hēlocyte

Clinical-Stage Immunotherapy

AUGUST 2018

Forward-Looking Statements

Statements in this presentation that are not descriptions of historical facts are forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. We have attempted to identify forward-looking statements by terminology including “anticipates,” “believes,” “can,” “continue,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “should,” or “will” or the negative of these terms or other comparable terminology. Forward-looking statements are based on management’s current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock price. Factors that could cause actual results to differ materially from those currently anticipated are risks relating to: our growth strategy; results of research and development activities; uncertainties relating to preclinical and clinical testing; our dependence on third party suppliers; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; our ability to attract, integrate, and retain key personnel; the early stage of products under development; our need for substantial funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in our parent company’s SEC filings. We expressly disclaim any obligation or undertaking to update or revise any statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances after the date of this presentation.

Overview

- Novel Immunotherapies to Prevent and Treat Cytomegalovirus
  - Based on Research from City of Hope National Medical Center
  - Potential of Lower Toxicity, Increased Durability over Antivirals

- Two Novel Biologics
  - **Triplex**: Universal Multi-Antigen MVA Vaccine for CMV Control
    - Phase 1: safe, highly immunogenic; presented at **ASH,** published in ***Blood***
    - First Phase 2: allo stem cell transplant (matched related-unrelated, n=102)
      - Primary Endpoint reached in 1Q2018 (*blinded*), completion by 4Q2018
      - Final DMC Review: no safety issues (2Q2018)
    - Multiple Other Studies Ongoing, Planned
  - **ConVax**: Universal Multi-Antigen MVA Vaccine for CMV Prevention and Control
    - Cellular and humoral immunity (stable expression of 8 antigens)
    - Non-clinical development ongoing; IND filing by 4Q2019

- First-In-Class, Best-In-Class Vaccine for CMV Control (Triplex)
- Well-Defined Markets, No Approved Immunotherapy
- Biologic Exclusivity (Orphan for Triplex), Robust IP Portfolio
- Significant Grant Funding (NCI, ACTG, NHLBI), $2.5B+ Proxy for Triplex (CMRX)

Leadership

Fortress Biotech Management

Lindsay A. Rosenwald, M.D. Executive Chairman	20+ years experience Life Sciences Entrepreneur and Investor
Michael S. Weiss, J.D. Executive Vice Chairman	20+ years experience Life Sciences Entrepreneur and Investor

Helocyte Management

Lindsay A. Rosenwald, M.D. Co-Founder and Executive Chairman	20+ years experience Life Sciences Entrepreneur and Investor
Frank Taffy, J.D. Co-Founder, President and Chief Executive Officer	15+ years experience **Forest Labs:** former Head of Business Affairs
David J. Horin, C.P.A. Interim Chief Financial Officer	15+ years experience **Chord Advisors:** Managing Partner
Elizabeth Moore, M.S. Executive Vice President Regulatory Affairs	30+ years experience **Pfizer La Jolla**: former Head of Regulatory Affairs

Helocyte Board of Directors

Lindsay A. Rosenwald, M.D. Executive Chairman
Michael S. Weiss, J.D. Director
Kenneth W. Cappell, M.B.A. Director
Frank Taffy, J.D. Director

Helocyte Scientific Advisory Board

Don J. Diamond, Ph.D. Co-Founder and Chairman of Scientific Advisory Board	**City of Hope**: Chair of Experimental Therapeutics
Additional SAB Members	TBA

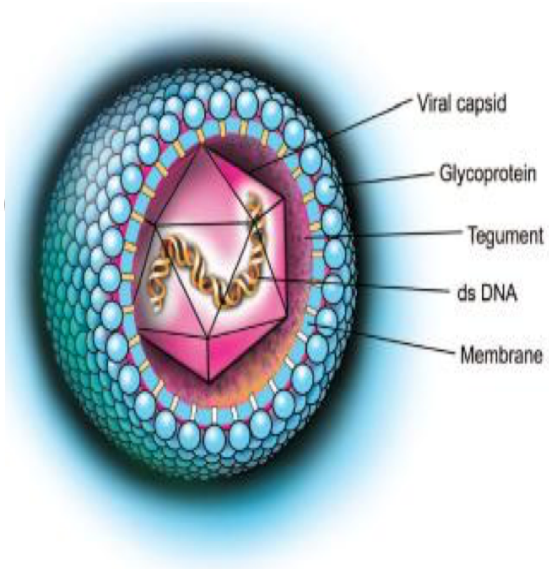
Development Pipeline

TRIPLEX	Pre-Clinical	Phase 1	Phase 2	Phase 3
Allogeneic Stem Cell Transplant (MRD/MUD)	Fully-Accrued, Data by 4Q2018 (n=102)			
Allogeneic Stem Cell Transplant (Haploidentical)	Open (n=108)			
Allogeneic Stem Cell Transplant (Pediatric)	Open (n=72)			
Allogeneic Stem Cell Transplant (Donor Vaccination)	Open (n=36)			
Autologous Stem Cell Transplant (NK Cell Recon)	Open (n=20)			
CMV-HIV Co-Infection on ART	To Open 4Q2018 (n=90)			
Kidney Transplant	To Open 1Q2019 (n=72)			
Liver Transplant	To Open 3Q2019 (n=72)			
Expand CMV-Specific T Cells	To Open 4Q2019			
CONVAX				
CMV Prevention & Control	IND by 4Q2019			

Novel Immunotherapies For Common Virus

- CDC estimates 50-80% infected with Cytomegalovirus (CMV) by age of 40
  - Easily transmitted: saliva, urine, and in utero
  - Life-long infection, asymptomatic in healthy individuals

- Life-Threatening in Those With Weak Immune Systems
  - Allogeneic Hematopoietic Stem Cell Transplant Recipients
  - Solid Organ Transplant Recipients ("SOT")
  - Developing Fetus or Newborn Children



- Standard of Care: often toxic, moderately effective antivirals

- Helocyte Vaccines
  - Triplex: T Cell Response to Control CMV in Transplant Recipients
  - ConVax: Antibody Response to Prevent CMV Transmission (+ T Cell Response to Control CMV)

