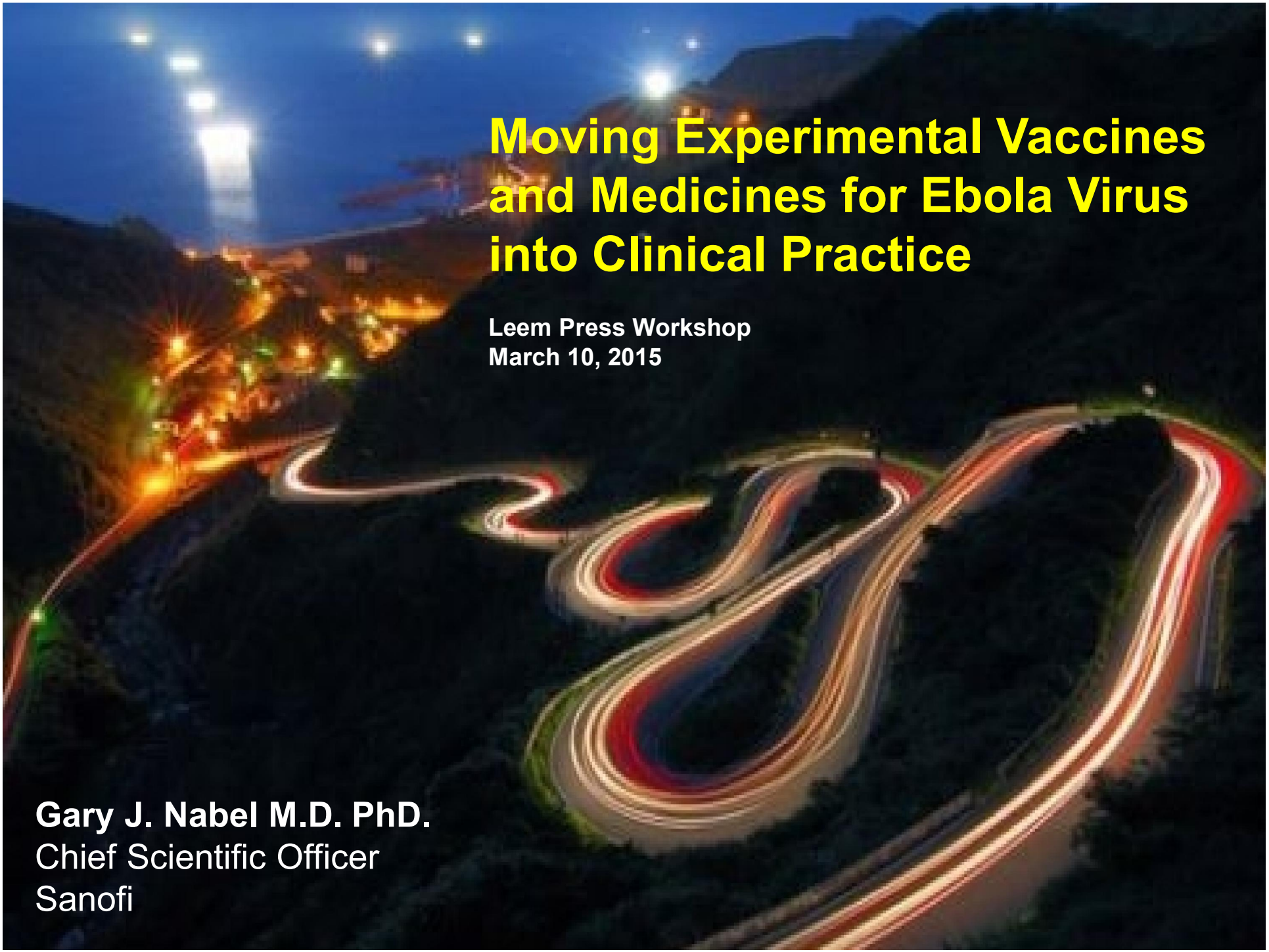
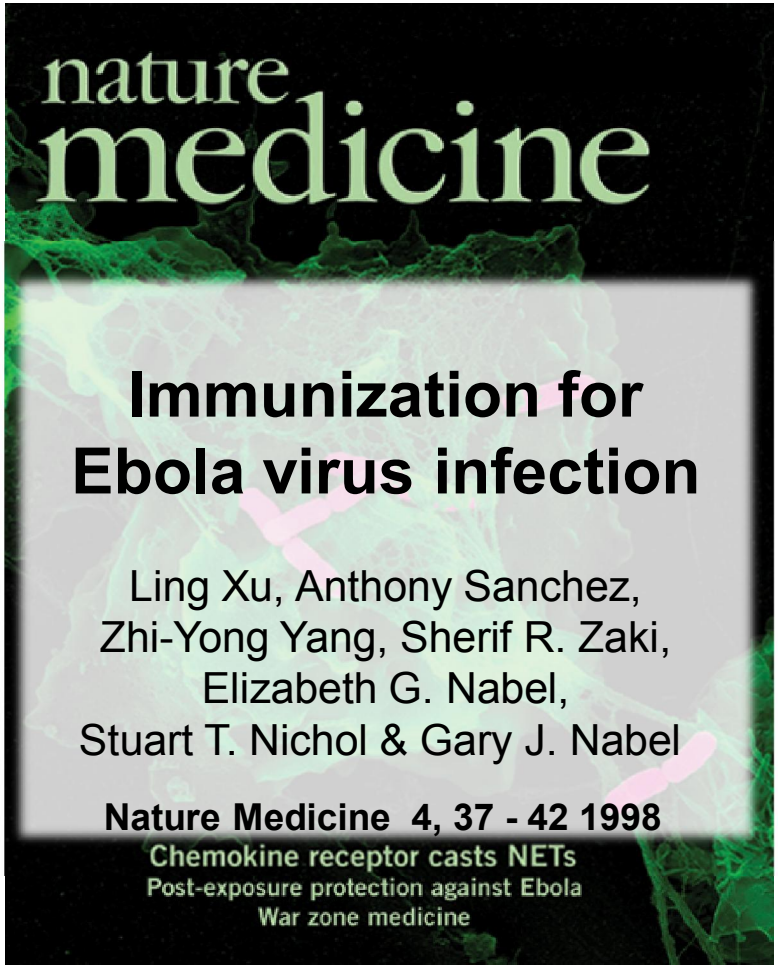


