HB-101 CMV Vaccine

Phase 2 Trial in Kidney Transplantation

Preliminary Results of Interim Analysis

November 30, 2020

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HB-101 Phase 2 Interim Analysis Data Overview

- HB-101 is a Cytomegalovirus (CMV) vaccine based on HOOKIPA's non-replicating technology
- This interim analysis of the ongoing Phase 2 study of HB-101 supports dose-finding for the 3-dose schedule
- The 3-dose schedule of HB-101 has demonstrated:
  - Good tolerability profile
  - Promising immunogenicity
  - Encouraging interim efficacy in decreasing rates of viremia, antiviral use, and CMV disease
- While from a small number of patients, early efficacy data show the potential of HB-101 to help address the unmet need in CMV

Cytomegalovirus (CMV) in Solid Organ Transplant Recipients

CMV can cause severe complications in solid organ transplant recipients

CMV viremia	CMV syndrome	CMV disease
CMV detection in body fluid	Fever, malaise, leukopenia, and/or thrombocytopenia	End organ disease, pneumonia, hepatitis, rejection

TWO TREATMENT APPROACHES

Pre-emptive antivirals
vs.
Prophylactic antivirals

CMV Risk to Organ Recipient

Donor	-	-	+	+
Recipient	-	+	+	-

Majority of kidney donors are deceased; living donor transplants offer the ideal opportunity to assess post-transplant efficacy relatively quickly

Kotton CN et al. The Third International Consensus Guidelines on Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation. 2019;102:900-931; Ljungman P et al. Definitions of Cytomegalovirus Infection and Disease in Transplant Patients for Use in Clinical Trials. Clinical Infectious Disease. 2017;64(1):87-91; Global Observatory on Donation and Transplantation. 2019; Azevedo LS et al. Cytomegalovirus infection in transplant recipients. Clinics. 2015;70(70):515-523.

HOOKIPA's HB-101: Arenavirus-based Prophylactic Vaccine to Prevent CMV Infections or Reactivations in Immuno-Compromised Populations

HB-101 Product Details

- **Uses our proprietary non-replicating technology, with two arenaviral vectors (LCMV)**
- **Bi-valent vaccine incorporating 2 CMV antigens:**
  - Glycoprotein B ("gB") fusion protein, a B cell antigen
  - Phosphoprotein 65 kDa ("pp65"), a T cell antigen
- **Vaccine stimulates both arms of the adaptive immune system:**
  - Antibodies against gB fusion protein
  - T cells against pp65 T cell antigen
- **Intra-muscular delivery**

HB-101 Ongoing Phase 2 Clinical Trial: Prophylactic CMV Vaccine in Kidney Transplant Patients

Patients Eligible for a Kidney Transplant from a Live Donor

Randomized to HB-101 or Placebo Pre-transplant
Stratified by Post-transplant Treatment Intent

	Pre-transplant	Post-transplant
ARM 1: CMV- Recipients	**HB-101** 2-3 doses pre-transplant **Placebo**	Pre-emptive antiviral therapy
ARM 2: CMV- Recipients	**HB-101** 2-3 doses pre-transplant **Placebo**	3-6 months prophylactic antiviral therapy
ARM 3: CMV+ Recipients	**HB-101** 2-3 doses pre-transplant	Pre-emptive or prophylactic SoC[1]

