HOOKIPA PHARMA

Supercharging Immunotherapy

May 2023

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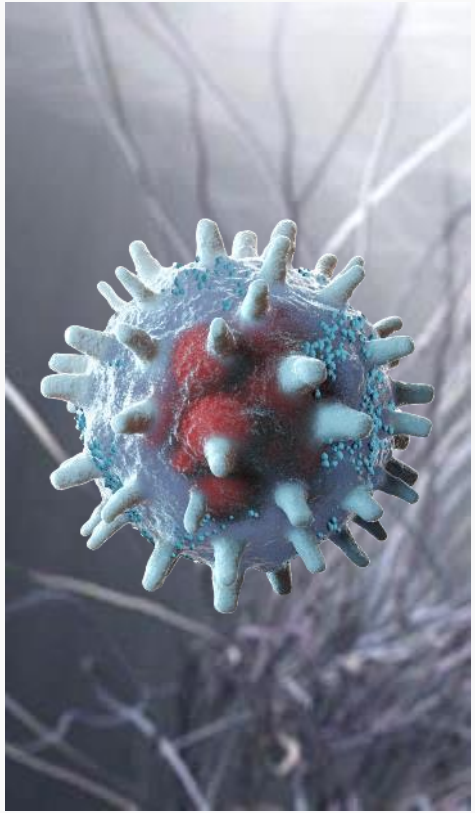
Directing the Power of the Immune System Against Serious Diseases



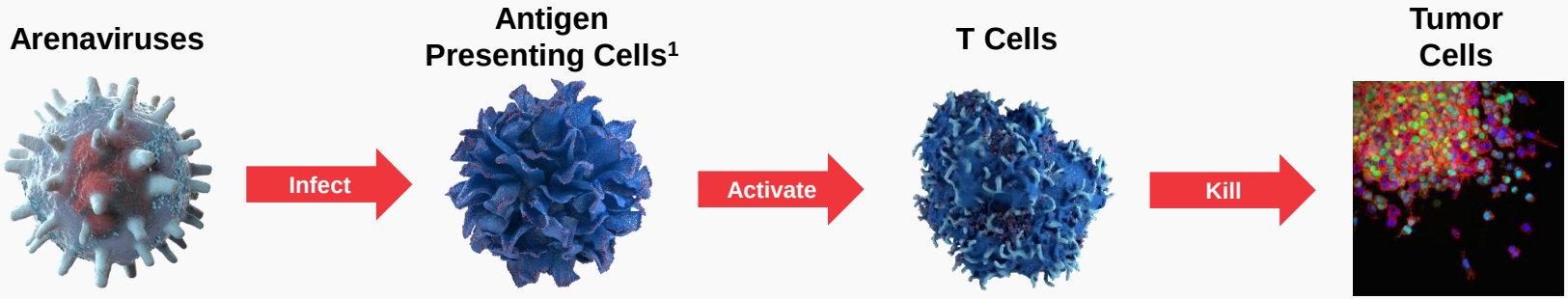
Vision A world in which cancers are chronically managed or eradicated

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

Strategy Targeted T cell induction and amplification as a backbone to immunotherapies lacking T cells at the tumor to be effective

Arenaviruses Naturally Target Immune Cells to Activate T Cells, Using This Mechanism to Direct T Cells to Specifically Kill Malignant Cells