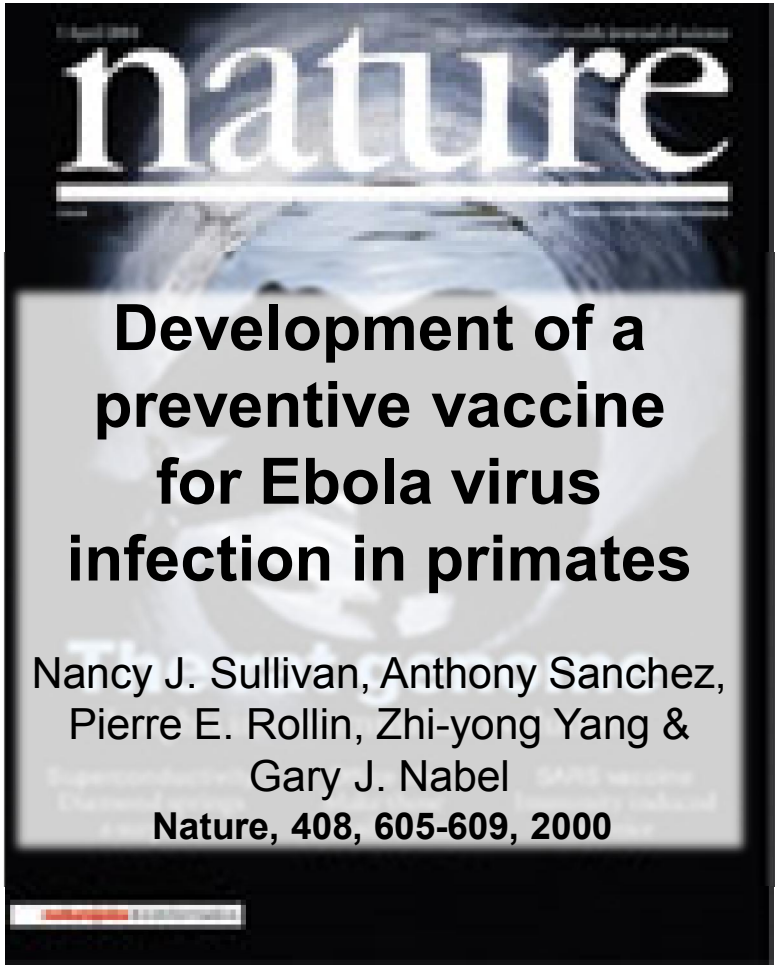
Moving Experimental Vaccines and Medicines for Ebola Virus into Clinical Practice