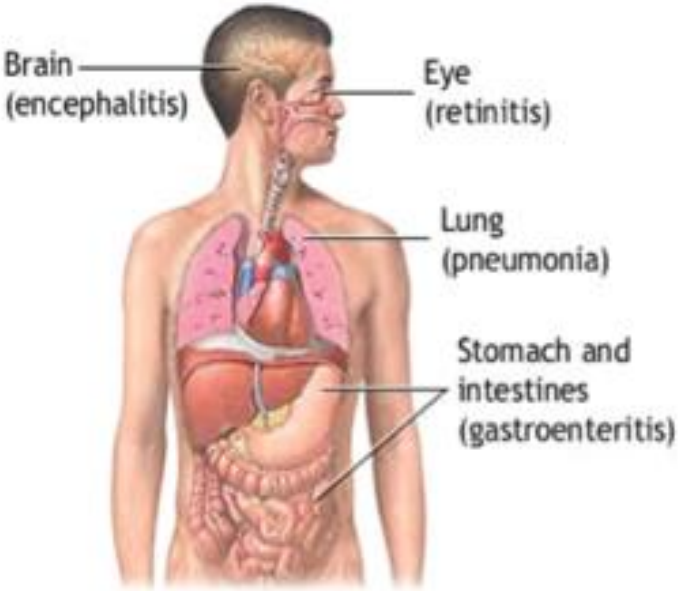
Complications of Cytomegalovirus

Direct Effects

- Viral Syndrome: fever, malaise, myalgia, leukopenia, thrombocytopenia
- Tissue Invasion (End Organ Disease): hepatitis, colitis, nephritis, pancreatitis, retinitis, encephalitis, pneumonia
- Other: bacteremia, fungemia, graft versus host disease

Occurrence

- Early and late after allogeneic HSCT and SOT
  - Late CMV (after Day 100) following antiviral use
- Evident at birth upon transmission from mother to fetus



Triplex Overview

- Universal Multi-Antigen MVA-based CMV Vaccine
- Mechanism: Cellular Immunity
  - T Cell Response to: pp65 + IE1 + IE2
- Indication: CMV Control in Post-Transplant
- Phase 1 in 24 Healthy Volunteers
  - Safe, Well-Tolerated at Three Dose Levels
  - Robust, Durable Immunogenicity
  - Presented at **ASH** (12/2015)
  - Published in **BLOOD** (11/2016)
- First Phase 2 (n=102): Matched Related, Unrelated HSCTs
  - Primary Endpoint Reached 1Q2018 (***BLINDED***)
  - Final DMC Review: no safety issues (04/2018)
  - Study Completion by 4Q2018
  - Supported in part by grants from NCI

Triplex: Phase 1

- **Phase 1 Data: Presented @ <u>ASH</u> (12/2015), Published in *<u>Blood</u>* (11/2016)**
  - 24 Healthy Volunteers (3 Dose Levels)
  - Safety: well tolerated, no SAE or dose-limiting toxicities
  - Immunogenicity: robust, durable T cell responses observed even in
    - CMV-negative subjects with no prior immunity
    - CMV-positive subjects with low baseline immunity

ASH | 57th Annual Meeting & Exposition
Orlando, FL • December 5-8, 2015

3108 Safety, Maximum Tolerated Dose and Immunogenicity of CMV-MVA-Triplex in Healthy Volunteers with or without Prior Immunity to CMV and Vaccinia

Clinical Allogeneic Transplantation: Conditioning Regimens, Engraftment and Acute Transplant Toxicities Program: Oral and Poster Abstracts

Session: 721. Clinical Allogeneic Transplantation: Conditioning Regimens, Engraftment and Acute Transplant Toxicities: Poster II

blood®
Leading the way in experimental and clinical research in hematology

Safety, Maximum Tolerated Dose and Immunogenicity of CMV-MVA-Triplex in Healthy Volunteers with or without Prior Immunity to CMV and Vaccinia

Don J. Diamond, Corinna La Rosa, Jeffrey Longmate, Joy Martinez, Qiao Zhou, Theodora Kaltcheva, Jennifer Drake, Mary Carroll, Sanjeet Dadwal, Ibrahim Aldoss, Ryotaro Nakamura and John A. Zaia

Blood 2015 126:3108;

Triplex: Phase 2 in Allo-HSCT (Lead Indication)

- First Phase 2: CMV control in Allo-HSCT (matched related, unrelated donors)
  - Multi-Center, Double-Blinded Study in 102 Patients, Randomized (1:1) Vaccine / Placebo
  - Clinical Sites (3): top transplant centers in US
    - City of Hope (PI, Nakamura): primary site, opened June 2016
    - Dana Farber (PI, Baden): opened November 2016
    - MD Anderson (PI, Ariza-Heredia): opened February 2017
  - Primary Endpoint (CMV Events Thru Day 100): *reached 1Q2018 (**blinded**)*
  - Secondary Endpoint (Late CMV, Relapse, Survival Thru Day 365): *data by 4Q2018*

	Design	Dosing Schedule	1° Endpoint	2° Endpoint(s)
Phase 2 (Fully-Accrued)	Multi-Center, Randomized (1:1), Double-Blinded Study in 102 Allogeneic HSCT CMV(+) Recipients (MRD, MUD)	Two IM Vaccinations After Transplant: • Day 28 • Day 56	CMV Reactivation through Day 100 as monitored by PCR	• Immune Response • Viremia Duration • Antivirals Use • Relapse, Survival

Final DMC Review: No Safety Issues

Dear Drs. Nakamura and Aldoss

On April 18, 2018, the data monitoring committee assembled by conference call for the final review of COH IRB 14295, *A Phase II, Randomized, Placebo-controlled, Multicenter Trial to Evaluate the Protective Function of a CMV-MVA Triplex Vaccine in Recipients of an Allogeneic Hematopoietic Stem Cell Transplant*. Present for the open session of the call were Mitchell Horwitz, Bipin Savani and Krishna Komanduri, all from the DMC. Also present were Ryotaro Nakamura, Ella Ariza and Jeff Longmate representing the study teams from City of Hope and MD Anderson Cancer Center . Provided for DMC review was Data and Monitoring Committee Report #4, an unblinded and confidential dataset that was extracted on April 17, 2018 and prepared by Dr. Longmate.

As reported by Dr. Nakamura, 130 patients have consented for participation on the study to date, of whom 102 were randomized and received at least the first injection. As of April 17, 2018 (the date of data extraction), the target accrual has been met and the study is now closed to accrual.

After review of the unblinded dataset along with the monitoring report in closed session (Drs. Horwitz, Komanduri and Longmate), no safety issues were identified.

