIST v1.1 determined stable disease or partial response. Grayed out bars on the swimmers' plot represent patients currently on treatment without ≥1 scan. Pembrolizumab was added to the HB-200 therapy in 3 patients by investigators. Back slashes represent time on pembrolizumab plus HB-200 therapy. DL, dose level; IV, intravenous; PR, partial response; Q3W, every 3 weeks; SD, stable disease; SOD, sum of diameters; TL, target lesion; uPR, unconfirmed partial response.

HB-200 Demonstrates Promising Activity (DCR of 75%, PFS of 3.45 Months[1]) in Context of Historical 2L+ Data

	Phase 1 Patients: Median of 3 Prior Lines			L2+ Patients
	HB-201 IV DL1-DL3 Q3W	HB-202/HB-201 IV DL1-DL3 Q3W	HB-200 Blended	Nivolumab^ Pembrolizumab^ (HPV+)
N, evaluable (≥1 scan)	14	14	28	
Median time on treatment (days)	107	75		
ORR, n (%)	**2 (14.3%)**	**1 (7.1%)**	**3 (10.7%)**	**13%[2], 18%[3] (HPV+: 16%[2], 24%[3])**
PR, n (%)*	2 (14.3%)	1 (7.1%)		
SD, n (%)	8 (57.1%)	10 (71.4%)		
PD, n (%)	4 (28.6%)	3 (21.4%)		
DCR, n (%)	10 **(71.4%)**	11 **(78.6%)**	21 **(75%)**	**35%[3] (HPV+: 40%[2])**
PFS, median (mo)			**3.45**	**2.0[2]**

75% DCR is a very encouraging response in a later line Phase 1 population

[1]As of 01 Nov 2021.

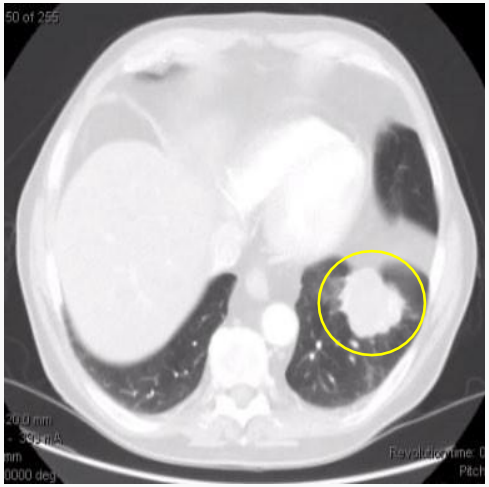
*Evaluable patients are those who had at least one evaluable anti-tumor activity scan. *PR include 1 confirmed PR and 2 unconfirmed PRs.*

^Historical, not head-to-head data comparisons. [2]Ferris et al, NEJM 2016; 375: 1856-1867; [3]Mehra R et al. British J of Cancer. 2018; 119:153-159.

Data cut-off: 01 Nov 2021. Some data added post data cut-off date due to missing/incorrect data entry on EDC as of the data transfer date. DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; SD, stable disease.

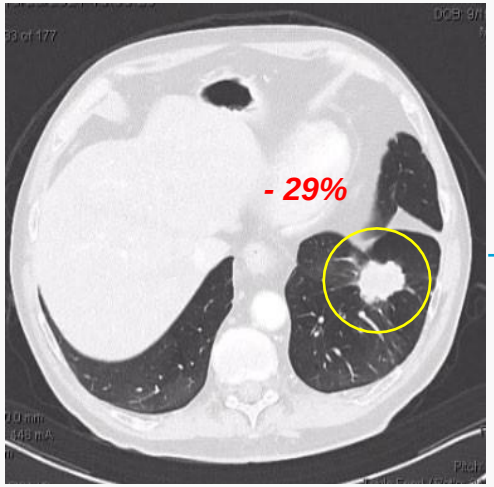
Metastatic HNSCC Patient On HB-202/HB-201 Dose Level 3 Demonstrates Strong Tumor Control Response After Progression on Pembro