Leem Press Workshop
March 10, 2015

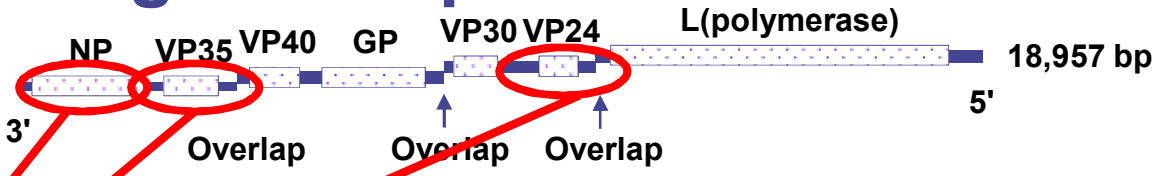
Gary J. Nabel M.D. PhD.
Chief Scientific Officer
Sanofi

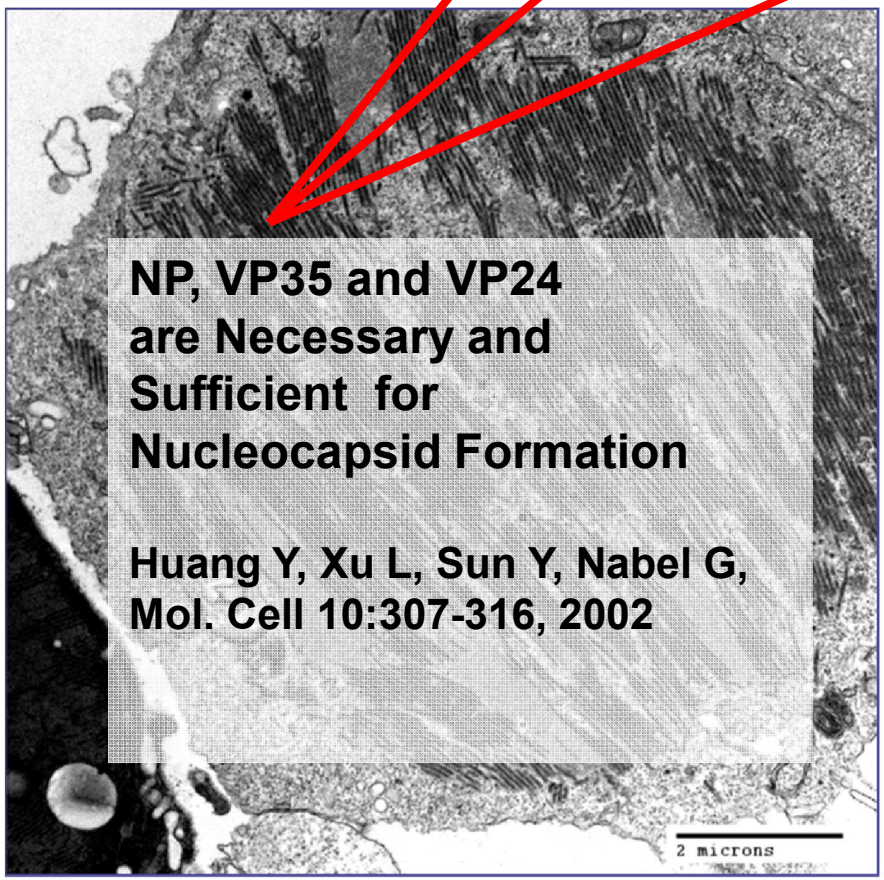
Gene-based vaccination for Ebola Virus





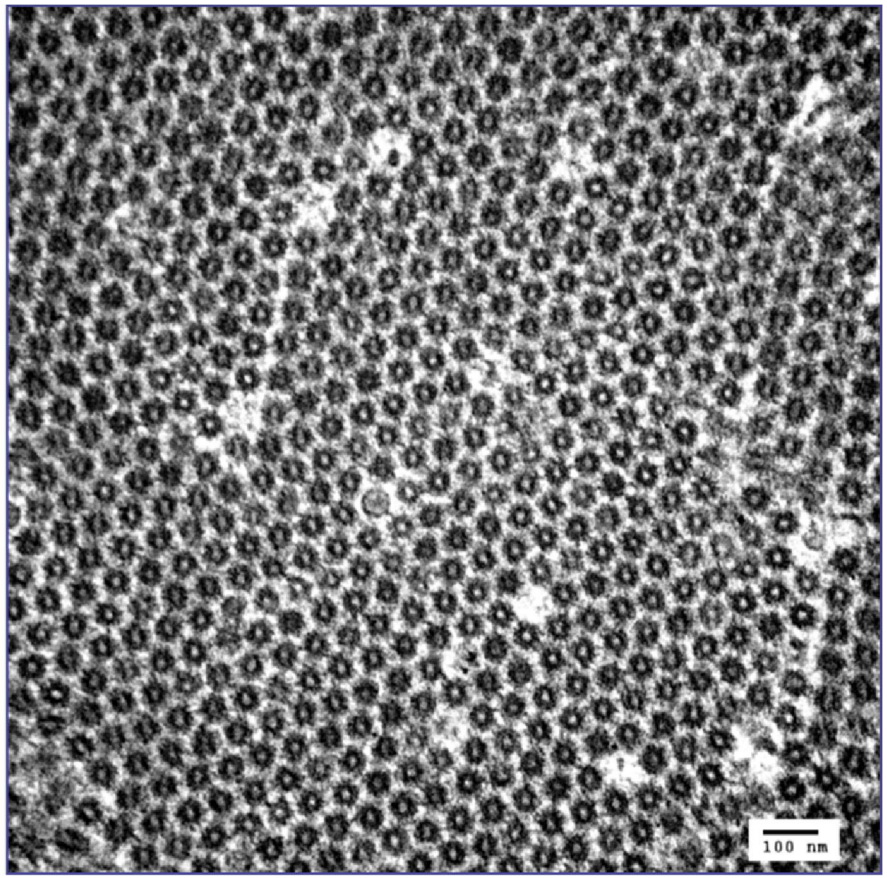
The Genetic Economy of Ebola Virus- a Tool for Vaccine and Drug Development