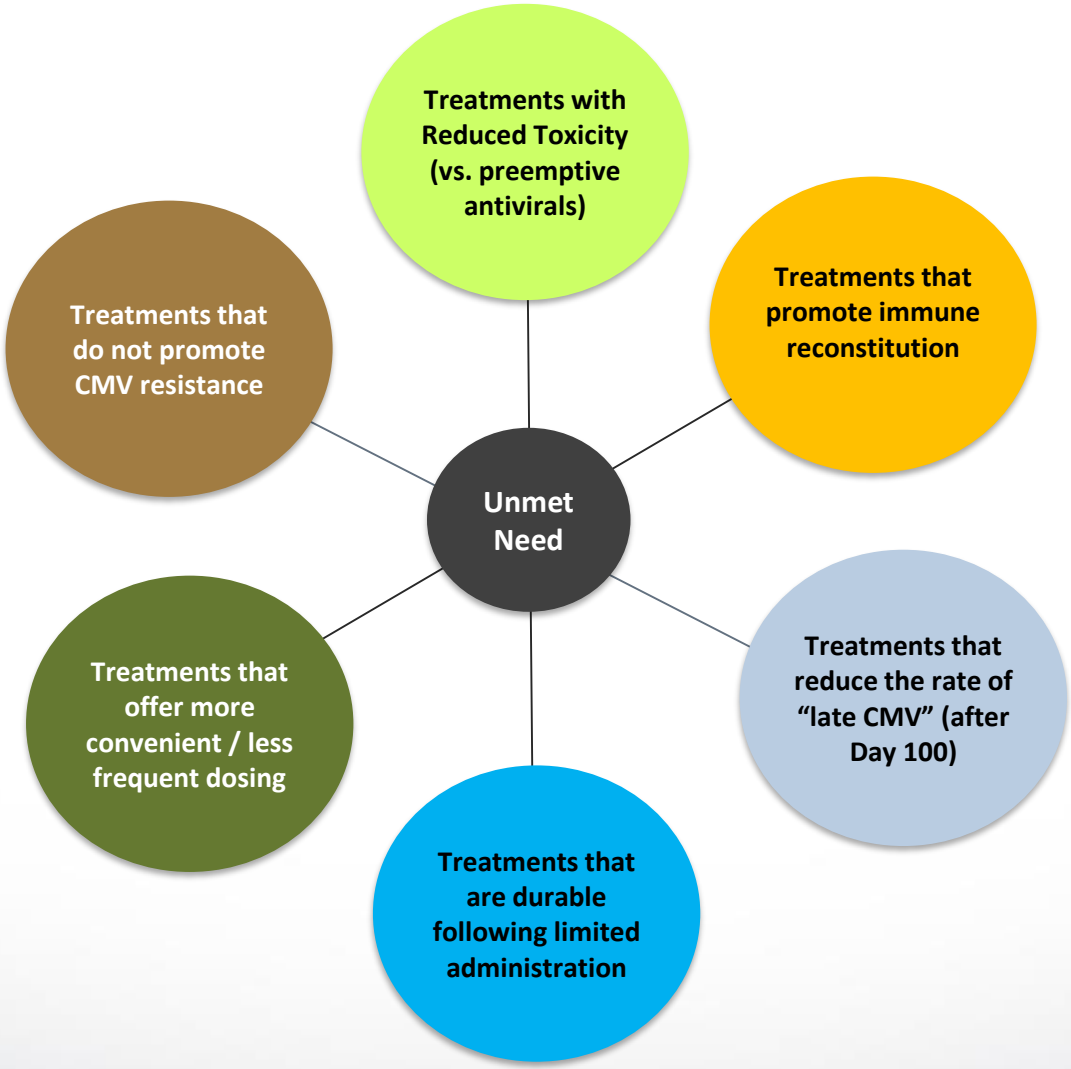
The DMC congratulates the study team on timely completion of the study.

Triplex: Development Strategy

- **Develop Across Entire Spectrum of Post-Transplant**
  - *CMV Control in Allogeneic Stem Cell Transplant*
    - Matched Related, Unrelated Donors: Phase 2 data by 4Q2018 (n=102)
    - Haploidentical Donors: Phase 2 open as of 1Q2018 (n=108)
    - Pediatric Recipients: Phase 1/2 open as of 1Q2018 (n=12+60)
    - Donor Vaccination: Phase 2 open as of 3Q2018 (n=36)
    - Future Studies: mismatched donors, cord blood, in combo with Prevymis™
  - *CMV Control in Solid Organ Transplant*
    - Patients likely more immuno-competent when vaccinated (vs. HSCTs)
    - Kidney Transplant: Phase 2 to open in 1H2019 (n=72)
    - Liver Transplant: Phase 2 to open in 2H2019 (n=72)
    - Future Studies: heart, lung transplant
  - *Autologous Stem Cell Transplant (NK Cell Reconstitution)*
    - Lymphoma / Myeloma: Phase 1/2 open as of 2Q2018 (n=20)
- **Expand to Other Non-Transplant Indications**
  - HIV: Phase 2 to open 4Q2018 (n=90)
  - In combo with CAR-Ts: City of Hope Lymphoma SPORE (2H2019)

hēlocyte

Unmet Need in Post-Transplant CMV Control
Addressed by Triplex



hēlocyte

Triplex: Standard of Care, Incidence

- **Antivirals: Standard of Care for CMV Control in Post-Transplant Setting**
  - Moderately effective, often toxic (*Black Box Warning for Preemptive*)
  - Mechanism: merely suppress CMV during course of treatment
    - Delay immune reconstitution, "late CMV" after discontinuation
  - Preemptive: upon CMV detection (weekly via PCR)
  - Prophylactic: upon transplant, see Prevymis™ (approved 11/2017)
  - Overall Burden: $58K to $74K per patient (Jain, Cytotherapy 2014)

Procedure	US Incidence	EU Incidence
Allogeneic Stem Cell Transplant	**~8,000**	**~15,000**
Solid Organ Transplant (Kidney)	**~15,000**	**~15,000**

ConVax Overview

- Universal Multi-Antigen MVA-based CMV Vaccine
- Mechanism: Humoral + Cellular Immunity
  - Neutralizing Antibody Response to: Pentamer, gB
  - T Cell Response to: pp65 + IE1
- Indication: CMV Prevention & Control
- Development Status:
  - IND-enabling studies in progress
  - Immune responses demonstrated in mice, rabbits, rhesus macaques
  - IND filing in 2019

Congenital CMV: Overview

- CMV Most Common Congenital Infection: 0.5%-2% of all pregnancies (38K in US / year)
  - Institute of Medicine ranks new vaccine as "Highest Priority"
  - Severe Complications (10-15%): hearing loss, mental retardation, retinitis