Trial Objectives

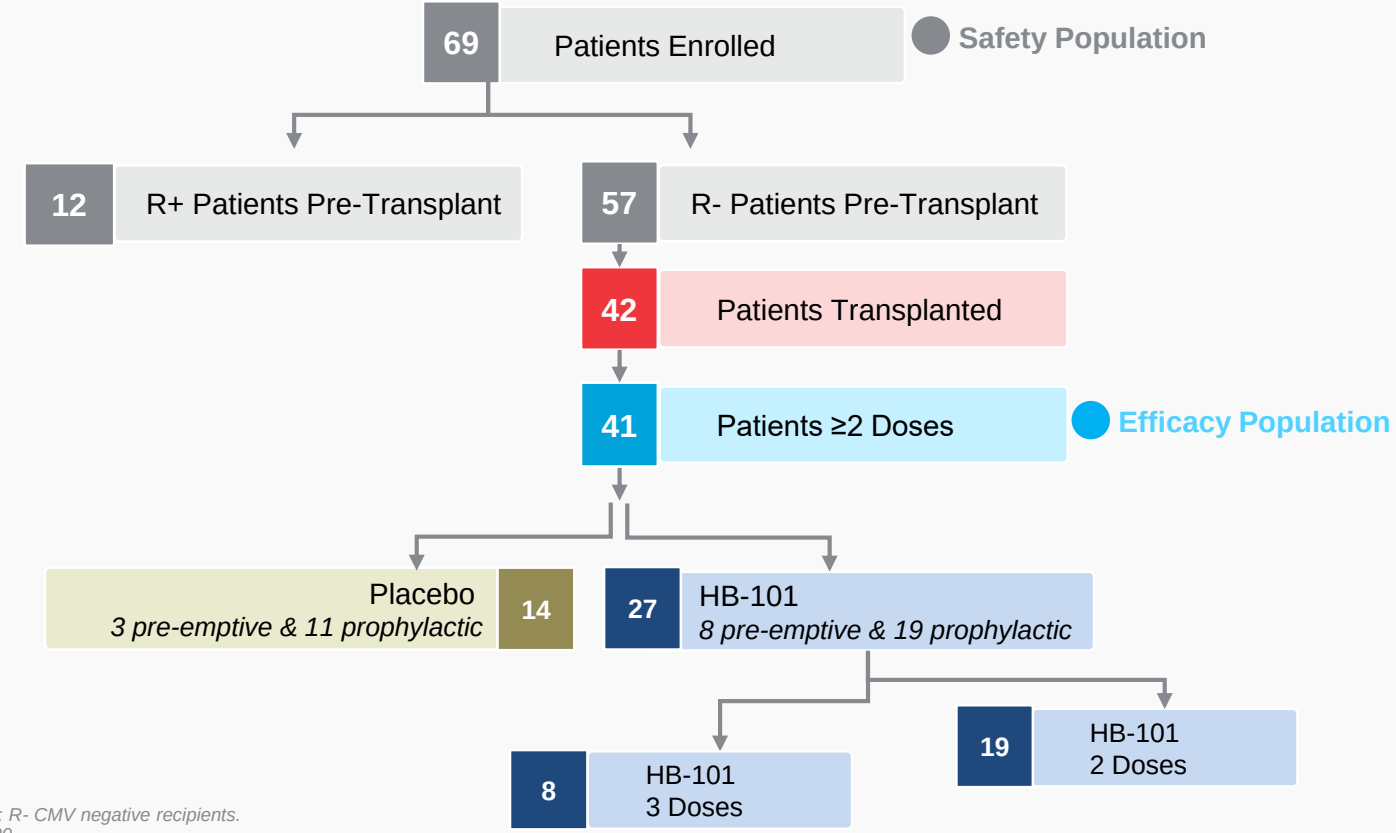
Measure decrease of post-transplant viremia in the absence and presence of antivirals

Endpoints

- Primary: immunogenicity & safety
- Secondary: CMV viremia, antiviral use, CMV disease, transplant rejection

[1]SoC: Standard of care.

HB-101 Phase 2 Interim Analysis: Safety on All 69 Enrolled Patients and First Efficacy Analysis of 41 CMV Negative Recipient Transplanted Patients



R+ CMV positive recipients; R- CMV negative recipients.
Data cut-off August 24, 2020.

HB-101 Phase 2 Interim Analysis Preliminary Safety[1]

Pre-Transplant AEs Related to Study Medication	N (%)
Grade 1 – Mild	8 (11.6%)
Grade 2 – Moderate	2 (2.9%)
Grade 3 – Severe	2 (2.9%)*
Grade 4 – Life-Threatening	0 (0.0%)
Death	0 (0.0%)
Serious (SAE)	2 (2.9%)*
Discontinued Study Medication Due to AE	0 (0.0%)

**Recipient HLA-sensitization*

Safety Population:

- 69 patients prior to kidney transplantation

Most common mild AEs:

- Influenza-like illness (N=2)
- Injection site pain (N=2)

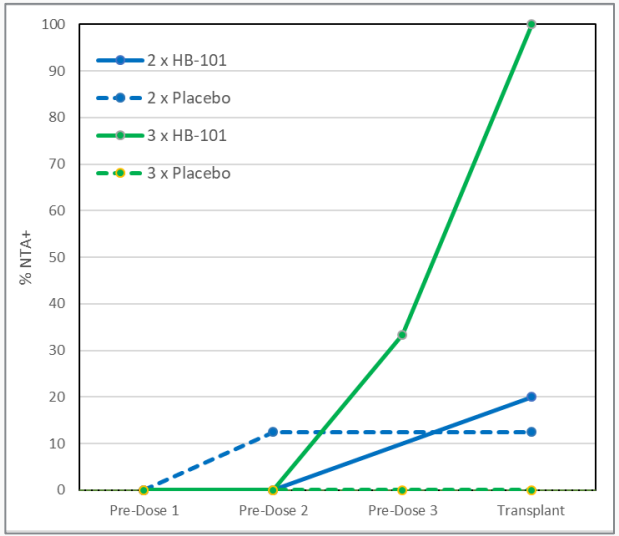
Human Leukocyte Antigen (HLA) Sensitization:

- HLA-sensitization is a known complication in renal dialysis patients awaiting transplantation, occurring at a rate of 4%[2]
- HLA sensitization requires identification of a new donor organ; it can be managed clinically via risk stratification based on recipient's HLA profile
- 2 cases were classified as both severe and serious AEs; 1 additional case was not considered an AE

[1]Data cut-off August 24, 2020. [2]Nephrol Dial Transplant (2013) 28: 2908-2918.