NP, VP35 and VP24 are Necessary and Sufficient for Nucleocapsid Formation

Huang Y, Xu L, Sun Y, Nabel G, Mol. Cell 10:307-316, 2002



Longitudinal

Transverse

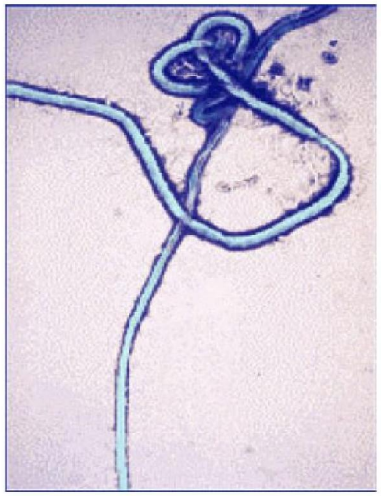
NIH NEWS RELEASE

Tuesday, November 18, 2003

National Institutes of Health

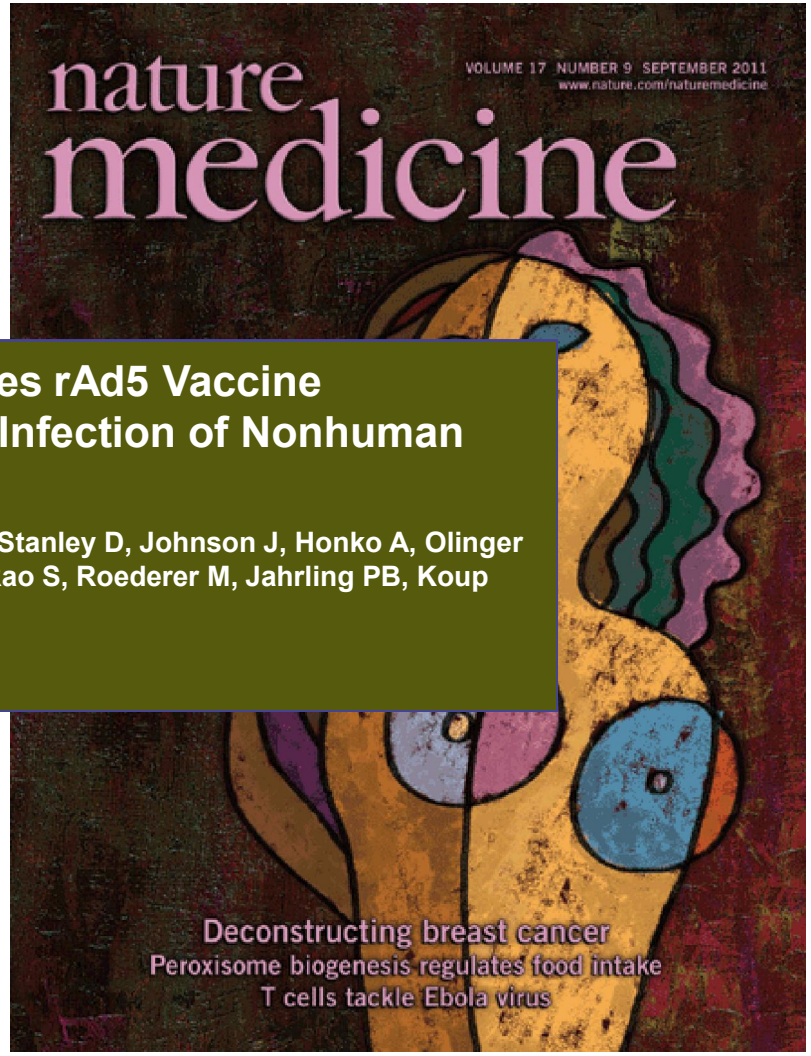
National Institute of Allergy and Infectious Diseases