Arenavirus Vector Mode of Action

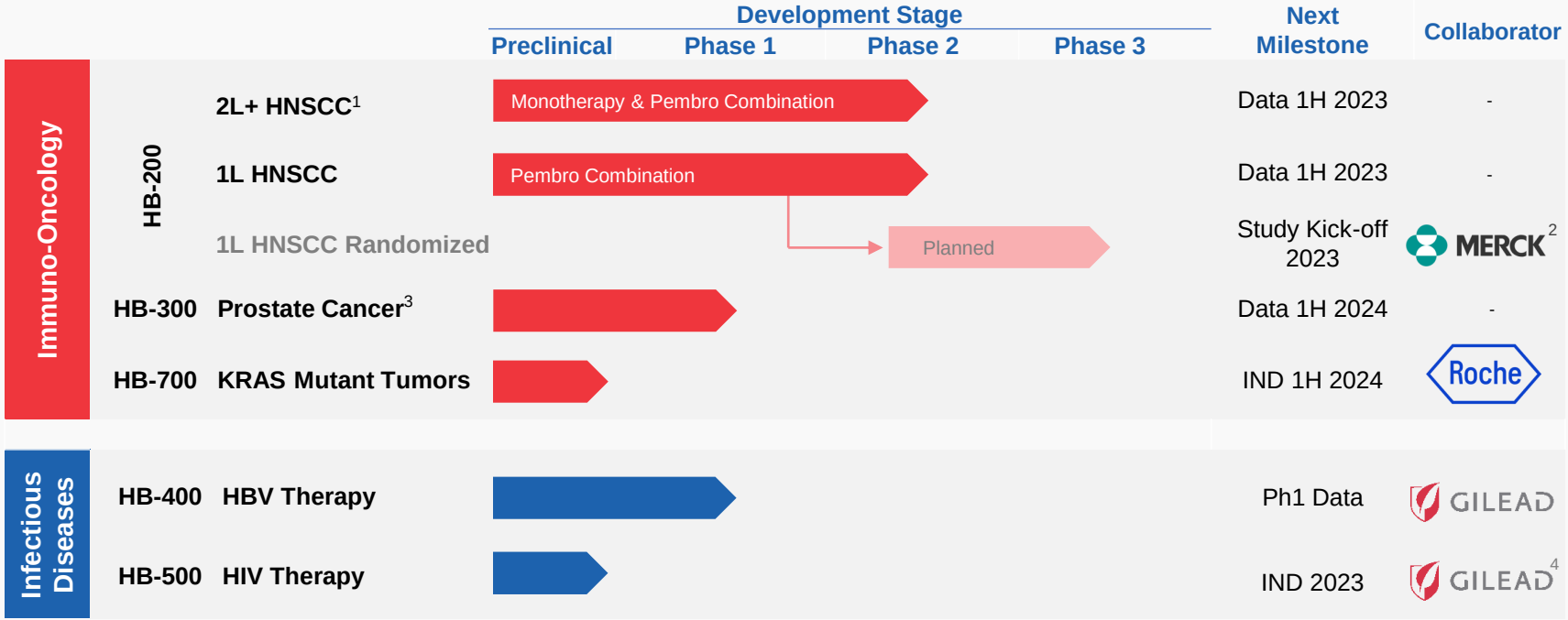


Potent characteristics of arenavirus

- In vivo (IV administration)
- Off-the-shelf
- Repeat administration
- Well tolerated, safely combinable with other IO agents

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

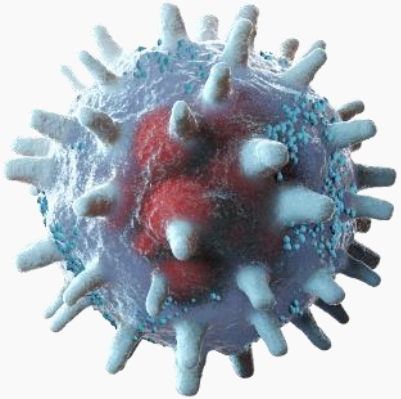
Diverse Oncology Pipeline, Upside from Partnered Infectious Disease Programs



HNSCC, Head and Neck Squamous Cell Carcinoma; 1L/2L+, line of therapy; HIV, Human Immunodeficiency Virus; HBV, Hepatitis B Virus

[1]ClinicalTrials.gov: NCT04180215; [2]Clinical supply agreement for pembrolizumab. Phase 2 1L randomized trial to be informed by non-randomized ongoing Phase 2 1L data; [3]ClinicalTrials.gov: NCT 05553639; [4]HIV Therapy: Upon completion of Phase 1b study, Gilead has exclusive right for further development.