- 75-year-old male diagnosed in 2012 with Stage III HPV16+ HNSCC
- Prior therapies:
  - carbo/taxol+RT; 2016 lung metastases
  - 2L pembro for 2 months with progressive disease
  - 3L FU/carbo/cetuximab for 4 months with progressive disease
  - 4L pembrolizumab+CCR4i with prolonged stable disease for 19 months, followed by progression
- Entered HB-200 study 2 months after progression on pembro/CCR4i



Baseline CT scan

Near PR



First scan after HB-202/HB-201 treatment

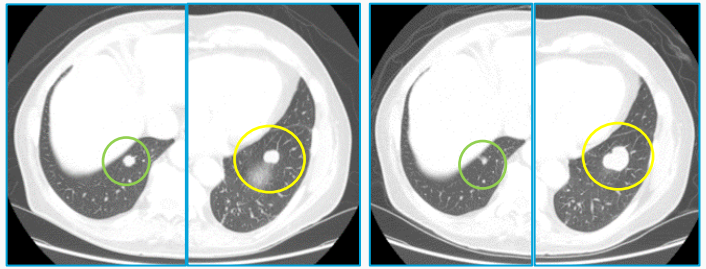
Patient remains on trial

2/3/4L, line of treatment; PR, partial response; RT, radiation therapy.

Metastatic HNSCC Patient On HB-202/HB-201 Dose Level 3 Demonstrates Strong Tumor Control Response After Progression on Pembro

- 65-year-old male diagnosed with Stage III oropharynx/ larynx cancer in 2019
- Prior therapies
  - Definitive chemo/radio-therapy
  - 2020 bilateral lung metastases
  - PD-L1 CPS<1

Dec. 2020:
Metastatic 1L Pembrolizumab + TKI started

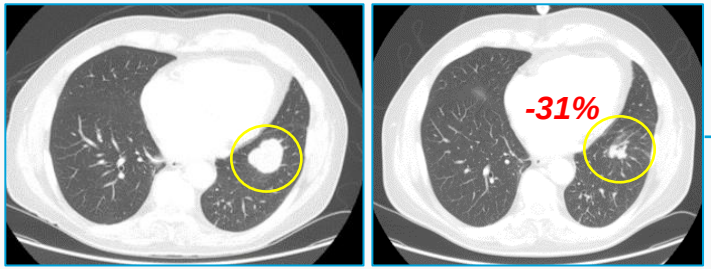


Prior to Starting 1L Pembrolizumab+TKI | **Confirmed Progression**

Mar. 2021:
Pembrolizumab + TKI confirmed progression.
One lesion responded; one lesion progressed

HB-202/HB-201 monotherapy started: “Refractory” lesion resolving, 31% uPR and ongoing

Apr. 2021:
Patient starts HB-202/HB-201 monotherapy



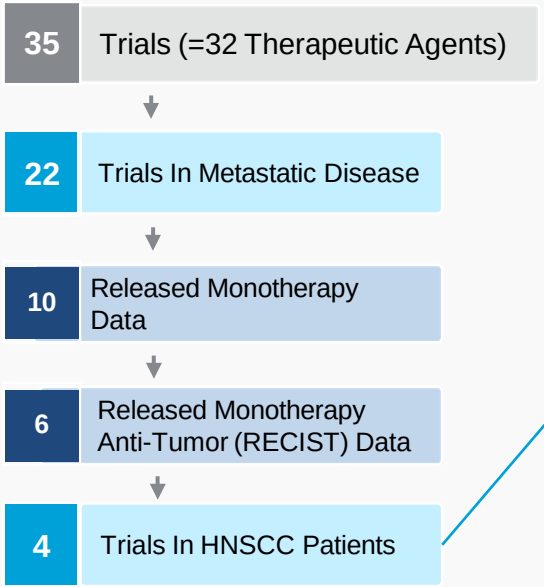
Baseline CT | **Third Scan**

Patient remains on trial

1L, line of treatment; POD, progression of disease; uPR, unconfirmed partial response.