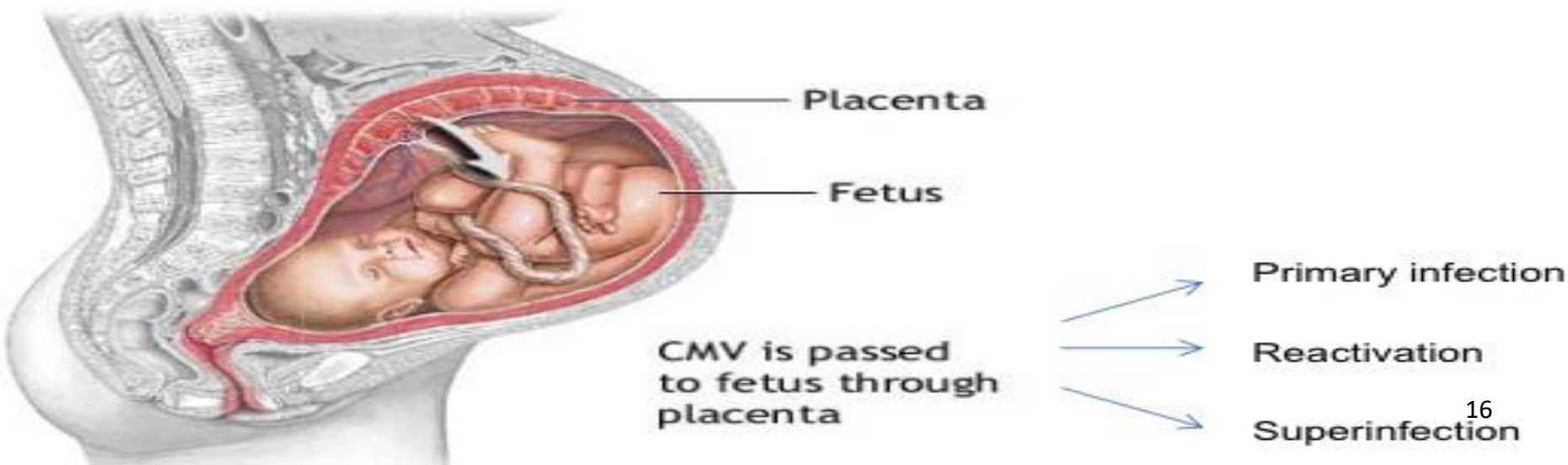
- Prevention requires humoral (NAb) response (vs. cell-mediated for HSCT, SOT)

The New York Times

HEALTH

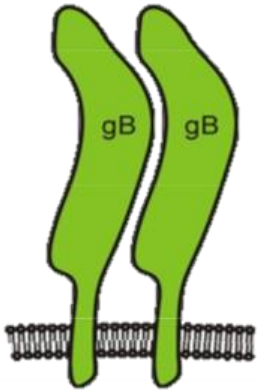
CMV Is a Greater Threat to Infants Than Zika, but Far Less Often Discussed

By CATHERINE SAINT LOUIS OCT. 24, 2016

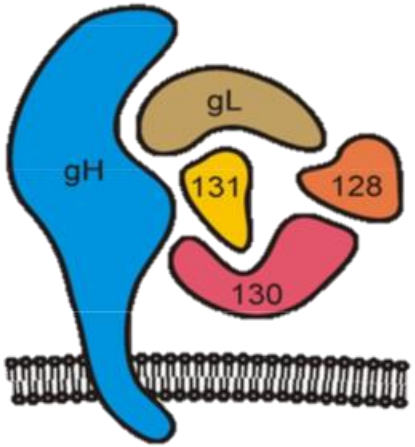


CMV Transmission Pathway

- Glycoprotein B (gB)
  - Essential for Virus Entry into Host Fibroblasts
  - Target of Neutralizing Antibodies (NAbs)
  - Fusion protein of, and triggered by, Glycoprotein H (gH)
  - Recombinant gB Subunit Vaccine (Sanofi)
    - Only ~50% Efficacy in Preventing Primary Infection



- gH/gL complex (gH/gL-PC)
  - Pentamer (gH, gL, UL128, UL130, UL131)
  - Allows Entry into Epithelial/Endothelial Cells (Epi/EC)
  - Major target of NAbs
  - Absent in Lab Strains (AD169, Towne)