HB-200 Monotherapy Activity in Recurrent/Metastatic HPV16^{+} HNSCC Patients Progressed on Standard of Care



- **Monotherapy results**
  - Phase 1 anti-tumor activity
  - Strong translational data
  - Favorable safety & tolerability profile

- **Phase 2 ongoing for HB-200 in combination with pembrolizumab**
  - FDA Fast Track Designation
  - Clinical supply agreement with Merck & Co. for pembrolizumab

HB-200 Program in HPV16^{+} Cancers

HB-200 Market
Large Unmet Medical Need to Treat HPV16⁺ Head & Neck Cancers

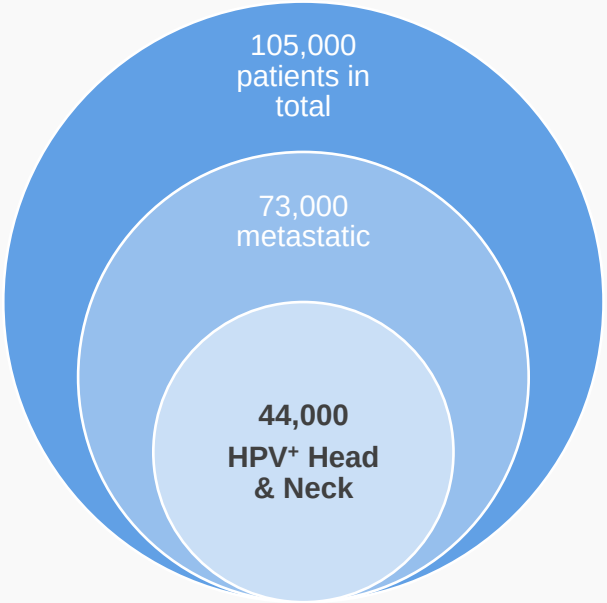
The HPV⁺ Cancer Challenge

- 60% of all head & neck cancers (HNSCC) are HPV⁺
- Poor outcomes with SOC (CPI), e.g. Pembrolizumab:

Endpoint	1L	2L
ORR	19 - 23%	16%
mPFS (months)	3.2	2.0 - 2.1
mOS (months)	12.3	7.5 - 8.4

- >80% of patients are refractory to SOC/CPI
- HB-200 goal: ORR of SOC x 2

Growing HPV⁺ Cancer Market
(Expected 2030 Patient Incidence)



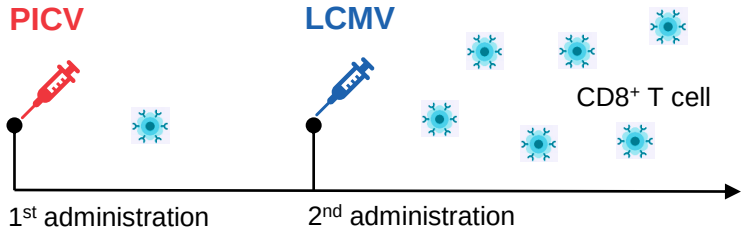
SOC, standard of care; HNSCC, head and neck squamous cell carcinoma. https://gco.iarc.fr/tomorrow/en/dataviz/tables; https://seer.cancer.gov/statfacts/html/oralcav.html; https://www.cdc.gov/cancer/hpv/statistics/cases.htm; https://gynoncrp.biomedcentral.com/articles/10.1186/s40661-017-0047-8; https://pubmed.ncbi.nlm.nih.gov/22966247/; 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; https://www.keytrudahcp.com/efficacy/hnscc-first-line-monotherapy#clinical-findings-from-keynote-048

Novel Arenavirus-based Product Candidate HB-200 Has Ideal Profile to Treat HPV16+ Head & Neck Squamous Cell Carcinoma