Measured Against Other Monotherapy Data Disclosed for HPV+ Cancers[1] Hookipa Leads on Disease Control Rate, Strong ORR

- HOOKIPA: Similar anti-tumor activity to TCRs in HPV+ HNSCC
- Most companies targeting HPV+ indications (32 agents with 35 trial read-outs) released limited-to-no Phase 1 metastatic monotherapy dose escalation data other than T cell metrics and safety before advancing to combinations



Technology	N	PRs	ORR	DCR
HOOKIPA HB-200	**28**	**3**	**10.7%**	**75%**
TCR A	8	3	38%	63%
TCR B	12	2	17%	58%
Complex Antibody/ Protein Biologic	38	1	3%	33%
Cell-based Therapy	10			40%

[1]Data sets derived from competitor data press releases and medical conference posters. DCR, disease control rate; HNSCC, head and neck squamous cell carcinoma; PR, partial response; ORR, overall response rate; TCR, T cell receptor.

HB-200 Phase 1/2: Vast Potential to Improve Patient Outcome in 1st Line and 2nd Line HPV16+ HNSCC Patients in Combination with Pembrolizumab

Phase 1 part (monotherapy)

Strong tumor-specific T cell responses and promising early signs of clinical efficacy

Phase 2 part[1] (combinations)

1st line HPV16+ HNSCC	Current SOC efficacy [2]:
HB-200 + Pembrolizumab (CPS≥20)	23% ORR 14.9mo OS 3.4mo PFS
HB-200 + Pembrolizumab + platinum+5FU (CPS ≥1<20)	

2nd line HPV16+ HNSCC	Current SOC efficacy[3]:
HB-200 + Pembrolizumab	15% ORR 8.0mo OS 2.1mo PFS
HB-200 + platinum	

2022 data

Path to registration

Randomized Phase 2

MERCK Supply agreement

Confirmatory Phase 2b

Potential fast-track for patients who have failed prior lines of treatment

[1]The Phase 1 part is ongoing for the HB-202/201 cohorts. The decision whether to progress the program in the 3rd line/post-CPI setting as a monotherapy will be determined in early 2022; [2]Pembro alone 1st line, Burtness, et al. Lancet 2019 Nov 23; 394(10212):1915-28; Rischin ASCO 2019; [3]Pembro alone 2nd line, Bauml JCO 2017.

Earlier I/O Programs

Arenavirus Platform Can Target a Broad Range of Antigen Types

Plug & Play system to express variety of known and novel epitopes

- Off-the-shelf: avoids patient-specific / ex vivo manipulation
- Able to express full length antigens, avoiding MHC restrictions

Oncoviral Antigens

- **HPV**
- EBV
- HBV
- HTLV

Tumor Associated Self-Antigens

PAP, PSA, PSMA, AFP, Tyrosinase, Melan-A, CEA, MART-1, HER2, WT1, MUC1, MAGE, GAGE, NY-ESO-1, …

Neoantigens

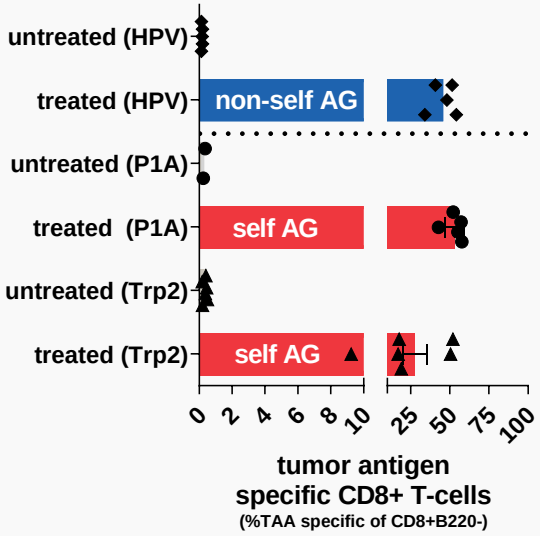
- Shared driver mutations: **KRas,** p53, BRAF, PIK3CA…

MHC, major histocompatibility complex.

