Supercharging Immunotherapy

MARCH 2024

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Investment highlights

Robust proof-of-concept

Arenavirus T cell activation mechanism has potential across multiple disease areas and indications

ORR is double standard of care

42% ORR In phase 2 of the HPV16+ head and neck cancer oncology program vs historical 19% ORR for pembrolizumab alone

Focused clinical plan

Additional Phase 1/2 combination data (Q2 2024);
Pivotal Phase 2/3 trial HB-200 + pembrolizumab in 2024

Strong partnerships

GILEAD MERCK

Meaningful clinical catalysts

KRAS IND-submission (April 2024);
HIV clinical trial start (Q2 2024)

Strong cash position

$117.5m cash as of 12/31/2023

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Generating best-in-class T cell activation to drive tumor-killing

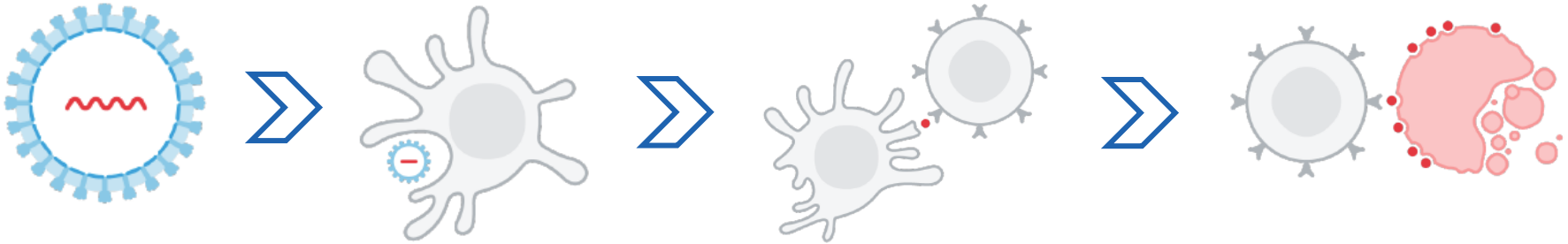
Engineered arenavirus supercharges natural action of immune system

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



Simple approach; powerful results

1. Ability to modify arenavirus with multiple target antigens for maximum immune response
2. Arenavirus has natural tropism to dendritic cells (DC); once infected, DCs are alerted to the antigen as a threat to the body
3. DCs are the immune system's primary messengers, notifying T cells to activate against the target antigen
4. Once activated, T cells circulate the body to detect and eliminate the tumor cells associated with the target antigen

Key differentiation

- Unprecedented levels of cancer-specific T cells with polyfunctionality that grows over time
- Clinical anti-tumor activity as monotherapy and in combination with checkpoint inhibitor
- Well tolerated, safe in combination with other IO agents
- Off-the-shelf drug product availability

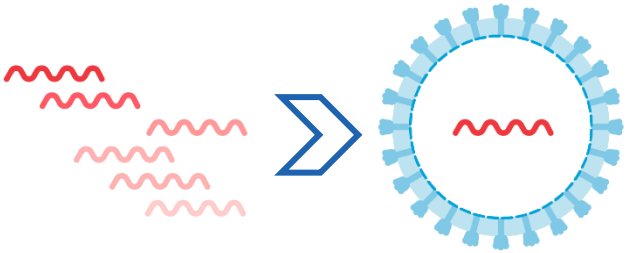
Deep pipeline of novel arenaviral therapies

The platform is scalable across disease areas and multiple antigen classes

		INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Oncoviral antigens	**HB-200**	HPV16+ HNSCC	1L Pembrolizumab Combination			Planned pivotal trial 2024 Additional Phase 2 1L data Q2 2024
Neo antigens	**HB-700**	^{mut}KRAS tumors	IND April 2024 Preclinical data Q2 2024			
Infectious disease	**HB-400**	HBV	GILEAD Phase 1 Trial (Gilead-led)			
Infectious disease	**HB-500**	HIV	GILEAD Phase 1 Trial Q2 2024			

Potential for plug & play development under drug master file

Ability to accelerate early-stage clinical development and target a broad range of antigen types in multiple disease areas



- Arenavirus platform can be the foundation for multiple target indications
- Drug master file offers the ability to accelerate development of current and future antigens

Viral Antigens	Tumor Associated Self-Antigens	Neoantigens (Shared Driver Mutations)
HPV for HPV+ cancers HIV, HBV, other infectious diseases	PAP, PSA, PSMA for prostate cancer CTA targets for solid tumors	^{mut}KRAS: Pancreatic, colorectal, lung cancers, etc.