HB-200's Potential Solution

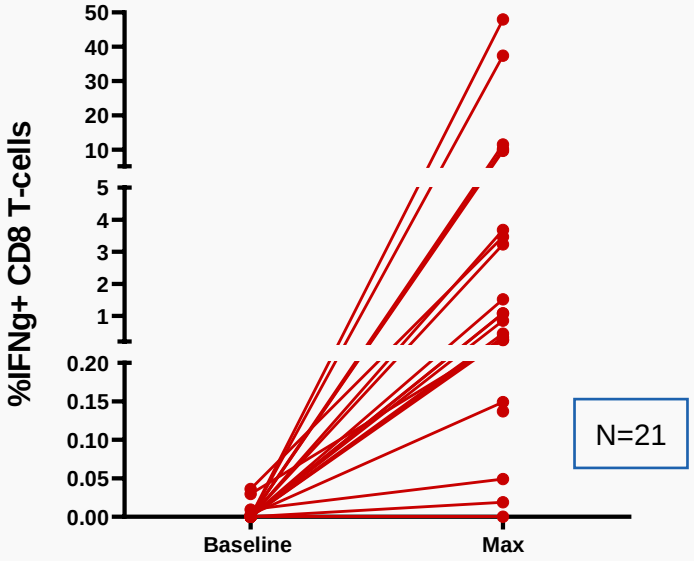
- Intravenous delivery (i.v.)
- 2 different replicating arenaviral vectors encoding the same non-oncogenic HPV16+ E6/E7 fusion antigens
  - HB-201 = Lymphocytic Choriomeningitis Virus (LCMV) carrying E6/E7
  - HB-202 = Pichinde Virus (PICV) carrying E6/E7
- Phase 2 expansion cohorts ongoing

Alternating 2-Vector Therapy



Alternating 2-vector therapy focuses amplification on the target antigen since PICV and LCMV have different backbones

HOOKIPA's Arenaviral Platform Ideally Suited to Induce Strong Specific CD8+ T Cell Responses



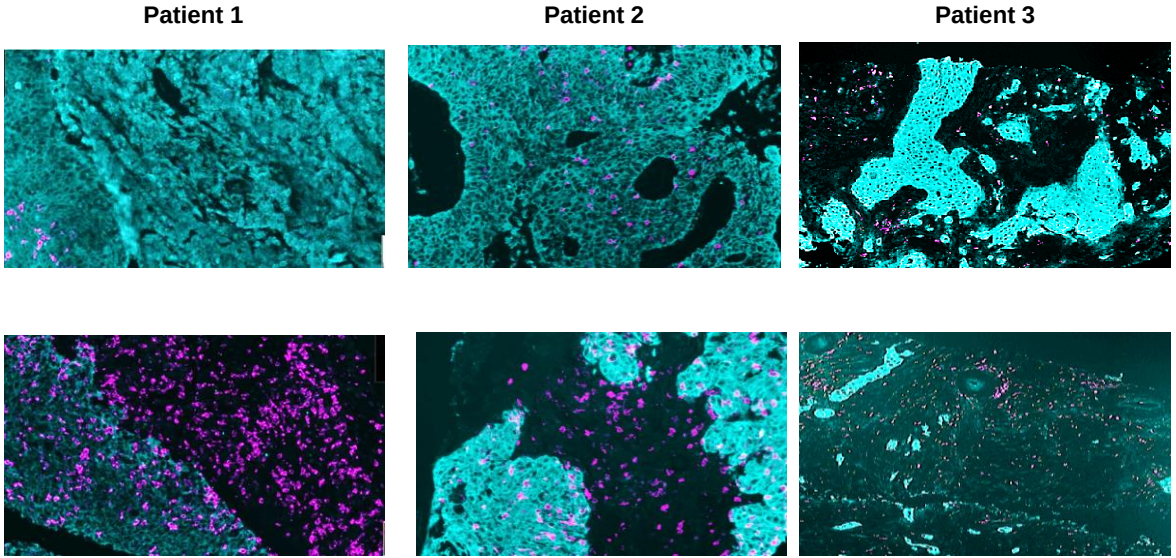
Direct measurement without prior in vitro expansion of cells; majority of patients show peak responses 2-3 weeks post first administration.

Fast and durable induction of active tumor-specific T cell responses in nearly all patients:

- ~80% of patients have measurable tumor specific T cell response after first administration
- ~90% of patients have measurable T cell response after second, third and fourth administrations
- In 57% of patients HB-202/201 breaks the above 1% threshold of tumor specific systemic CD8+ T cells

Phase 1: HB-200 CD8+ T Cells Traffic Tumors

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



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).

