Where no QP has gone before?

Challenges for a QP working on the borderline between startup and early/mid clinical stage

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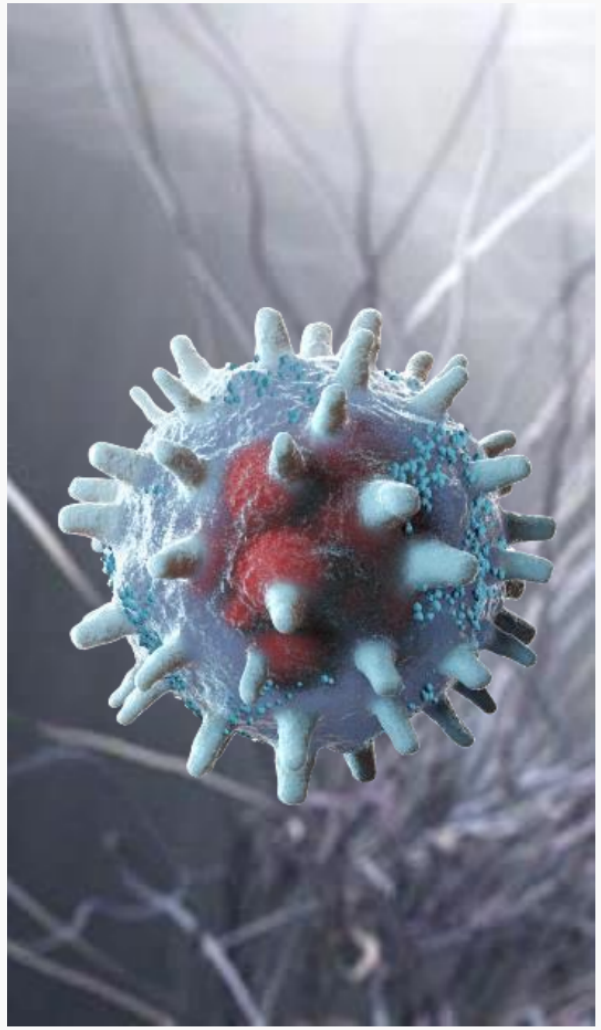
Disclaimer

Any views or opinions represented in this presentation are personal and do not represent those of people or companies the presenter is associated with.

About me

- 2010: QC and RA at Polymun Scientific Immunbiologische Forschung GmbH
- 2012: RA at Polymun Scientific Immunbiologische Forschung GmbH
- 2017: 3rd QP at Polymun Scientific Immunbiologische Forschung GmbH
- 2019: Manager – QM/QP at HOOKIPA Biotech GmbH
- Aug 2020: Sr. Manager – QA/QP at HOOKIPA Biotech GmbH

Directing the Power of the Immune System Against Serious Diseases



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

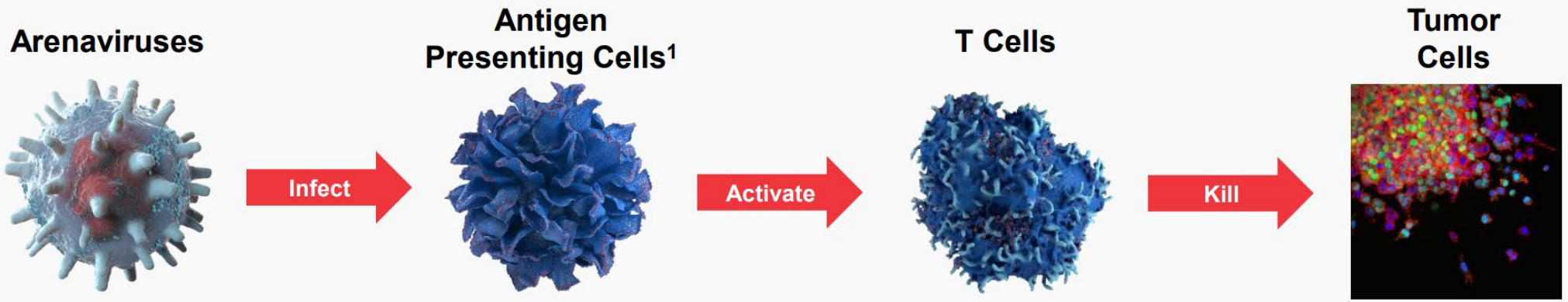
Mission Advancing the field of immunotherapy by using a novel, arenavirus-based antigen delivery system