NIAID Ebola Vaccine Enters Human Trial



The first human trial of a vaccine designed to prevent Ebola infection opened today. Scientists from the Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), one of the National Institutes of Health (NIH), designed the vaccine, which was administered to a volunteer at the NIH Clinical Center in Bethesda. The vaccine does not contain any infectious material from the Ebola virus.

CD8 Cells Mediate Ad Vaccine Protection Against Ebola

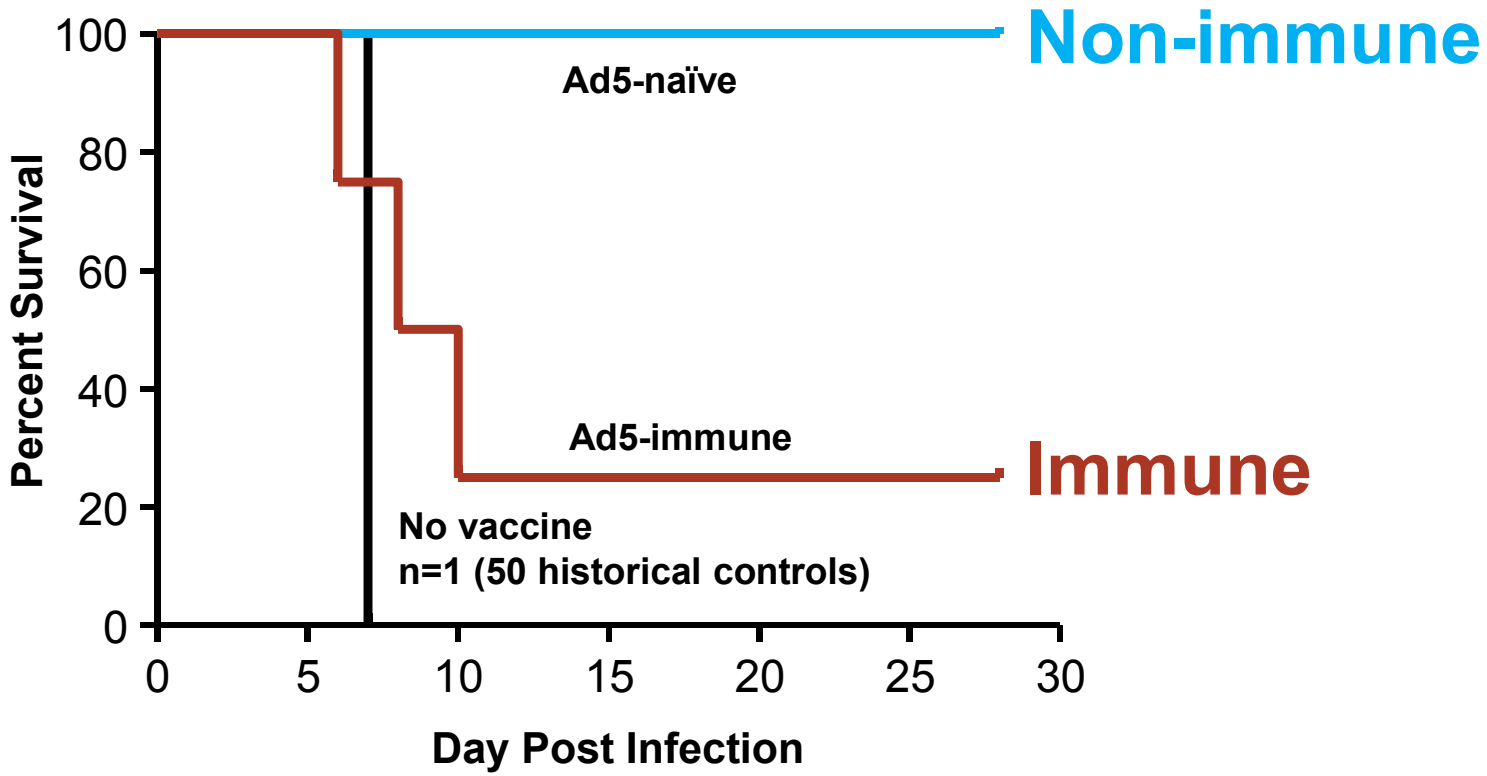