+ Future potential for additional indications

Oncology indications	Infections disease indications
Examples: melanoma, ovarian, uterine, etc.	Potential for both therapeutic and prophylactic approaches

1 HPV16+ Oropharyngeal Cancer

2 Additional Oncology Opportunity

3 Infectious Disease Programs Partnered with Gilead

4 Rich Upcoming Milestones

The totality of the HB-200 data represents clinical proof-of-concept

Favorable safety profile

Across all cohorts in monotherapy and
in combination with pembrolizumab

Unprecedented T cell activation

HB-200 driving expected antigen-specific T cell activation

Monotherapy clinically active

44% disease control rate; 33% of patients show tumor shrinkage

Best-in-class results in combination

Confirmed ORR of 42% in combination with pembrolizumab
vs. 19% for pembrolizumab alone

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HB-200 Monotherapy: Vaccine with demonstrated monotherapy activity

44% disease control rate; 33% of patients show tumor shrinkage

Observed association of HB-200 induced CD8 T cells and clinical benefit[1]

44% Disease Control Rate (12/27)

- 1 confirmed PR
- 11 confirmed SD
  (DCR = SD+PR+CR)

33% patients with tumor shrinkage (9/27)

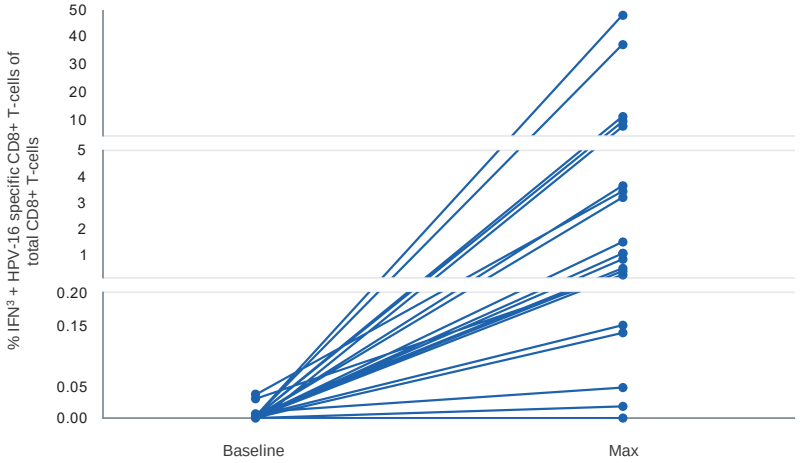
Overall Survival data still maturing (ITT: 29 patients)

- mOS approx. 13 mo.,
- median follow-up time 6.3 mo.

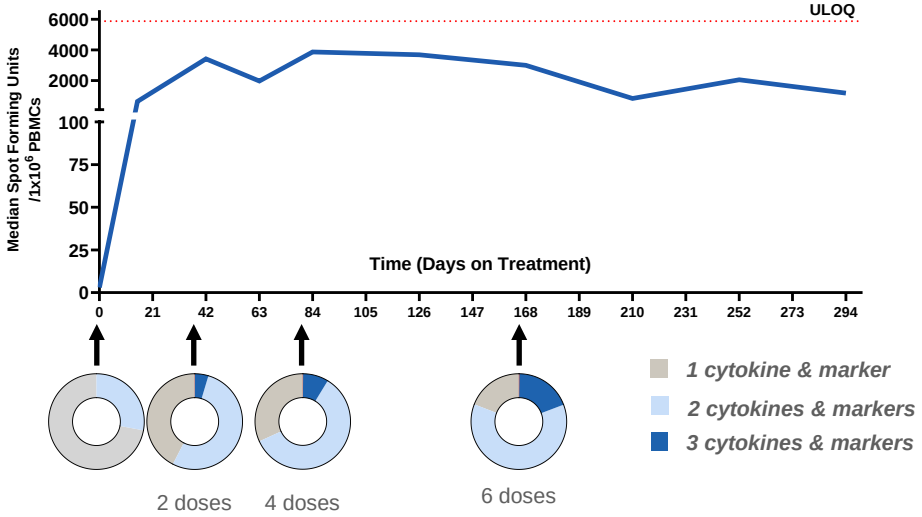
[1] Presented SITC 2023
Responses assessed by RECIST v1.1 per investigator assessment;
RECIST: Response Evaluation Criteria in Solid Tumors