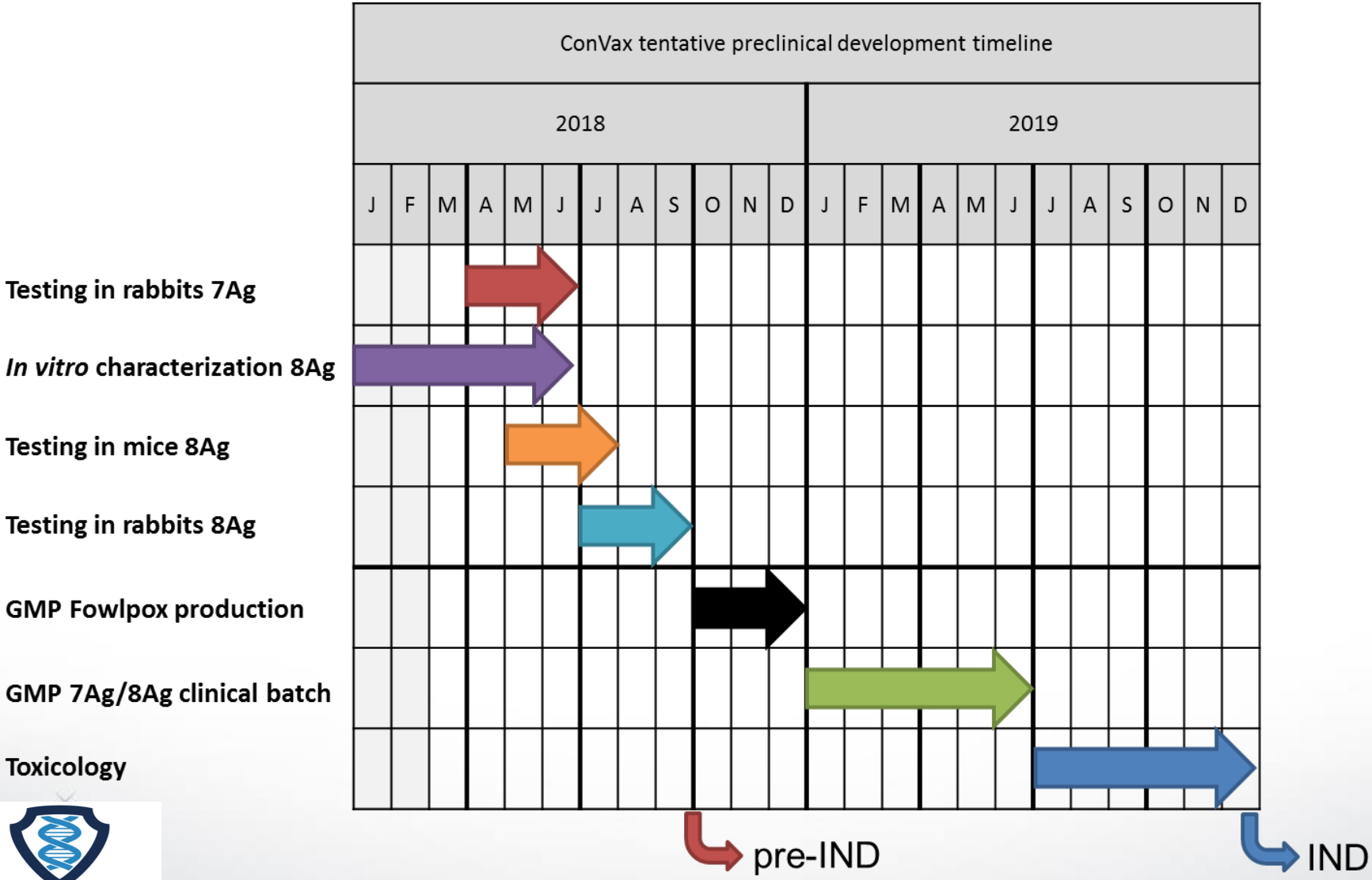
ConVax: CMV Prevention & Control

- **Overview**
  - Universal MVA-Based Vaccine Induces Humoral AND Cellular Immunity
  - Indication: prevention and control of CMV
    - Prevention: requires neutralizing antibodies (pentamer, gB)
    - Control: requires virus-specific T cells (pp65, IE1, IE2)

- **Development Candidates (3)**
  - First Vaccine Candidate (Pentamer)
    - Stable expression of six antigens (pentamer + gB)
  - Second Vaccine Candidate (Heptamer)
    - Stable expression of seven antigens (pentamer + gB + pp65)
  - Third Vaccine Candidate (Octamer)
    - Stable expression of eight antigens (pentamer + gB + pp65 + IE1)
  - Development Status
    - Tested in mouse models, rabbits, rhesus macaques
    - Robust, durable immune responses observed
    - Current Plan: enter clinic with Octamer (IND in 2019)

hēlocyte

ConVax: Non-Clinical Development Timeline



hēlocyte

Regulatory & IP Exclusivity

- Regulatory
  - Orphan Exclusivity (applicable to Triplex): 7 Years (US), 10 Years (EU)
  - Biologic Exclusivity (applicable to Triplex & ConVax): 12 Years (US), 11 Years (EU)

- Triplex IP
  - HCMV Antigens Expressed in MVA, Methods (7,163,685), expires 2024
  - rMVA Vaccines and Methods of Prep Thereof (14/075,975), expires 2030
  - rMVA Vaccines and Methods of Prep Thereof (8,580,276), expires 2031
  - Other applications relating to MVA construct extend protection to 2033
  - Patent Term Adjustment, Patent Term Extension possible

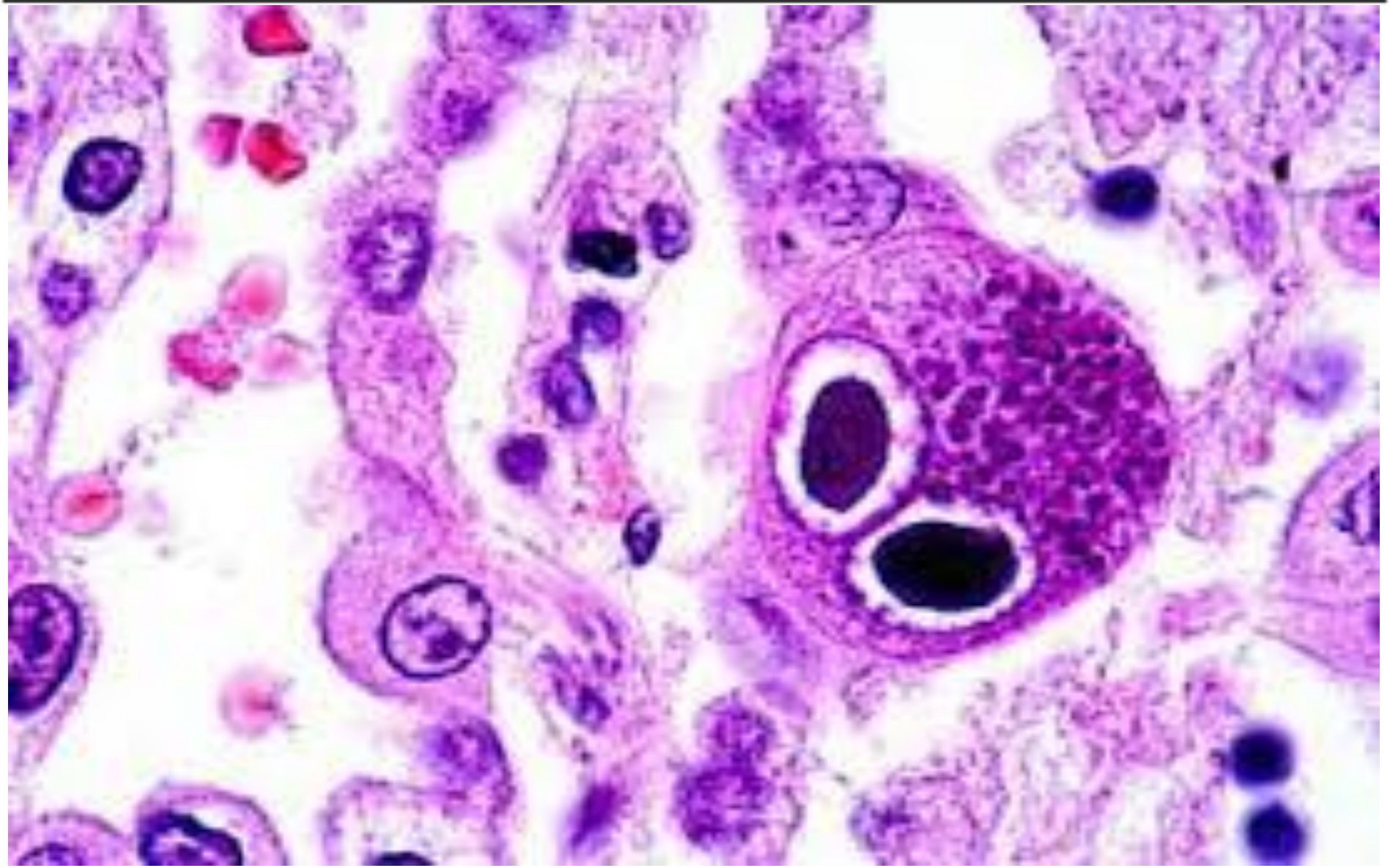
- ConVax IP
  - MVA Vaccine UL128 Complex, Methods (PCT/US2013/32554)
  - Additional IP covering new constructs filed (not yet published)

