

MAY 2024

Supercharging Immunotherapy



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Investment highlights

Unprecedented T cell activation

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

Defined path to registration

Phase 2/3 start in Q4 2024, primary read-out expected in 2026 with potential filing for Accelerated Approval

Meaningful clinical catalysts

Update on H&N Phase 2 data in ASCO oral presentation; Additional oncology pipeline with KRAS IND clear by FDA

Convincing Phase 2 data

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

Regulatory alignment

Pivotal Phase 2/3 trial design and protocol aligned with FDA; EMA PRIME Designation

Strong partnerships & cash position

Gilead-partnered HBV and HIV programs in Phase 1; \$93m cash as of 03/31/2024

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

Engineered arenavirus supercharges natural action of immune system

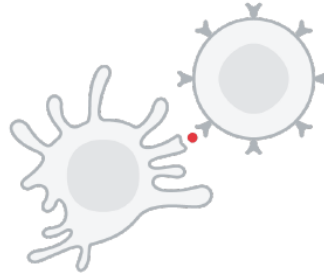
- 1** Modification of arenavirus with target antigen



- 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

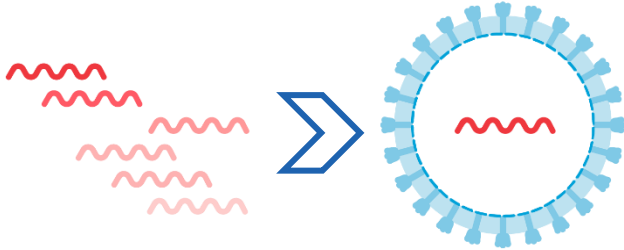
Deep pipeline of novel arenaviral therapies

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		Pivotal trial start: Q4 2024 Additional Phase 2 1L data Q2 2024	
Neo antigens	HB-700	^{mut} KRAS tumors	IND Cleared April 2024 Preclinical data Q2 2024			
Infectious disease	HB-400	HBV	 Phase 1 Trial (Gilead-led)			
Infectious disease	HB-500	HIV	 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

HPV for HPV+ cancers
HIV, HBV, other infectious diseases

Tumor Associated Self-Antigens

PAP, PSA, PSMA for prostate cancer
CTA targets for solid tumors

Neoantigens (Shared Driver Mutations)

^{mut}KRAS: Pancreatic, colorectal,
lung cancers, etc.

+

Future potential for additional indications

Oncology indications

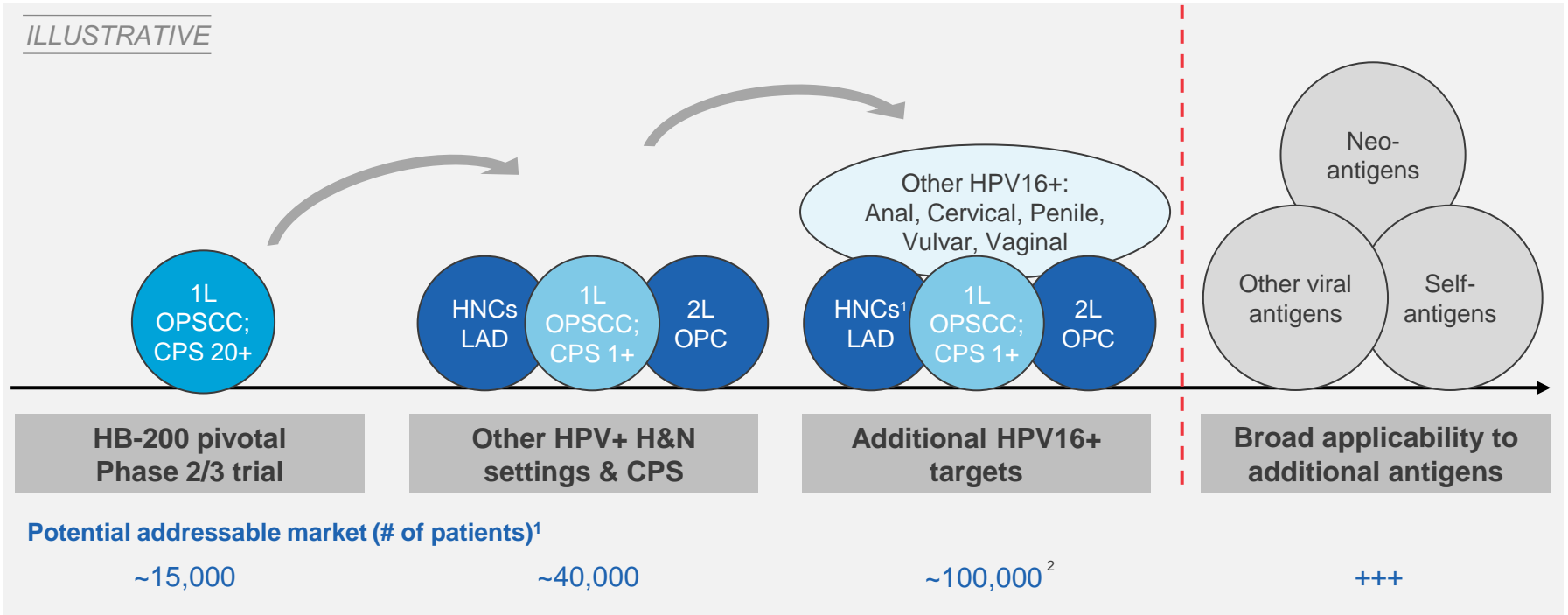
Examples: melanoma, ovarian, uterine, etc.