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

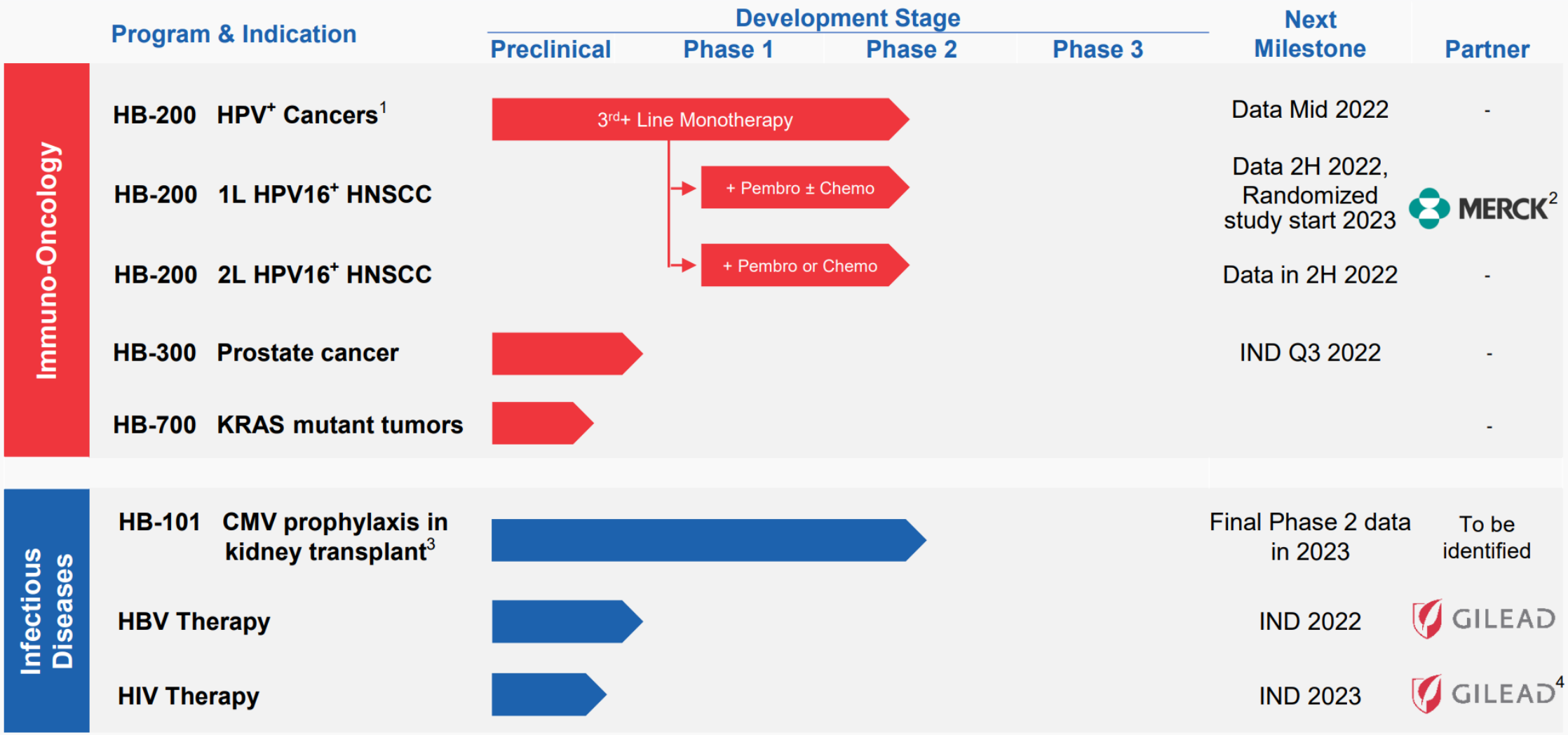


Potential to design drugs that are:

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

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

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.

Challenges

Novelty of platform

- Initially, limited experience on GMP production of arenaviruses:
  - Limited number of CMOs and CLOs capable of handling BSL-2 attenuated viral vectors
    - Dependency
    - Complex contractor landscape (improved)
    - Harmonization of processes and methods between different contractors
    - Assure adequate quality oversight (deviations, OOS,…)
  - Limited manufacturing experience in case of new vectors (antigens)
    - Difficult to define specifications (e.g. yield experience may not fully translate to new antigens)
- Implementing increasing process knowledge and experience
  - Adaption of manufacturing process
  - Comparability (the process is the product)
  - Compliance with GMP
  - Compliance with regulatory filings
- Ongoing stability program
  - Frequent extension of shelf-life

Challenges

Company structure

- Clinical Operations and Regulatory Affairs mainly located in US
  - Disciplined communication required
  - Align on regulatory expectations (e.g. ATMP vs. Vaccine, phase I requirements US vs. EU, IND vs IMPD, label requirements)
  - Working in different time zones

Changing regulatory requirements

- Annex 1?
- Clinical Trial Regulation (Annex 13 vs “GMP for IMPs” vs GMP for ATMPs)

Storage and shipping conditions

- Limit time at RT during manufacture (avoid hold times)
- Store and ship at ≤ -65 °C (dry ice shipments)
- "The patient is waiting at the site. Can we use the product?”