Monotherapy: Driving best-in-class T cell activation in HPV16+ HNSCC

HB-200: unprecedented, long-lasting polyfunctional CD8+ T cell response



- Up to 48% conversion to functional tumor-specific CD8+ T cells, median 2%



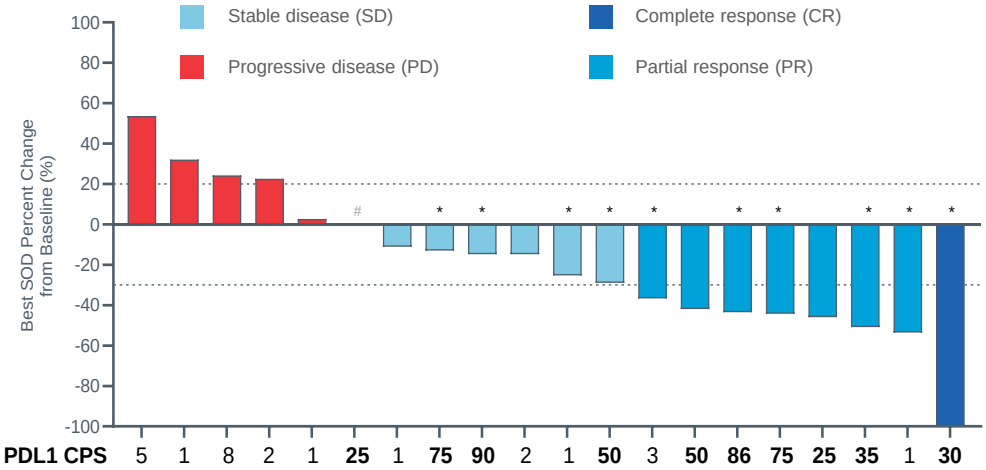
- Rapid polyfunctional CD8+ T cell increase sustained > 9.8 months

Presented SITC 2023

Left: HPV-16 E6 and E7 specific CD8+ (killer) T cells out of total CD8+ T cells measured by intracellular cytokine staining; Right: HPV-16 E6 and E7 specific cell kinetics by ELISPOT

HB-200 in combination with pembro: ORR of 42% as 1L treatment

All responses confirmed under RECIST 1.1



* Patients still on treatment

\# Patient discontinued prior to tumor scans due to covid-related death

Objective Response Rate : 42% (8/19)

- 1 confirmed Complete Response
- 7 confirmed Partial Response

Disease Control Rate is 74% (14/19)
(DCR = SD+PR+CR)

Pembrolizumab 1L:
ORR: 19-24% DCR: 40-47% [1]

Presented ESMO 2023: 19 evaluable oropharynx cancer patients with at least 3 mo. follow up (≥ 2 scans); Responses assessed by RECIST v1.1; SOD: sum of diameters of target lesions

[1] Harrington Updated Data KEYNOTE-048 JCO 2023; Seiwert, KEYNOTE-012, Lancet Oncology, 2016; Mehra, R. Br J Cancer, 2018 (N=45 HPV+ subgroup analysis in Keynote-012);

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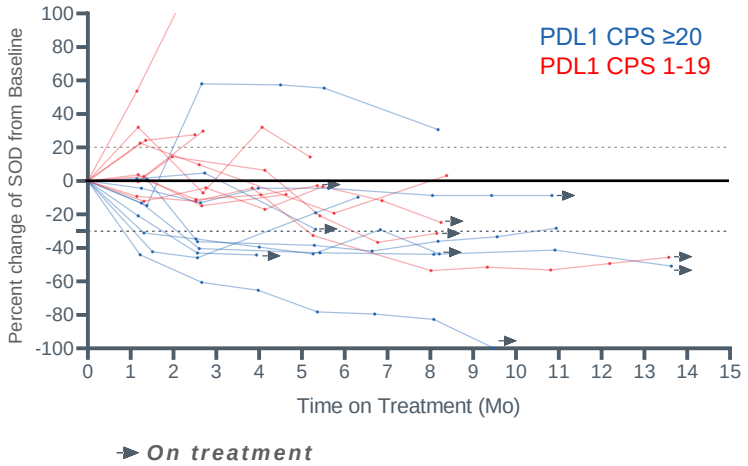
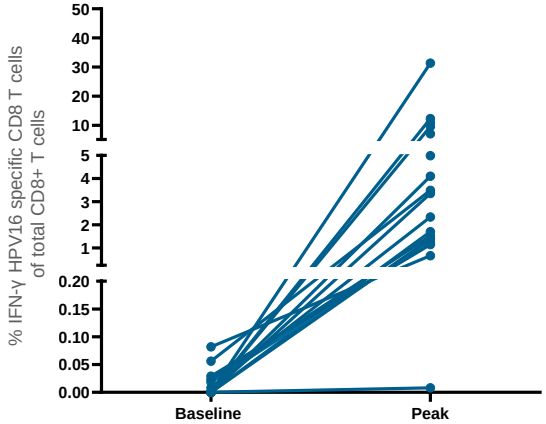
Pembro Combinations:
Durable response and prolonged disease control