CD8+ Cellular Immunity Mediates rAd5 Vaccine Protection Against Ebola virus Infection of Nonhuman Primates.

Sullivan NJ, Hensley L, Asiedu C, Geisbert TW, Stanley D, Johnson J, Honko A, Olinger G, Bailey M, Geisbert JB, Reimann KA, Bao S, Rao S, Roederer M, Jahrling PB, Koup RA, Nabel GJ.

Nat Med. 2011 Aug 21;17(9):1128-31.

Pre-existing Ad5 Immunity Abrogates Ebola Vaccine Protection in NHP



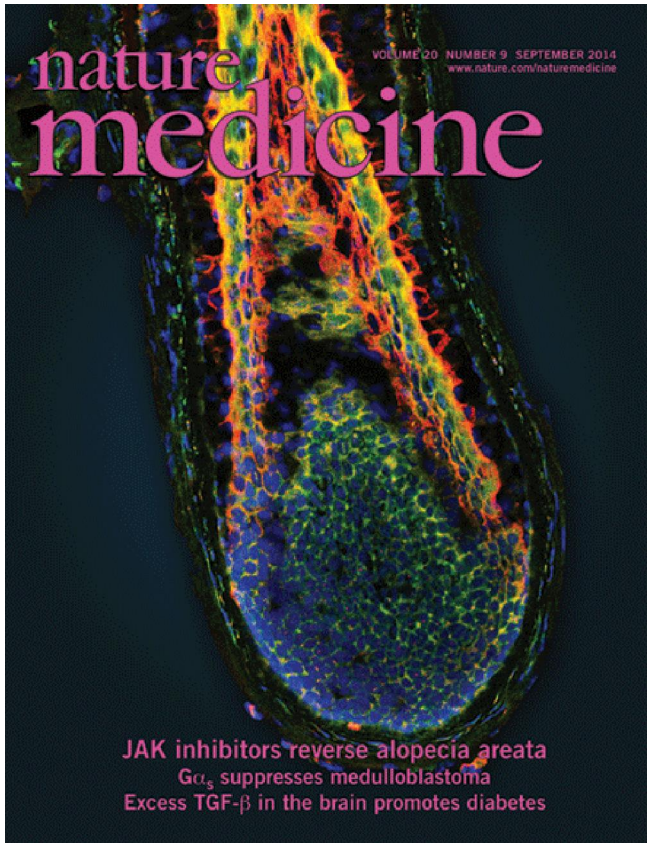
- Ad5-immune and –naïve macaques
- Vaccinate with rAd5-GP
- Immune response and challenge at 4 wks

Definition of an Ebola Vaccine with Rapid Onset and Durable Protection in Monkeys