Phase 1 HB-200 Tolerability Profile: Ideal Candidate for Combination Therapy

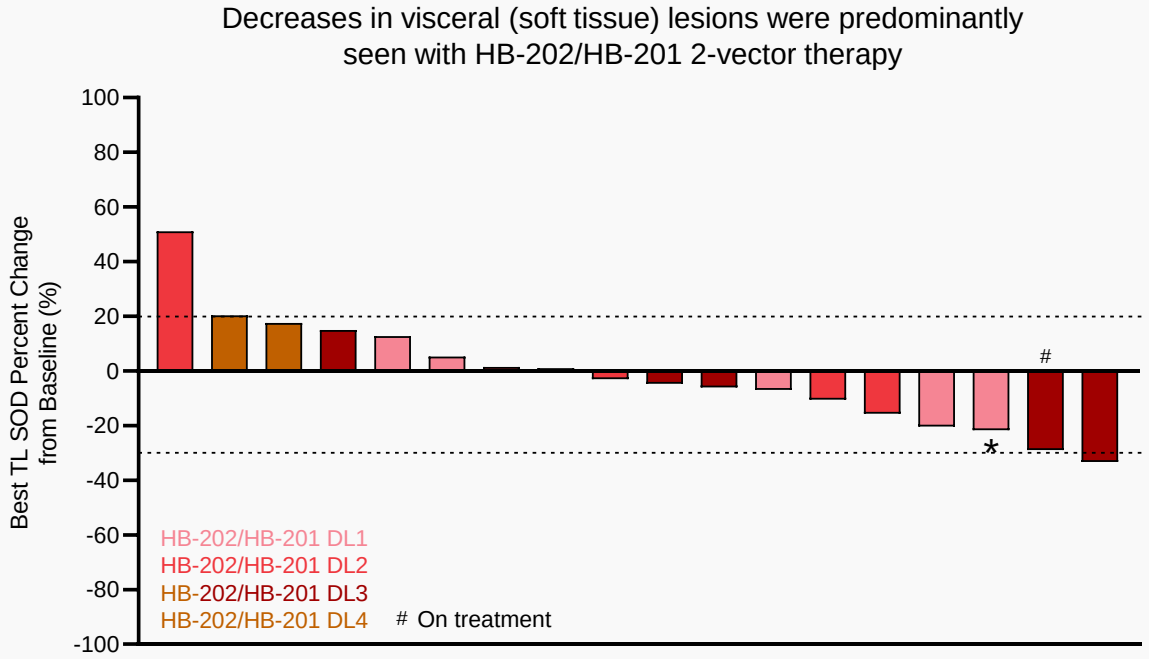
All Groups, All Cohorts (N=68)	Treatment Related AEs	All AEs
Any event	HB-201: 43 (63%) HB-202: 21 (75%)	67 (99%)
Grade ≥3	6 (9%)	29 (43%)
Serious	2 (3%)	17 (25%)
Leading to dose reduction	1 (2%)	1 (2%)
Leading to discontinuation	2 (3%)	6 (9%)
Deaths	0	3 (4%)

Data as of 31 Mar 2022. Preliminary Data: Includes unmonitored and unverified data based on current EDC data or data provided by Investigators. Data is subject to change.

- Median 3 prior lines of treatment (range 1-11)
- Most common AE: flu-like symptoms, lasting 24-72 hours; no recurrence following additional administrations
- No treatment-related deaths
- 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)

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

Phase 1 HB-200 Anti-Tumor Activity: 56% of Target Lesion Shrinkage



Data cut-off: March 31, 2022. Best overall response indicates the patients who have a RECIST v1.1 determined stable disease or partial response. DL, dose level; TL, target lesion; SOD; sum of diameter.

**Pembrolizumab was added to the HB-200 therapy upon disease progression at the investigators' discretion. Data shown here excludes changes after the addition of pembrolizumab.*

Phase 1 80% DCR in 2-Vector RP2D Group Is Competitive in a Post-SOC Population When Compared to Earlier Line CPIs

	HB-200 Phase 1 Patients: Median 3 Prior Lines of Therapy		Earlier Line Checkpoint Inhibitors: L2+ Patients	
	All HNSCC Q3W IV Patients	HB-202/HB-201 @RP2D	Nivolumab[1] (HPV+)	Pembrolizumab[1] (HPV+)
N, evaluable (≥1 scan)	**34**	**5**		
ORR, n (%)	**3 (8.8%)**	**1 (20%)**	**13%[2]** (HPV+: 16%[2])	**18%[3]** (HPV+: 24%[3])
DCR, n (%)	**22 (65%)**	**4 (80%)**	**HPV+: 40%[2]**	**31%[3]** (HPV+: 32%[3])
PFS, median (mo)	**2.56**	**Unreached**	**2.0[2]**	

Data cut-off: March 31, 2022.