Infections disease indications

Potential for both therapeutic and prophylactic approaches

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

ILLUSTRATIVE



¹ Source: SEER; GLOBOCAN 2022; Clinical Trials.gov; NCCN Guidelines; ClearView Analysis.

² Systemic therapy patients only, assumes non-resectable or partially resectable only

LAD = Locally Advanced Disease

1 HPV16+ Head & Neck Cancer

2 Additional Oncology Opportunity

3 Infectious Disease Programs Partnered with Gilead

4 Rich Upcoming Milestones

Treatment paradigm: Limited treatment options and sub-optimal outcomes for majority of patients

Physicians and patients must choose between low probability or high toxicity treatment options

- **Low response rates** with pembrolizumab monotherapy (current standard of care)
- Combination with chemotherapy improves response rates, but **adds toxicity with a lower median duration of response** than with pembrolizumab alone
- Strong medical **desire to move away from chemotherapy** due to toxicity profile
- **Need for targeted treatment approach** with immunotherapy combinations for improved outcomes

Summary findings of KEYNOTE-048 ¹	ORR PD of Pembro mono (as best response ¹)			mDoR (months)	TRAEs	
	Total ²	CPS ≥ 20	CPS ≥ 1		All Grades	≥ Grade 3
Pembrolizumab	17% 41%	23% 32%	19% 39%	23.4	58%	17%
Pembro + Chemo	36% 17%	44% 15%	37% 17%	6.7	96%	72%
Cetuximab + Chemo	36% 12%	~37% ~9%	~36% ~13%	4.5	97%	69%

¹ Harrington Updated Data KEYNOTE-048 JCO 2023 ² Includes patients with CPS = 0
 ORR: Objective response rate; PD: Progressive disease; mDoR: Median duration of response;
 TRAE: Treatment-related adverse event

Our advantage: clear path to registration for HB-200

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

Convincing Phase 2 clinical data:

- Achieved >2x ORR increase over SOC¹
- Able to combine without adding toxicity
- Update on ~40 patients in an ASCO presentation

Defined, fast path to registration:

- Patient population most likely to benefit
- Phase 2 readout in 2026, potential for accelerated approval filing

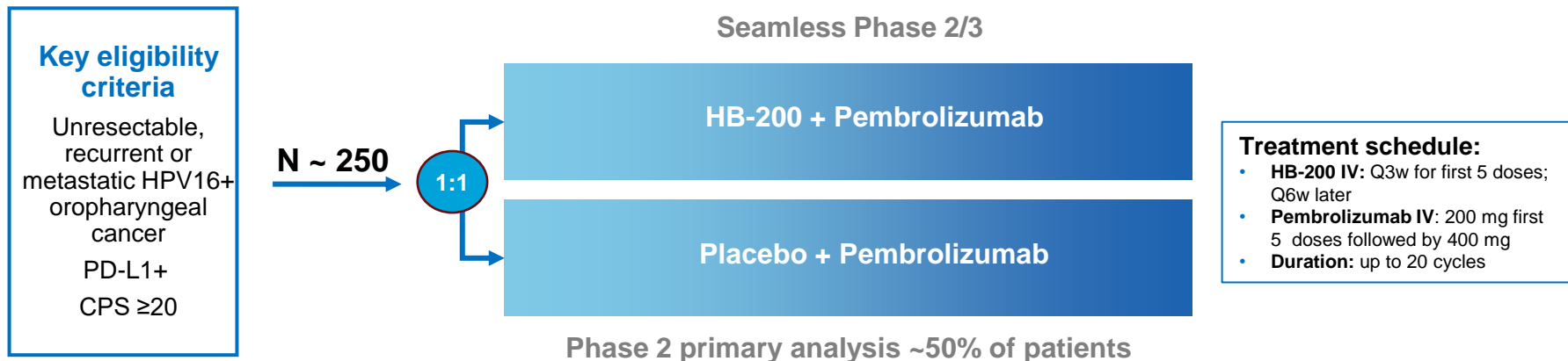
Positive regulatory interactions:

- 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

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

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



Expected Milestones & study endpoints:

Study start: Q4 2024

Phase 2 primary analysis: 2026, subsequent filing for AA

Phase 3 primary analysis: 2028

Primary endpoints:

- Phase 2: ORR
- Phase 3: OS

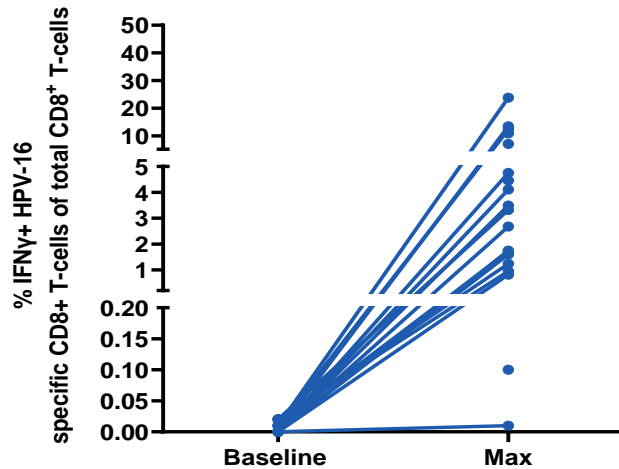
Secondary endpoints (Phase 2/3):

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

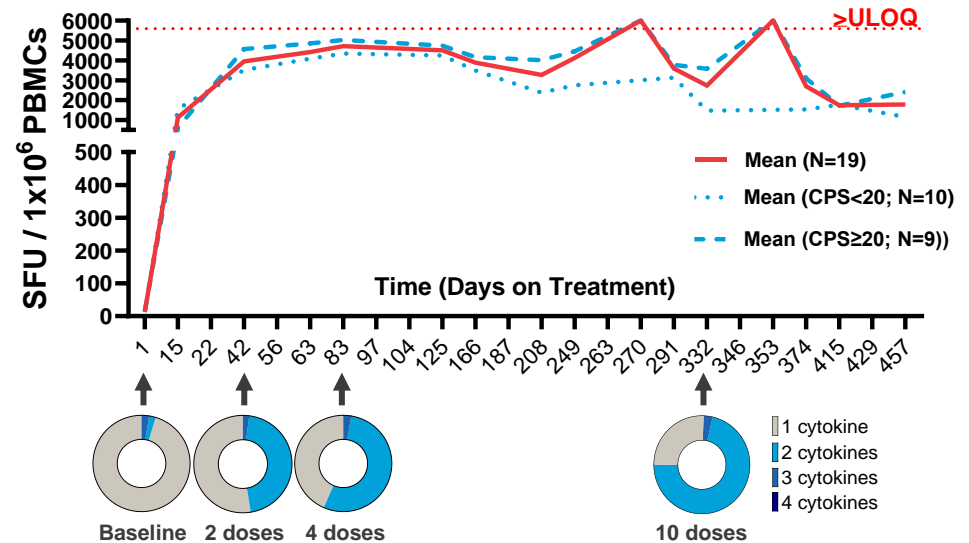
HB-200 + pembrolizumab: Unprecedented antigen-specific T cell activation

Meaningful and durable increases in antigen-specific T cells for patients observed