Sustained disease control in majority of patients



Meaningful antigen-specific T cell reactivity



Presented ESMO 2023;median follow-up 8.31 mo
Responses assessed by RECIST v1.1; SOD: sum of diameters of target lesions

HB-200: favorable safety profile as monotherapy and in combination

No treatment related deaths and de minimis treatment-related discontinuations

HB-200 safety & tolerability

- Majority of reported adverse events (AE) were mild to moderate with the most common AEs being flu-like symptoms
- Only a limited number of patients had serious AEs related to treatment
- Treatment-related adverse events leading to dose reduction or discontinuation: only 4 patients across all cohorts
- No treatment-related deaths
- **Data suggest that Arenaviral therapies can safely be added to other immuno-therapy**

HB-200 Safety Profile n (%)	Monotherapy[1] (n=93; 2L+)		In combination with Pembrolizumab[2] (n=20; 1L)	
	Treatment-related AE	All AE	Treatment-related AE	All AE
Any event	77 (83%)	92 (99%)	19 (95%)	20 (100%)
Grade ≥3	11 (12%)	43 (46%)	4 (20%)	8 (40%)
Serious	5 (5%)	31 (33%)	2 (10%)	31 (33%)
Leading to dose reduction	2 (2%)	2 (2%)	0 (0%)	0 (0%)
Leading to discontinuation	3 (2%)	14 (15%)	1 (5%)	2 (10%)
Deaths	0	5 (5%)	0	1 (5%)

[1] Presented SITC 2023; data cutoff March 31, 2023;
93 patients with any HPV16+ cancer in 2L+ setting (72 HNSCC and 21 non-HNSCC)
[2] Presented ESMO 2023; data cutoff August 7, 2023;
20 patients with HPV16+ oropharyngeal HNSCC in 1L setting

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Addressing a significant unmet need

Potentially best-in-class treatment for recurrent, metastatic HPV16+ oropharyngeal cancers

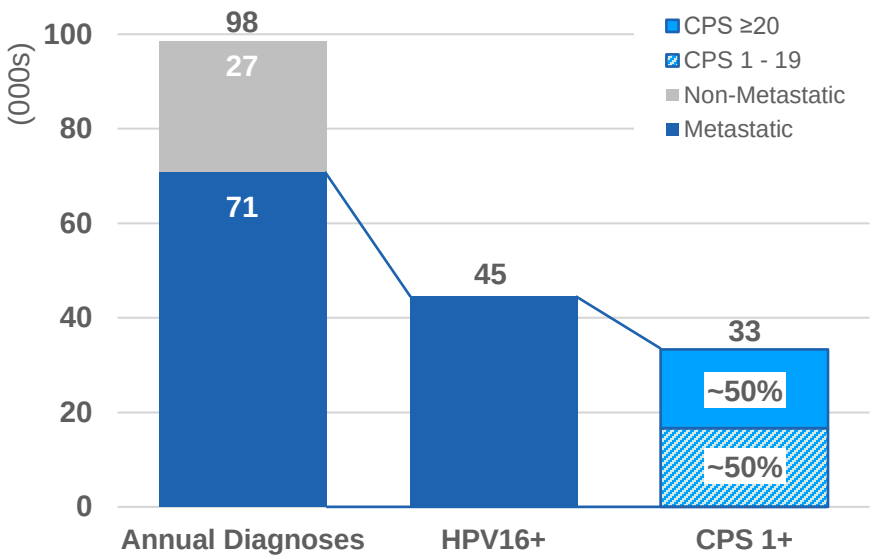
The Challenge:

- 98,000 annual diagnoses of oropharyngeal cancers globally[1]
  - ~60-65% of oropharynx cancers are HPV16+ (~45,000 metastatic diagnoses) [1]
- **No approved HPV-specific treatment options for oropharyngeal cancers**
- Only ~24% of patients with HPV16+ oropharynx cancer respond to approved standard of care CPI