ChAd3 Prime MVA Boost

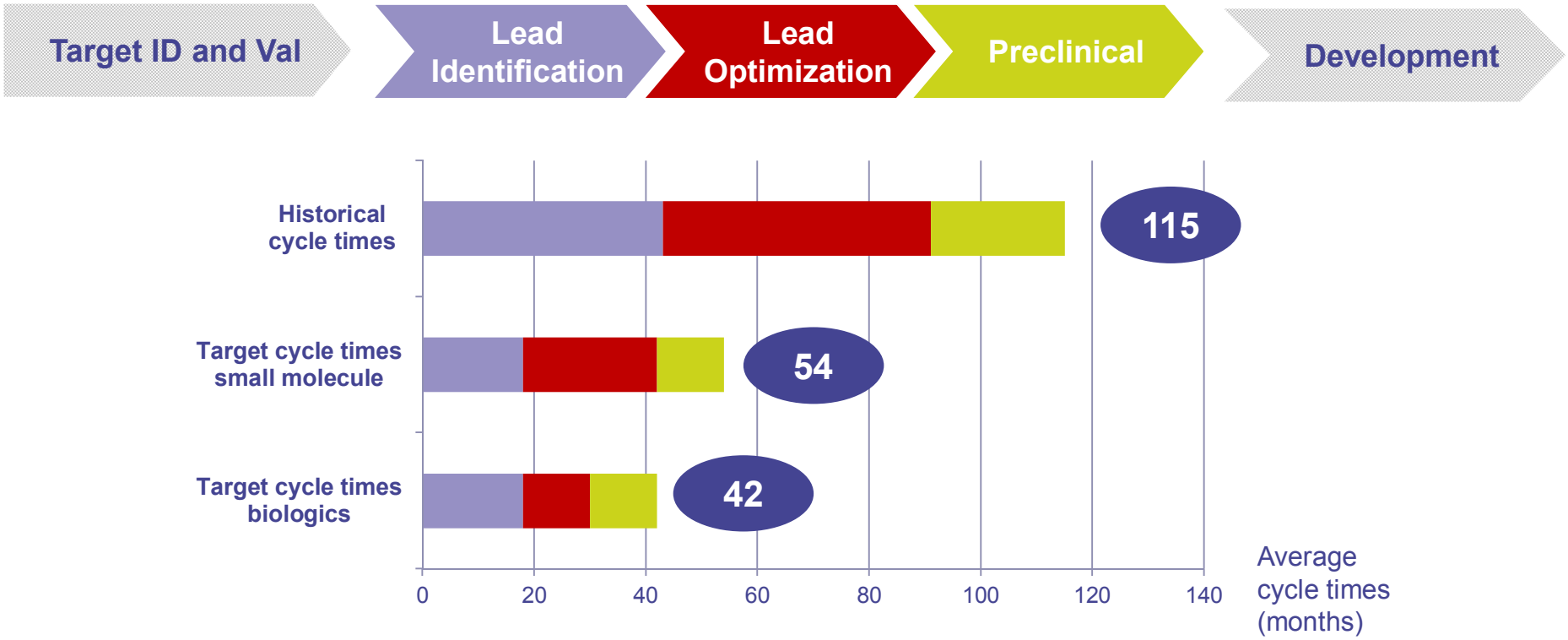
Chimpanzee adenovirus vaccine generates acute and durable protective immunity against ebolavirus challenge

Daphne A Stanley[1], Anna N Honko[2,7], Clement Asiedu[1,8], John C Trefry[2], Annie W Lau-Kilby[1], Joshua C Johnson[2,7], Lisa Hensley[2,7], Virginia Ammendola[3], Adele Abbate[3], Fabiana Grazioli[3], Kathryn E Foulds[1], Cheng Cheng[1], Lingshu Wang[1], Mitzi M Donaldson[1], Stefano Colloca[3], Antonella Folgori[3], Mario Roederer[1], Gary J Nabel[1,7], John Mascola[1], Alfredo Nicosia[3–5], Riccardo Cortese[6], Richard A Koup[1] & Nancy J Sullivan[1]



Received 18 August; accepted 2 September; published online 7 September 2014;
doi:10.1038/nm.3702

Pharmaceutical Drug and Vaccine Development-A Slow Process



Sanofi names chief scientific officer Gary Nabel as Sanofi Ebola response coordinator