DCR, disease control rate; RP2D, recommended Phase 2 dose; SOC, standard of care; L2+, line of therapy, ORR, objective response rate; PFS, progression-free survival.

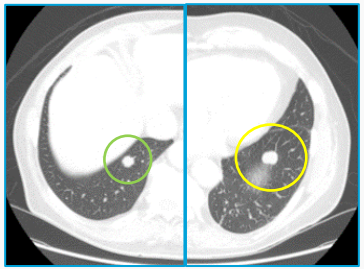
[1]Historical, not head-to-head data comparisons; [2]Ferris et al, NEJM 2016; 375: 1856-1867; [3]Mehra R et al. British J of Cancer. 2018; 119:153-159.

HB-200 Metastatic HNSCC Patient on 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
- 3 prior therapies to HB-202/HB-201

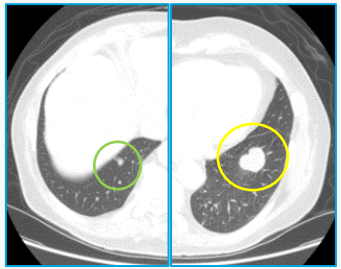
Prior to HB-200

Prior to starting 1L Pembrolizumab+TKI



Dec. 2020:
Metastatic 1L Pembrolizumab + TKI started

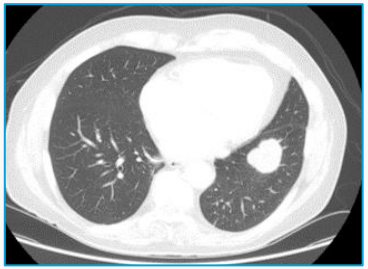
Confirmed progression



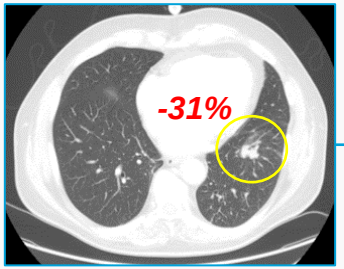
Mar. 2021:
Pembrolizumab + TKI confirmed progression. One lesion responded; one lesion progressed

HB-200 Treatment

HB-202/HB-201 alone therapy: "Refractory" lesion responds



Apr. 2021: **Baseline CT**
Patient starts HB-202/ HB-201 vector-only therapy



Dec. 2021:
4th scan
Confirmed PR -31%

After 5th scan in Jan. 2022 (-33%), patient came off study to pursue resection of lung metastasis in Mar. 2022

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

HB-200 Phase 2 Clinical Development Strategy in 1st and 2nd Line HPV16+ HNSCC Patients

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

HB-200 + Pembrolizumab

Current SOC efficacy[2]:

19-23% ORR
47-53% DCR

2nd line HPV16+ HNSCC

HB-200 + Pembrolizumab

(other potential combinations under discussion)

Current SOC efficacy[3]:

15% ORR

1H 2023 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]Phase 2 part of Phase1/2 trial; monotherapy part is also ongoing for the HB-202/201 cohorts and a decision to progress the program in the post SOC setting as a monotherapy will be determined in 1H2023; [2]Pembro alone 1st line, Burtness B et al. Lancet 2019; [3]Pembro alone 2nd line, Cohen et al. Lancet 2019.