HB-200 combination with pembrolizumab shows promising and consistent outcomes:

- ORR 42% vs. pembrolizumab 19-24%[2]
- DCR 74% vs. 47% of pembro alone[2]
- mPFS and mOS favorable, not reached

Unmet medical need:
Global Oropharyngeal Cancers[1]



[1] Source: World Health Organization, Globocan 2020; ClearView Healthcare Partners
[2] Sung, H. CA Cancer J Clin, 2021. Harrington, KJ. J Clin Oncol, 2023 (N=301 pembrolizumab treatment group in Keynote-048); Mehra, R. Br J Cancer, 2018 (N=45 HPV+ subgroup analysis in Keynote-012); Chaturvedi AK. J Clin Onc, 2011.

1 HPV16+ Oropharyngeal Cancer

2 Additional Oncology Opportunity

3 Infectious Disease Programs Partnered with Gilead

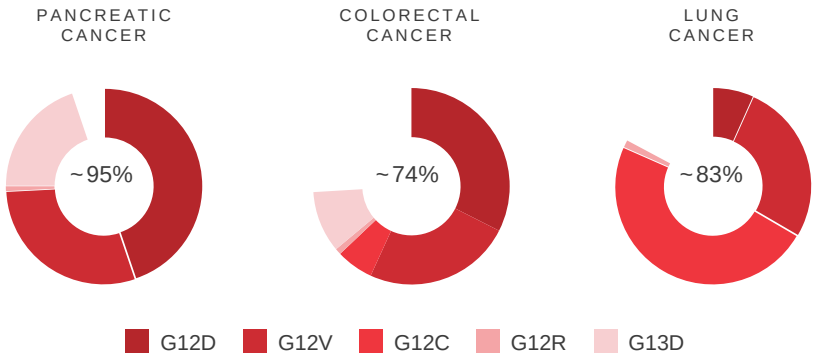
4 Rich Upcoming Milestones

HB-700: One product targeting five KRAS mutations

Targeting the most prevalent KRAS mutations in pancreatic, colorectal, and lung cancers

HB-700: Arenaviral vectors encoding ^{mut}KRAS neoantigens

Mutational pancreatic, colorectal, lung cancers driven mainly by 5 mutations[1]



KRAS cancers – large unmet medical need

- Gene acts as on/off-switch for cell growth
- KRAS mutations are most common genetic causes of cancer[2]

Prevalence

- ≥ 80% in pancreatic, ~30% in colorectal, 15-20% in lung cancers have KRAS mutations[3]
- Of those 95% (pancreatic), 74% (colon), and 83% (lung) of cancers carry at least one of these mutations

Market potential

- ≥ 200,000 patients with KRASmut pancreatic, colorectal, and lung cancers[4] in the US + EU

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

1 HPV16+ Oropharyngeal Cancer

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4 Rich Upcoming Milestones

Two independent collaboration development programs with Gilead

HB-400 HBV cure: Phase 1 trial ongoing

HOOKIPA responsibilities

- Vector design
- Manufacturing and supply of clinical material

Terms

- $190m development + commercialization milestones
- High-single digit to mid-teen % royalties
- All costs borne by Gilead, including full HOOKIPA R&D cost

Gilead responsible for clinical development

Milestone payment: start of Phase 2

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Two independent collaboration development programs with Gilead

HB-500 HIV cure: HOOKIPA to progress program through to Phase 1b study

HOOKIPA responsibilities

- Conducting Phase 1b clinical trial
- IND clearance Q4 2023; trial start Q2 2024

Terms

- $240 million development + commercialization milestones
- Mid-single digit to low double-digit % royalties
- $54m commitment from Gilead to fund

Gilead retains exclusive option post Phase 1

Milestone payment: first patient dosed

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1 HPV16+ Oropharyngeal Cancer

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Rich 2024 Value Inflection Points

PROGRAM	INDICATION	COLLABORATION	UPCOMING PHASES	DATES
HB-200	HPV16+ HNSCC		Phase 2 1L follow-up data	Q2 2024
		MERCK [1]	Pivotal Phase 2/3 1L start [2]	2024
HB-700	KRAS$_{mut}$ tumors		IND-submission	April 2024
HB-400	Hepatitis B	GILEAD		TBD: Gilead-led
HB-500	HIV	GILEAD	Ph1 Trial Start	Q2 2024

[1] Supply agreement
[2] Fast Track designation; rights 100% HOOKIPA.

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