HB-101 Phase 2 Interim Analysis of CMV-Neutralizing Antibody Responses: 3 Doses Induce 100% Seroconversion at Levels Superior to 2 Doses or Placebo

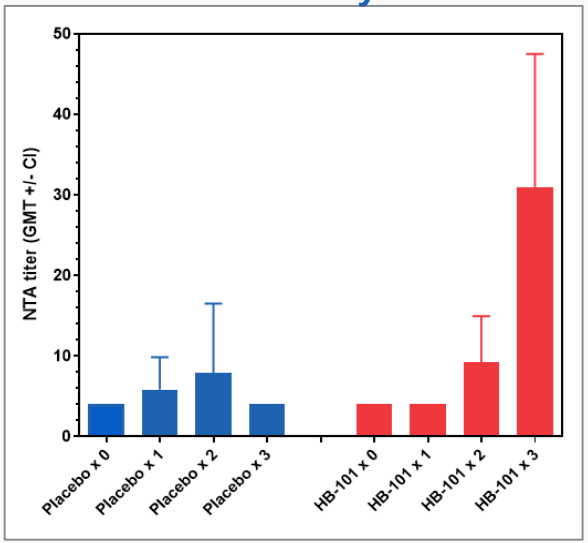
Seroconversion Rates



Rates of CMV-neutralizing antibodies development:

- 100% in 3 dose group (N=6)
- 20% in 2 dose group (N=15)

CMV Antibody Levels



33 R- patients measured on the day of transplant

- 21 patients received vaccine
- 12 patients received placebo

3 doses of HB-101 more immunogenic than 2 doses

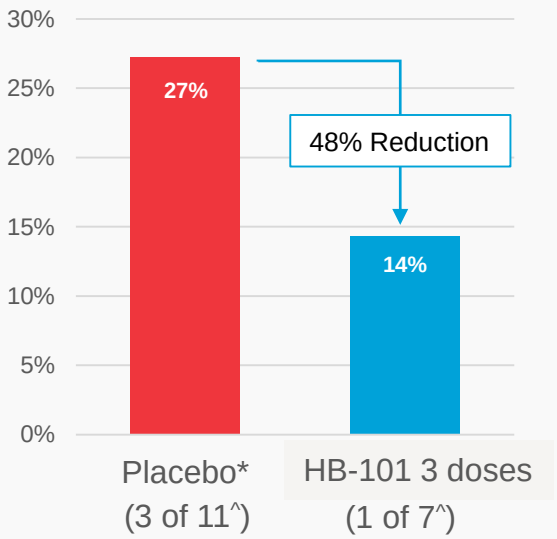
Antibody level induced by 3 doses of HB-101 was significantly superior to that induced by:

- 2 doses of HB-101 (p=0.03)
- Placebo (p=0.0095)

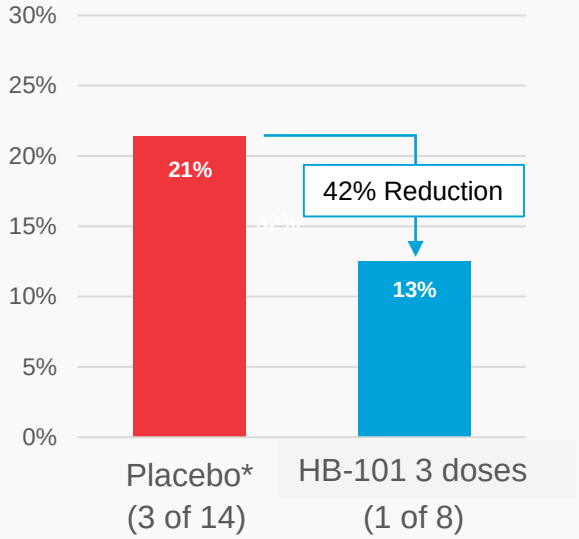
Assessment of antibody responses was completed for a subset of the 41-patient efficacy group at the time of cut-off. Data cut-off August 24, 2020.