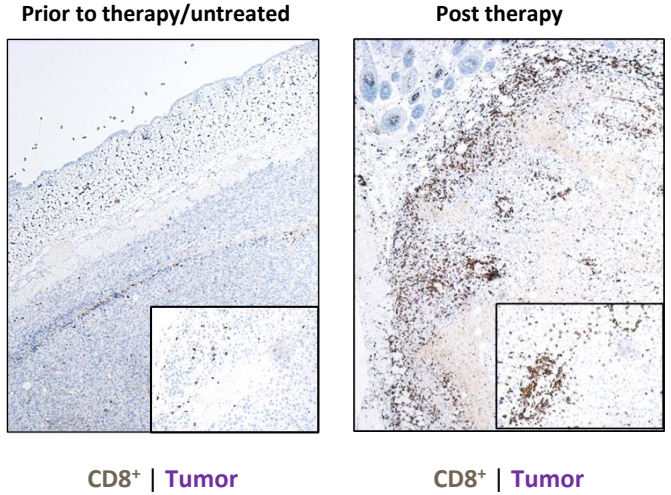
Preclinical Evidence Suggests that Arenavirus Vector Technology Works Against Self-Antigen Driven Cancers

Induction of self-antigen specific CD8+ T cell responses and increase in TILs is comparable to activity demonstrated against non-self antigen

Strong T cell generation in self-antigen models



Leading to tumor infiltration



Advancing Pre-clinical Programs Targeting Self-Antigens and Mutant Antigens to Address Sizeable Clinical Cancer Populations

Preclinical Proof of Concept

- ✓ Ability to break self-tolerance[1]
- ✓ Induction of >50% tumor self antigen specific $CD8^+$ T cells and elevation of TILs[2]
- ✓ Induction of high $CD8^+$ T cell levels against mutated epitopes[3]

Targeted Indications

Tumor self-antigens

- **HB-300: Prostate Cancer** targeting PAP, PSA & PSMA

Mutant antigens

- **HB-700: Colorectal, Pancreatic, Lung Cancer** targeting mutated KRAS

[1]Preclinical proof of concept with multiple self antigens such as Trp-2, gp70, P1A, GP100. Ring S et al Nature Communications volume 12, Article number: 4734 (2021), Bonilla WV Cell Reports Medicine2, 100209, March 16, 2021; Hookipa, data on file.

[2]Bonilla WV et al Cell Reports Medicine2, 100209, March 16, 2021.

[3]Preclinical proof of concept by expressing an isolated mutated epitope derived from the protein Adpgk (i.e. mutated neo-antigen) described by Yadav M, et al. Nature. 2014;515(7528):572-576; Hookipa, data on file.

Partnering Upside in Infectious Diseases

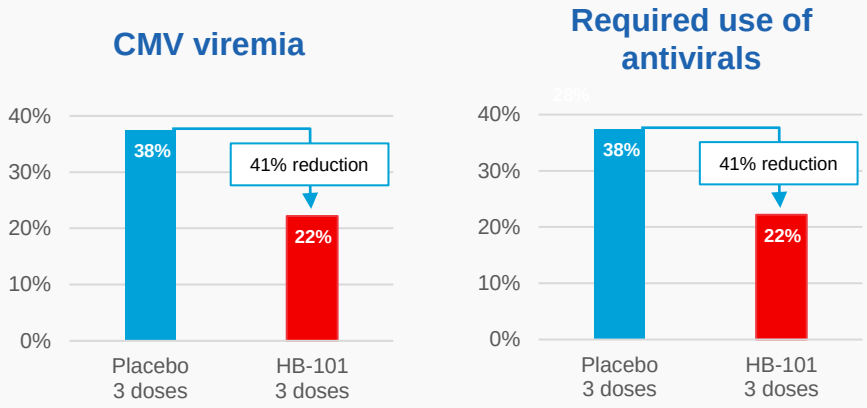
HB-101: Arenavirus-based Prophylactic Vaccine Candidate Reduces CMV Viremia and Use of Anti-virals