Challenges

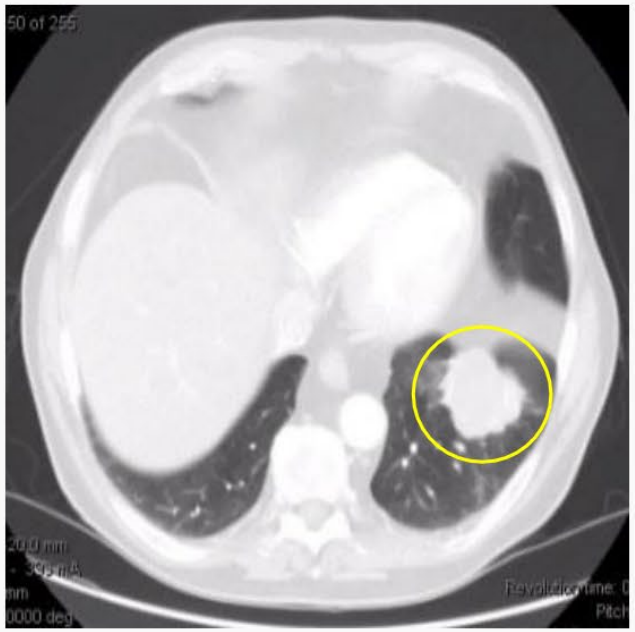
(source unknown; deliberately exaggerated)

Maturity

- Quality governance
  - Transitioning a stand-alone QMS into an integrated QMS
- GxP mindset not yet fully internalized across whole organization
  - "I have already requested a re-test"
  - "This is only for Phase I"
  - "Can we release this at a later point in time if needed?"
  - "We are only a little bit OOS“
- Challenging questions
  - "Does this need to be GMP?“
  - "Can we just change the specification?“
  - “How can we avoid temperature excursions”?

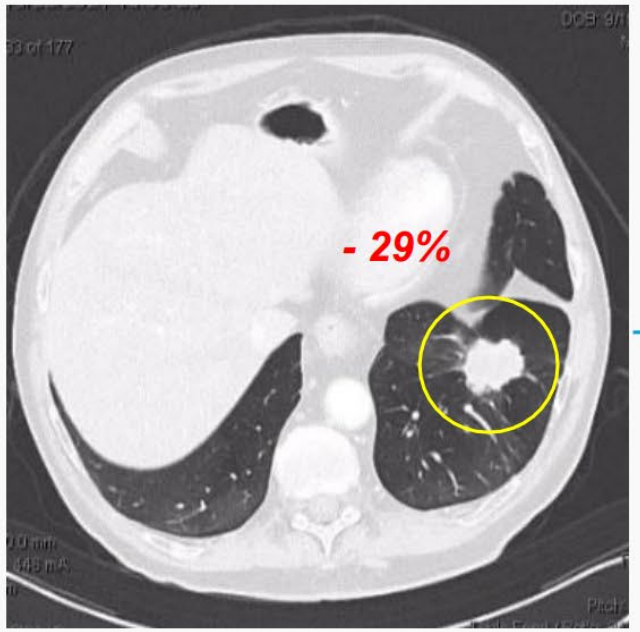
Gratification

- 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

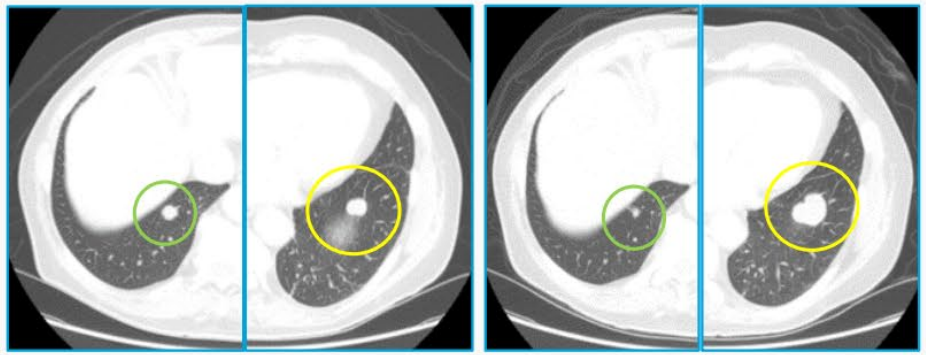
→ **Patient remains on trial**

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

Gratification

- 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



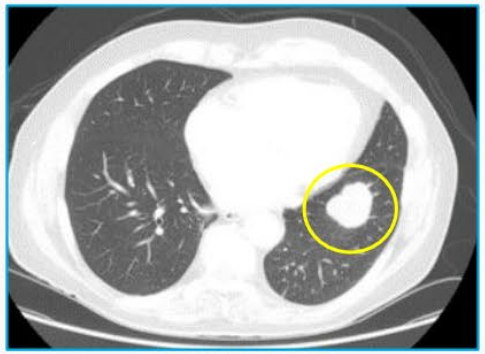
Prior to Starting 1L Pembrolizumab+TKI

Confirmed Progression

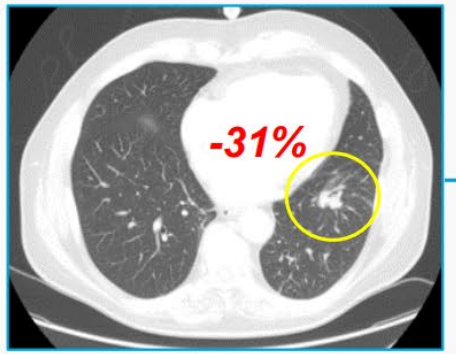
Mar. 2021:
Pembrolizumab + TKI confirmed progression.
One lesion responded; one lesion progressed

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.

Thank You!

Questions?