Investment Considerations

- Novel Biologic Immunotherapies Targeting $Billion Markets
- Triplex: First-in-Class, Best-in-Class Vaccine for CMV Control
  - Phase 1: Safe, Highly Immunogenic (Published in ***Blood***)
  - Phase 2: Fully-Accrued; Completion in 4Q2018
- Less Toxic, More Durable Alternative to Standard of Care (antivirals)
- Significant Grant Funding: Reduces Capital Requirements, Validates Approach

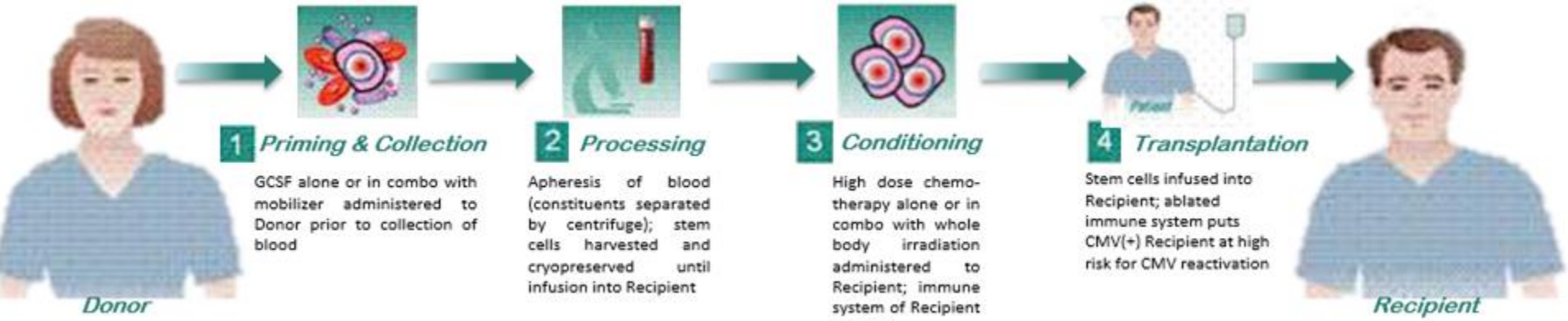
For More Information, Contact:
Frank Taffy, Co-Founder, President, CEO, Board Member
frank@helocyte.com

Backup Slides



CMV in Hematopoietic Stem Cell Transplant (HSCT)

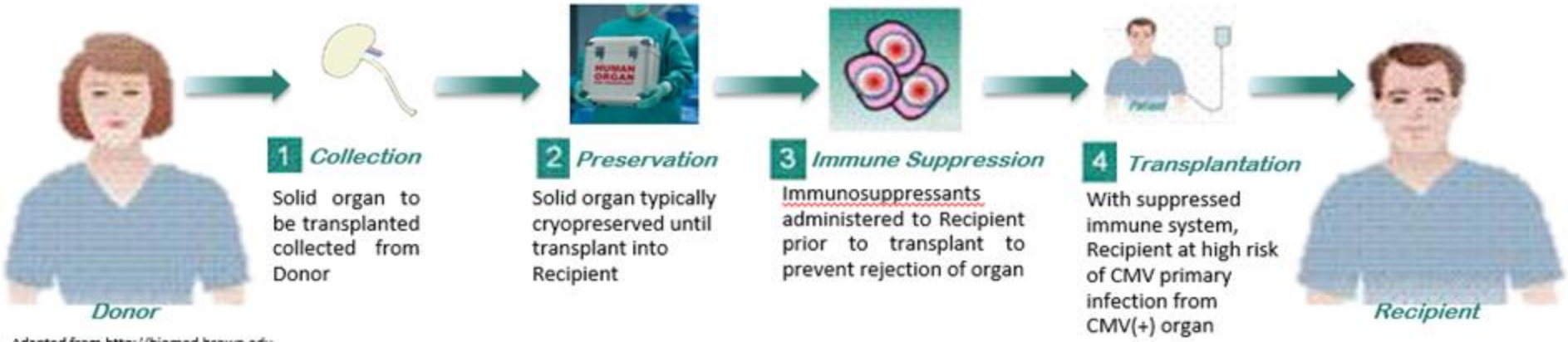
- Hematopoietic Stem Cell Transplant
  - Leading therapy for hematological malignancies (*e.g.,* chronic and acute leukemias)
  - Trend towards increased use (particularly in EU) as outcomes improve
  - Allogeneic: stem cells transplanted from healthy donor
- Process (Two Stages)
  - Conditioning: prior to transplant; high-dose chemo +/- radiation
    - Ablates bone marrow, cells needed to fight infection (CMV)
    - Immunosuppressants often administered to prevent rejection of graft, GvHD
  - Engraftment: occurs two to four weeks after transplant
    - Stem cells travel to bone marrow, produce WBCs, RBCs, platelets
    - Recovery of immune function can take 1-2 years in allogeneic HSCTs
- CMV Reactivation
  - Rate: ~30% between Days 40 and 100 after transplant; ~15% after Day 100 ("late CMV")
  - Most at Risk: seropositive allogeneic Recipient (R+), regardless of Donor status (D+/-)



Adapted from http://biomed.brown.edu

CMV in Solid Organ Transplant (SOT)

- Solid Organ Transplant
  - Recipients receive immuno-suppressants to prevent organ rejection, GvHD
- Process
  - Organ collected from Donor and cryopreserved until transplantation
  - Preserved, allogeneic organ transplanted into immunosuppressed Recipient
- CMV Infection
  - Rate: >50%, most common infectious complication after SOT
    - Most at Risk: seropositive Donor (D+), seronegative Recipient (R-); results in primary infection
    - Risk Factors: size of organ transplanted (viral load); level of immunosuppression (type, dose)