Development post Phase 2 trial follow-up only in partnership

CMV Unmet Medical Need

- **Key Prophylactic Indications:**
  - **Solid Organ Transplant (SOT) Recipients**
    20% - 30% or ~25,000 SOT recipients develop CMV disease annually worldwide[1,2]
  - **Neonates (Congenital)**
    20,000 - 30,000 birth defects due to CMV infection during pregnancy in the U.S. annually (0.5%-1.0% of births); higher incidence in low-income nations[3]
- **No licensed CMV vaccine exists**

Phase 2 Interim: Secondary efficacy endpoints



Reduction in viremia and required use of antivirals for patients who received 3 doses of HB-101 compared to placebo

[1]https://www.who.int/transplantation/gkt/statistics/en/, Accessed January 2021. [2]Ramanan P, et al. Infect Chemother. 2013;45:260-271.
[3]https://www.who.int/immunization/research/meetings_workshops/PDVAC_2017_CMV_Plotkin.pdf?ua=1, Accessed January 2021.

HIV News: HOOKIPA to Progress Program Through Phase 1b Study; Gilead Funding $54M in Initiation, Milestones and Equity at a Market Premium

GILEAD **Collaboration**

HIV Cure
Human Immunodeficiency Virus

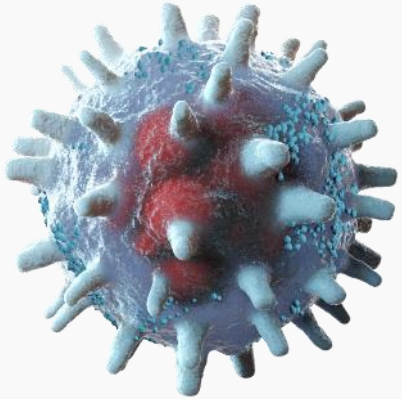
- Agreement amended on February 15, 2022
  - Hookipa responsible for Phase 1b clinical trial
  - Gilead retains exclusive option post Phase 1b
- Terms
  - $19m in a non-refundable payment in Q1 2022
  - Equity at a premium to market
    - $5m in Q1 2022
    - $30m any time before 12/2023
  - $240 million development + commercialization milestones
  - Mid-single digit to low double-digit % royalties

HBV Cure
Hepatitis B Virus

- Hookipa's responsibilities
  - Vector design
  - Manufacturing and supply of clinical material
- Terms
  - $190m development and commercialization milestones
  - High-single digit to mid-teen % royalties
  - All costs borne by Gilead, including full Hookipa R&D cost

Summary & Outlook

Investment Highlights



1. Off-the-shelf *in vivo* T cell technology

2. Robust PoC of T cell mechanism

3. Monotherapy anti-tumor activity in late stage HPV16^{+} HNSCC patients
   - >50% patients respond with tumor shrinkage
   - Disease control rate (DCR) of 75%
   - HB-200 post-CPI shows mPFS longer than CPI 2nd+L[1]

4. HB-200 in combination with pembrolizumab is safe, and may have additive or synergistic efficacy

5. *Pro forma* cash position[2]: $157 million, including proceeds from follow-on

[1]Historical, not head-to-head data comparisons. [2]Dec. 31, 2021 cash position $67m + Feb. 15, 2022 Gilead cash $20m + Mar. 1, 2022 follow-on offering $70m (net proceeds).

Rich Near Term Value Inflection Points

HB-200

Phase 1 HPV16^{+} Monotherapy Data: Mid 2022

Phase 2 HPV16^{+} HNSCC CPI Combination

- **1st Line Initial Data: 2H 2022**
- **2nd Line Initial Data: 2H 2022**
- **Randomized Phase 2 in 1st Line Start with Merck & Co.: 1H 2023** (Fast Track Designation)

HB-300

Prostate Cancer IND: 3Q 2022

HBV & HIV

GILEAD **Hepatitis B IND: 2022**

GILEAD **HIV IND: 2023**


HOOKIPA
PHARMA