HB-101 Phase 2 Interim Analysis Preliminary Efficacy: Reduced Incidence of CMV Infection, Reduced Use of Antivirals, and No CMV Disease

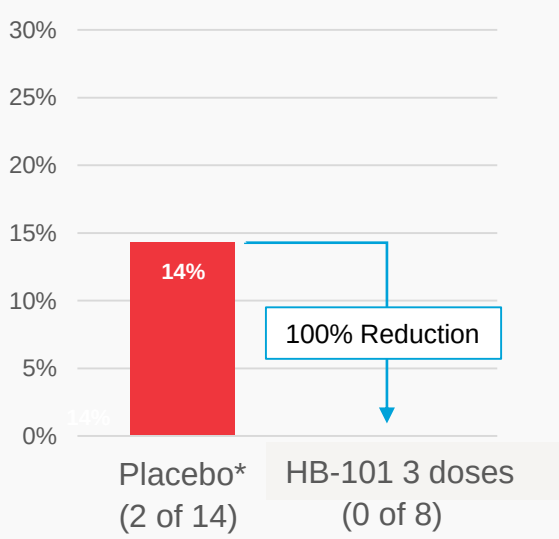
CMV Viremia



Required Use of Antivirals



CMV Disease



*Patients received either 2 or 3 doses of placebo.
^Not all patients had PCR data at the time of the August 24, 2020 data cut-off, and therefore some were not evaluable for CMV viremia assessment.

- No reduction in immune-mediated pathology

Based on Phase 2 Interim Analysis, HB-101 Appears to be Well Tolerated, and in Patients Receiving Three Doses, Immunogenic and Efficacious (Preliminary Data)

Safety:

- HB-101 appears to be well tolerated with a low incidence of adverse events (mostly mild to moderate)
- Three cases of HLA-sensitization were reported, two as serious adverse events

Immunogenicity:

- Patients who received three doses of HB-101 had 100% response rate for CMV-neutralizing antibodies (N=6)
- CMV-neutralizing antibody levels induced by the three doses of HB-101 are statistically superior to those seen with placebo (p=0.0095)
- Patients who received three doses of HB-101 had 100% response rate for CMV-specific cellular (T cell) responses (N=3, as reported in June 2020 interim analysis)

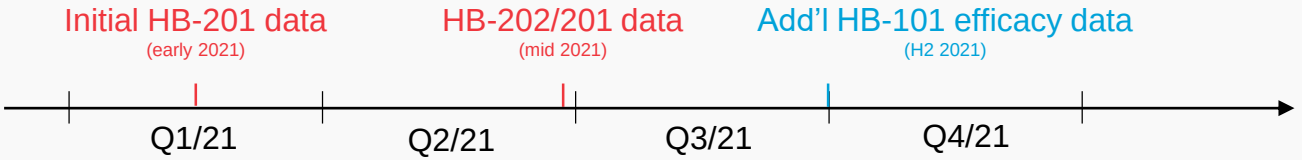
Efficacy:

- Reduced viremia in patients who received three doses of HB-101 compared to placebo by 48%
- Reduced antiviral use required in patients who received three doses of HB-101 compared to placebo by 42%
- No CMV disease in eight patients who received three doses of HB-101

HB-101 Phase 2 Dataset Continues to Build and Inform Path to Registration

- Interim Phase 2 safety and immunogenicity data have been reviewed with investigators:
  - Encouraged to complete the pre-transplant **three dose vaccination protocol** (whenever possible in the context of these live donor transplants) and thereby **maximize immunogenicity** at transplantation and **potential patients benefits**.
- Continuing accrual, as permitted by COVID-19 considerations at our participating sites
- Phase 2 data will enable us to explore a path to a Phase 3 registration study in a real world, all-comers population, wherein most recipients are on a transplant waiting list and a three-dose vaccination schedule is easily managed
- Next Phase 2 data update will be provided in H2 2021

2021 Outlook: Catalysts & Upcoming Immuno-Oncology Clinical Data



- From non-replicating to single-vector replicating to dual vector replicating technology
  - HB-101 is an immunogenic, single-vector non-replicating technology
  - HB-201 is expected to be more immunogenic, single-vector replicating technology
  - HB-202/HB-201 is expected to be most immunogenic, alternating two-vector replicating technology
- Based on published preclinical data, we hope to demonstrate
  - **Favorable safety** across the non-replicating and replicating platforms
  - **Increasing immunogenicity** and **efficacy** for single-vector replicating as compared to non-replicating
  - **Increasing immunogenicity** and **efficacy** for alternating two-vector replicating therapy as compared to single-vector replicating therapy
- Initial clinical data release from the HB-201 Phase 1/2 study is planned for early 2021
- Funded to reach beyond major value inflections: $82m cash (30 September 2020)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