Adapted from http://biomed.brown.edu

MVA as Delivery Vehicle

- Vaccinia strain *Ankara* passaged 570x in CEF (re-named Modified Vaccinia *Ankara)*
  - Propagates only in CEF but replicates DNA and prolific expression in eukaryotes
  - Head-head comparison to ALVAC™ shows superior immunogenicity
    - *Zhang et al, JVi 2007*

- Human MVA studies conducted in Germany in 1970's
  - 120K+ individuals (children, elderly) vaccinated
  - No significant adverse events reported

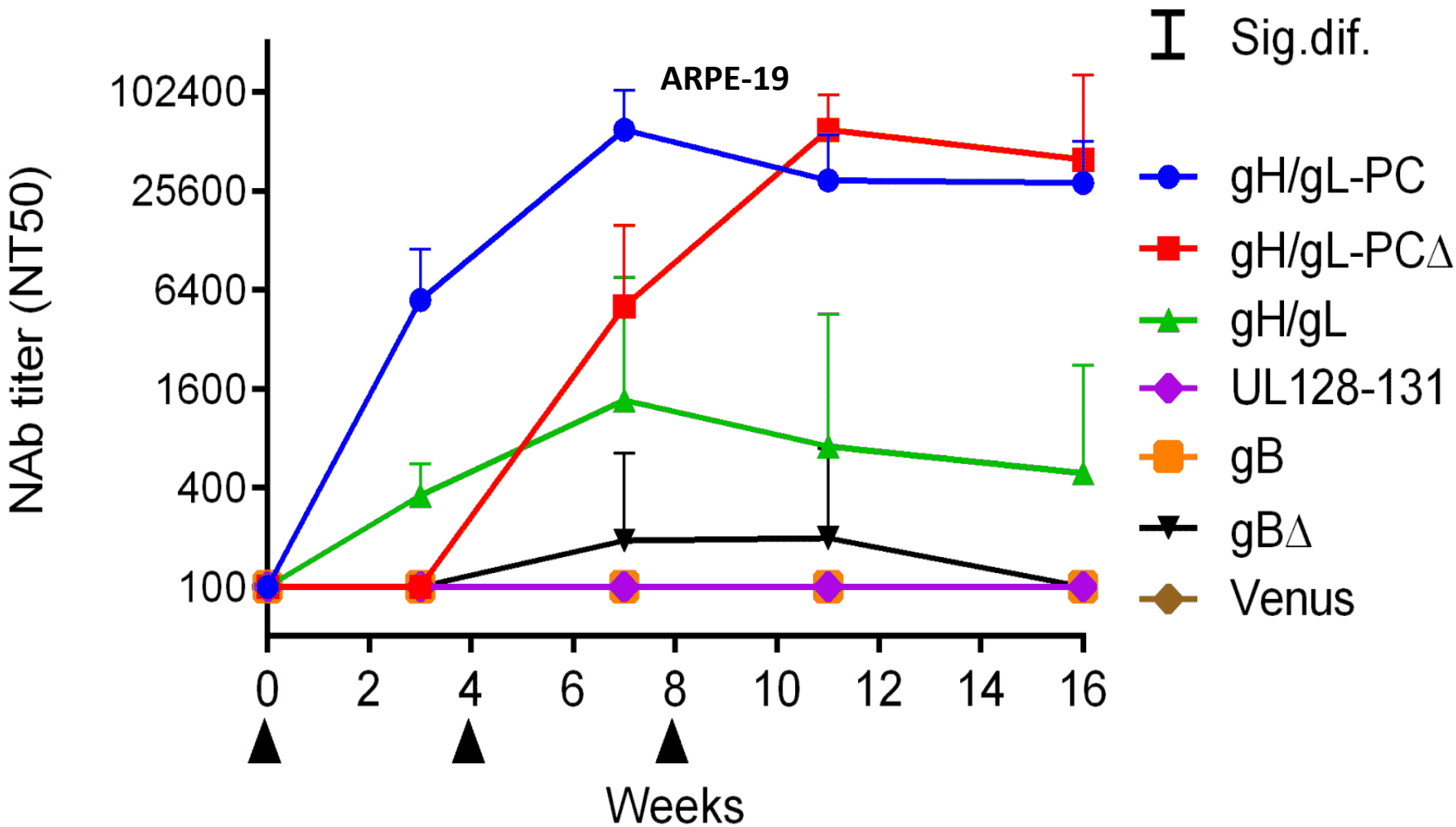
- Recent study by VRC shows safety in healthy vaccinia naïve and immune adults

- European study shows safety after immunization in HIV-infected adults

- Pre-clinical studies in R. macaques shows no propagation, pathogenesis in immunosuppressed animals