Meaningful antigen-specific T cell reactivity



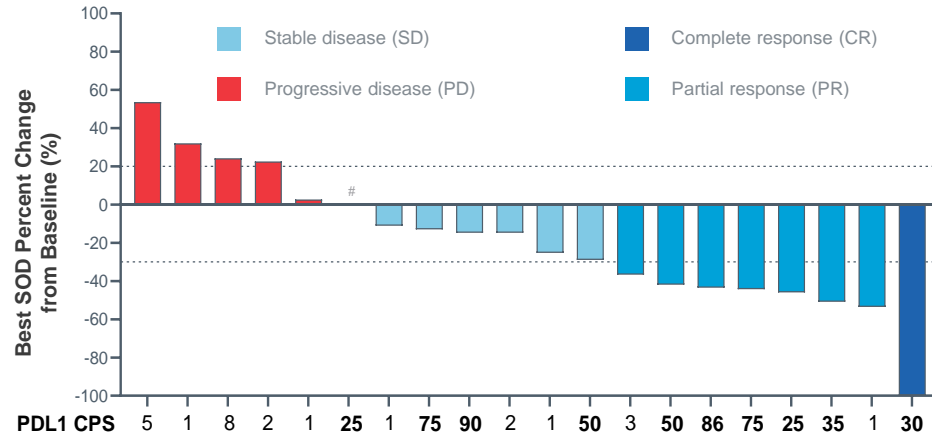
Long-lasting, healthy T cells with growing polyfunctionality over time



Left graph: Systemic HPV16 E6/E7 specific IFN- γ + CD8+ T cell responses at beginning of HB-200 treatment and peak responses (N=19 patients) determined by intracellular cytokine staining

Right graph: Systemic T cell kinetics per HPV16 E6/E7 specific ELISPOT (N=19pt) & analysis of polyfunctionality of E6/E7 specific CD8+ T cells by intracellular cytokine staining; cytokines analyzed were IFN- γ , TNF- β , IL-2

HB-200 + pembrolizumab: Delivers meaningful improvement to ORR



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

	ITT (N=20)	Evaluable (N=19)	Pembrolizumab ¹
ORR	40%	42%	19-24%
DCR	70%	74%	40-47%

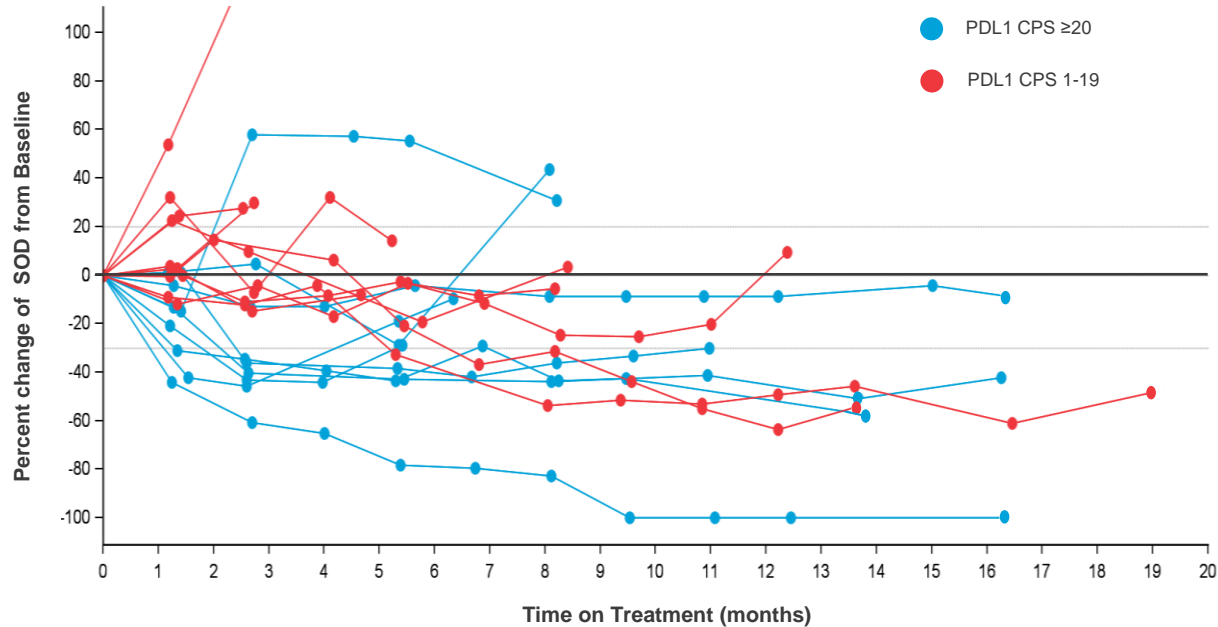
Patient population with CPS \geq 20 demonstrate highest probability of response to HB-200 + pembrolizumab

Presented ESMO 2023; Data cutoff: Aug 7, 2023; 19 evaluable oropharynx cancer patients with at least 3 mo. follow up (\geq 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

HB-200 + pembrolizumab: Durable responses and prolonged disease control

Rapid clinical responses for patients with CPS ≥ 20



Median follow-up time of 14 months (Mar. 8, 2024)