Earlier I/O Programs

Arenavirus Platform Can Target a Broad Range of Antigen Types

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

- Drug Master File cleared by FDA in July 2022 -

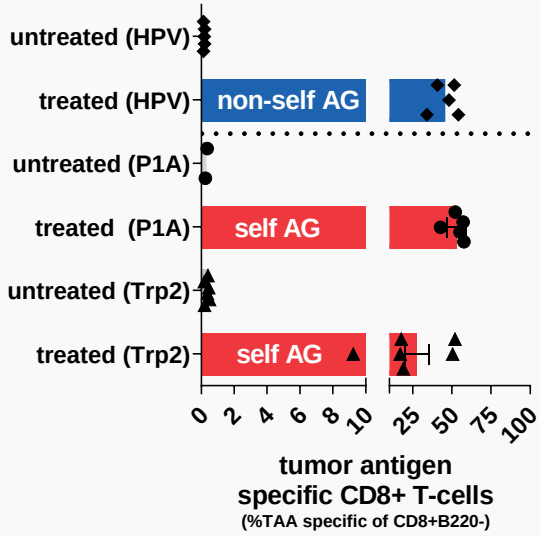
Oncoviral Antigens	Tumor Associated Self-Antigens	Neoantigens (Shared Driver Mutations)
HPV: Human papillomavirus **HBV**: Hepatitis B virus EBV: Epstein–Barr virus HTLV: Human T-lymphotropic virus 1	**PAP, PSA, PSMA**: Prostate Tyrosinase, Melan-A CEA MART-1, HER2, WT1, MUC1, MAGE, GAGE, NY-ESO-1, …	**KRAS**: Pancreatic, colorectal, lung cancers p53: Breast cancer, bone and soft tissue sarcomas, brain tumors and adrenocortical carcinomas BRAF: Melanoma, colorectal carcinoma, NSCLC PIK3CA: Breast, colon, endometrial cancers

Bolded *antigens represent targets under development internally or through partnership/collaboration*

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



HB-300: Unmet Medical Need in Metastatic Castrate-Resistant Prostate Cancer

The Prostate Cancer Challenge

- Very common cancer in men
- Disease progression ultimately leads to metastatic Castrate-Resistant Prostate Cancer (mCRPC)
- High unmet need with standard of care:
  - Androgen Receptor inhibitor (e.g. abiraterone, enzalutamide) +/- Androgen Deprivation Therapy or docetaxel regimens: rPFS 16m+ in 1L setting
  - Therapy is switched after progression on initial therapy for mCRPC

HB-300's Potential Solution

- Replicating arenaviral vectors each encoding prostate-specific antigens PSA and PAP
  - HB-301 = Lymphocytic Choriomeningitis Virus (LCMV)
  - HB-302 = Pichinde Virus (PICV)
- Alternating 2-vector HB-302/HB-301 Ph1 Enrolling
  - Regimen: Q3W for initial 5 administrations, then Q6W
  - Intravenous (IV) delivery
  - Minimal number of dose levels based on HB-200 experience: 2
  - Number of patients: ~35
  - Phase 1 primary endpoints:
    - Safety
    - Recommended Phase 2 Dose

NCCN Guidelines for Prostate Cancer Version 2.2022
CancerMPact Treatment Architecture EU, Prostate Cancer

Partnered Programs

HB-700: One Product For Three Cancers - Pancreatic, Colorectal, and Lung by Targeting Five KRAS Mutations

KRAS - Large Unmet Medical Need

KRAS

- KRAS is a gene that acts as an on/off switch for cell growth
- KRAS mutations are among the most common mutations that cause cancer[1]

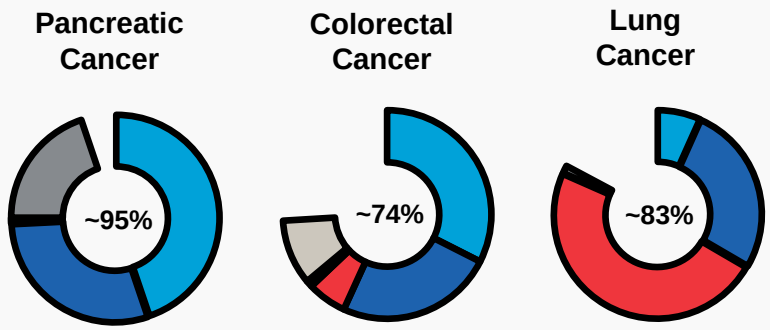
Prevalence

- ≥ 80% in pancreatic[2], ~30% in colorectal[2], 15-20% in lung[2]; also prevalent in many other cancer types

Market Potential

- 2021: ≥ 200,000 patients in the US and EU who could have benefited in just the pancreatic, colorectal, and lung indications[3]

Targeting Five Most Relevant Mutations



Analysis provided by Catenion.