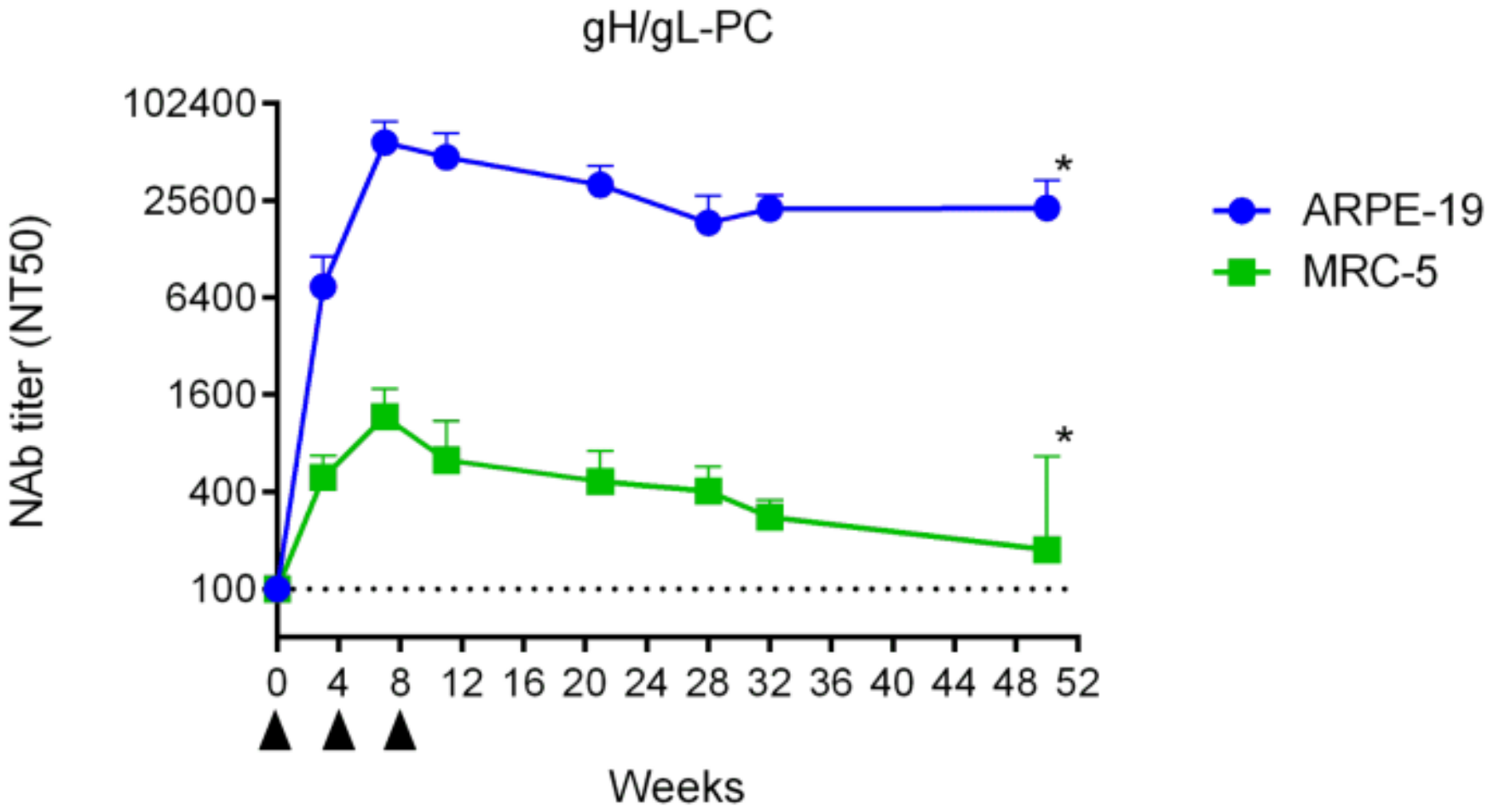
- PK studies shows rapid disappearance of the viral DNA within 6 weeks of administration

ConVax Stimulates Superior Murine NAbs: Inhibits HCMV Infection of Epithelial Cells



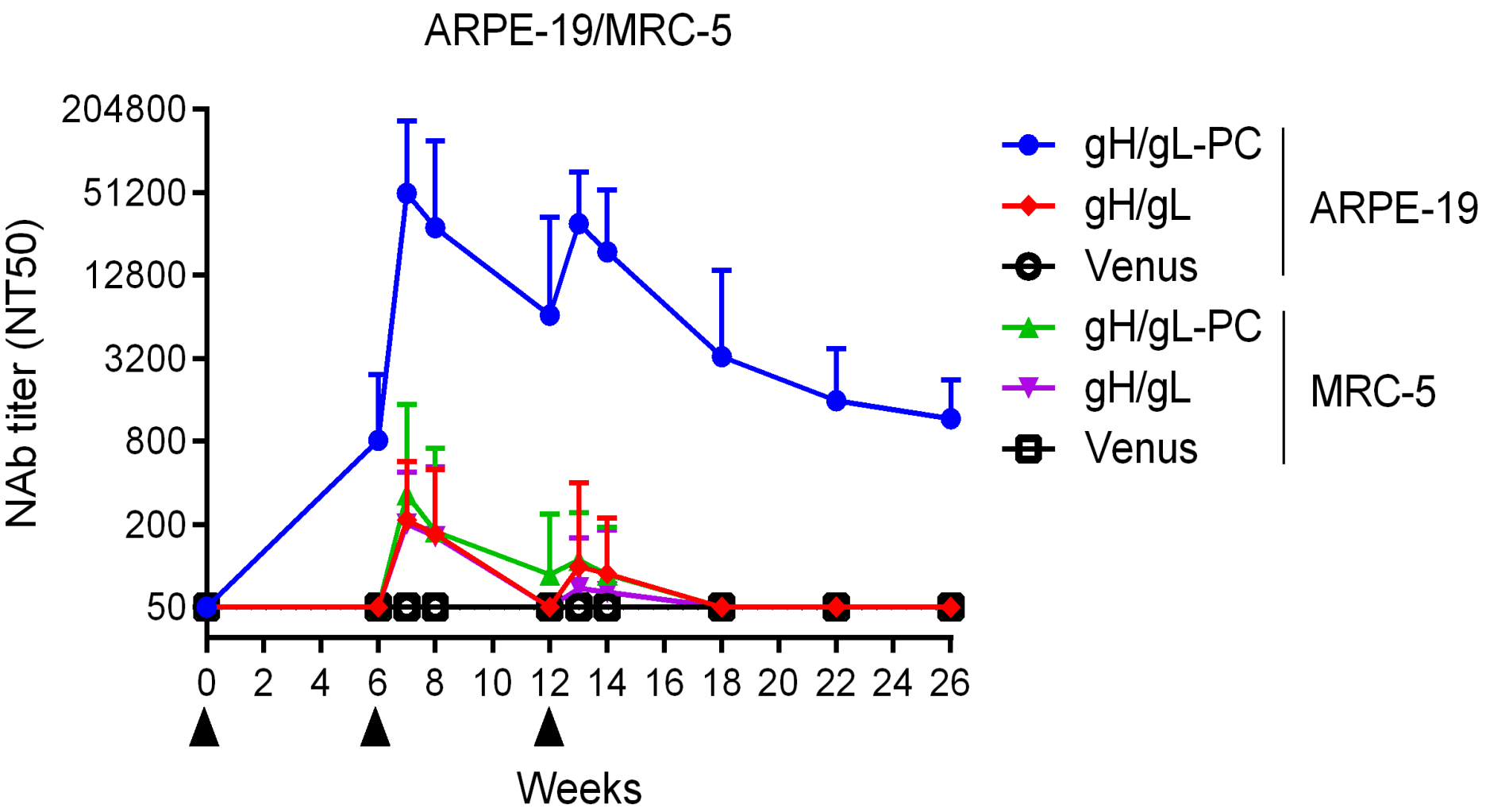
Wussow et al, PLOS Pathogens, 2014

ConVax: Durability of Murine NAbs



Wussow et al, PLOS Pathogens, 2014

ConVax Stimulates Superior Rhesus Macaques NAbs: Inhibits HCMV Infection of Epithelial Cells, Fibroblasts



Wussow et al, PLOS Pathogens, 2014