- Majority of responding patients remain on treatment
- DoR, PFS and OS continue to mature
- 18 of 20 patients are still alive at cutoff

HB-200 + pembrolizumab: Favorable safety profile

No treatment related deaths and minimal treatment-related discontinuations

HB-200 in combination with pembrolizumab safety & tolerability profile

- Majority of adverse events (AE) were mild to moderate; most common AEs were flu-like symptoms
- Low incidence of treatment-related, serious AEs
- One treatment-related AE leading to discontinuation
- No treatment-related deaths

All Participants (N = 20)	Treatment-Related AEs, n (%)	Treatment-Emergent AEs, n (%)
Any event	19 (95)	20 (100)
Grade \geq 3	4 (20)	8 (40)
Serious	2 (10)	5 (25)
Leading to discontinuation	1 (5)*	2 (10)
Deaths	0	1 (5)

*discontinued for treatment-related SAE of grade 3 CPI pneumonitis; resolved to grade 2

HB-200: Patient-centric path to registration aligned with FDA



Targeting high unmet need

- Disease-specific treatment



Data strongly support Ph 2/3 plans

- Doubles response of standard of care alone



ASCO oral abstract presentation

- Data from ~40 patients to be presented June 4



FDA-alignment on design / protocol

- Potential to file for accelerated approval



EMA Priority Medicines (PRIME)

- Enhances clinical development support



Oncology strategy built for growth

- Sequential opportunity for future expansion

1 HPV16+ Head & Neck Cancer

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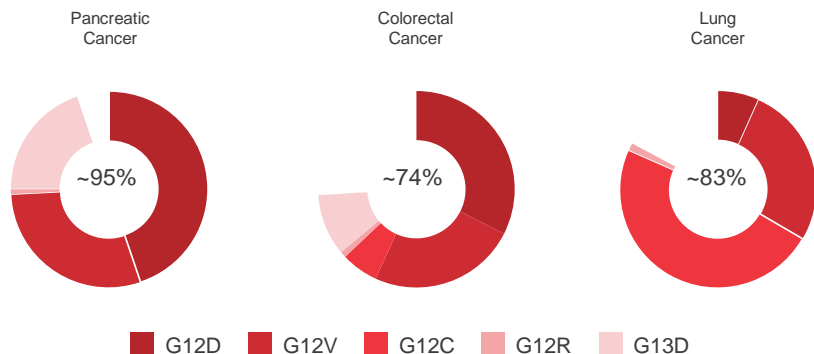
4 Rich Upcoming Milestones

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 mutations¹



KRAS cancers – large unmet medical need

- Gene acts as on/off-switch for cell growth
- KRAS mutations are most common genetic causes of cancer²

Prevalence

- ≥ 80% in pancreatic, ~30% in colorectal, 15-20% in lung cancers have KRAS mutations³
- Of those 95% (pancreatic), 74% (colon), and 83% (lung) of cancers carry at least one of these mutations

Market potential

- ≥ 200,000 patients with KRAS^{mut} pancreatic, colorectal, and lung cancers⁴ 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+ Head & Neck Cancer

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4 Rich Upcoming Milestones

Two independent collaboration development programs with Gilead

HB-400 HBV cure: Phase 1 trial ongoing; HB-500 HIV cure: Phase 1 study by HOOKIPA to start in 2Q24



HBV

Gilead responsible for clinical development

Milestone payment: start of Phase 2

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

HIV

Milestone payment: first patient dosed

Gilead retains exclusive option post Phase 1

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





1 HPV16+ Head & Neck Cancer

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4 Rich Upcoming Milestones

Rich Value Inflection Points

Program	Indication	Collaboration / Regulatory Designation	Upcoming Phases	Dates
HB-200	HPV16+ OPSCC	 U.S. Food & Drug Administration ¹	Phase 2 1L follow-up data	ASCO 2024
		 European Medicines Agency ²	Pivotal Phase 2/3 1L start	Q4 2024
HB-700	KRAS _{mut} tumors		Preclinical data	ASCO 2024
HB-400	Hepatitis B	 GILEAD		TBD: Gilead-led
HB-500	HIV	 GILEAD	Phase 1 start	Q2 2024

¹ U.S. Food and Drug Administration Fast Track Designation

² European Medicines Agency Priorities Medicine (PRIME) Designation

The logo consists of a stylized white graphic of three overlapping, curved segments that resemble a globe or a flower. The background is a dark blue gradient with a red-to-blue light flare on the left side.

HOOKIPA
PHARMA