[1]*Nature Reviews Clini Onc (2022) 19 637-655;* [2]*Cancer Res (2020) 80 (14); 2969-2974; COSMIC database;* [3]*Internally sourced reports.*

HB-700 Roche Collaboration: $25m Upfront, Up to ~$930m in Future Milestones And Up To Mid-teen Royalties

License for HB-700 KRAS program and option for a second undisclosed arenaviral immunotherapy

Development Path & Funding

Preclinical

- HOOKIPA responsible for all preclinical development
- Funded by upfront and milestone payments

Phase 1b

- HOOKIPA responsible for Phase 1b trial
- 50/50 cost-sharing
- Funded by IND related milestone payments

Further development

- Roche responsible for all R&D, manufacturing, commercialization
- Roche funds all post phase 1b

Financial Terms

Total of $955m in upfront and milestones

HB-700 KRAS mutant therapy

- R&D and commercial milestones
- Tiered royalties: high single-digit to mid-teens %

Undisclosed novel arenaviral therapy

- $15m at option exercise
- R&D and commercial milestones
- Tiered royalties: high single-digit to mid-teens %

HBV: Gilead on Track to Dose First Subject in 2023
HIV: HOOKIPA to Progress Program Through Phase 1b Study; IND in 2023

GILEAD **Collaboration**

HBV Cure
Hepatitis B Virus

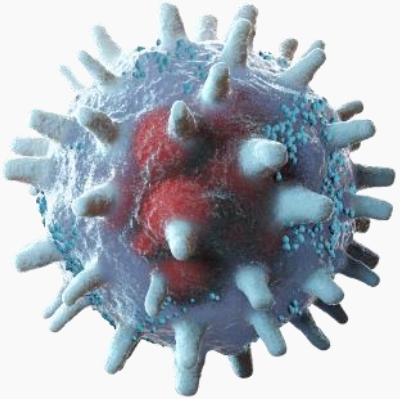
- Hookipa's responsibilities
  - Vector design
  - Manufacturing and supply of clinical material
- Terms
  - $190m development and commercialization milestones
  - High-single digit to mid-teen % royalties
  - All costs borne by Gilead, including full Hookipa R&D cost
- **FPI dosed in Q2 2023**

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
- Funding $54m to conduct Phase 1b
  - $19m in a non-refundable payment in Q1 2022
  - Equity at a market premium
    - $5m in Q1 2022
    - $30m any time before 12/2023
  - Substantial option exercise fee after Ph 1b or rights back
  - $240 million development + commercialization milestones
  - Mid-single digit to low double-digit % royalties
- IND 2023

Summary & Outlook

Investment Highlights



1. Robust PoC of Arenavirus T cell activation mechanism

2. Lead Phase 2 oncology program ‘HB-200 + pembrolizumab’ in HPV16^{+} head and neck cancer

3. 2 further clinical programs in 2023 in H1 2023
   - HB-300 prostate cancer
   - HB-400 HBV functional cure

4. Strong partnerships Roche GILEAD MERCK

5. $110.0m available cash as of 03/31/2023
   additional $30m Gilead equity facility

Rich Near Term Value Inflection Points

HB-200
HPV16+ HNSCC

HB-200 + Pembro Combination

- **Phase 2 1L Data: 1H 2023**
- **Phase 2 2L+ Data: 1H 2023**

MERCK **Randomized Phase 2 1L start: 2023**
(Fast Track Designation; 100% rights with Hookipa)

Post-SOC HB-200 Alone Phase 2 Data: 1H 2023

HB-300

Prostate Cancer Phase 1 Initial Data: 1H 2024

HB-700

Roche **KRAS IND: 1H 2024**

HBV & HIV

GILEAD **Hepatitis B FPI: dosed in 2023**

GILEAD **HIV IND: 2023**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