Monday, November 24, 2014 02:30 PM

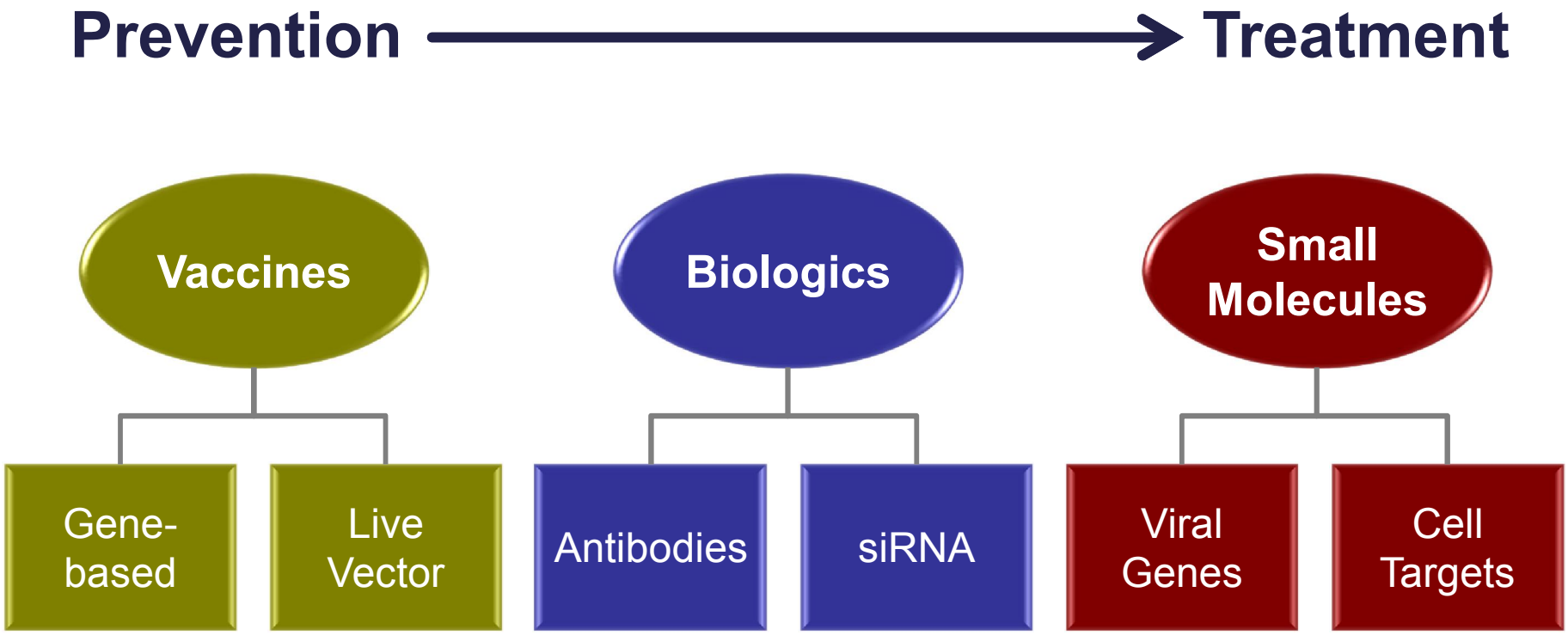
As part of its contribution to the global response to the Ebola epidemic, Sanofi has appointed chief scientific officer Dr. Gary J. Nabel, M.D., Ph.D., as its Ebola response coordinator.

In his mission, Dr. Nabel will identify how Sanofi can help advance countermeasures to contain the current outbreak and prioritize and foster opportunities to develop novel treatments for the future.

"Given his past experience in public health epidemics as director of the NIH Vaccine Research Center and his leadership in developing an Ebola vaccine at NIH, Nabel is uniquely qualified for this position," said Dr. Elias Zerhouni, M.D., president of Sanofi Global R&D. "Nabel is working with other organizations, including providing guidance to researchers based on the company's extensive experience in vaccine and drug development, to determine how Sanofi can assist in making progress with this global challenge."

"Working with our colleagues across the industry, Sanofi is helping to find ways to advance medicines to prevent or treat Ebola virus infection. We also are sharing our scientific, medical, regulatory and manufacturing expertise with the World Health Organization, government and non-governmental organizations—public and private—in an effort to contain this epidemic,". Nabel said.

A Spectrum of Ebola Countermeasures
From Vaccines to Anti-virals



Sanofi Priorities for Ebola Virus Countermeasures

Tier 1

Vaccines/Antivirals Already in Clinical Trials

Tier 2

Proof of Concept in NHP Not in Clinical Development

Tier 3

Antiviral activity but no NHP proof of concept

Diverse Target Product Profiles

	Modality		
Prophylaxis (Pre or Post Exposure)	Vaccines	Biologics	Small Molecules
Treatment, EBOV+ (early symptoms)	Vaccines	Biologics	Small Molecules
Ebola VHF (late stage)	Vaccines	Biologics	Small Molecules

PHRMA Response to Ebola Outbreak: Ebola Response Coordination Team (ERCT)

- Organized by BMAC Co-Chairs Elias Zerhouni and Tachi Yamada
- Chaired by Gary J Nabel, Sanofi CSO,
- Other Members:

Mark Feinberg, MD, PhD, Chief Public Health and Science Officer, Merck Vaccines, Merck & Co., Inc.
John Houston, PhD, Senior Vice President, Disease Sciences and Biologics, Bristol-Myers Squibb
Dale Kempf, PhD, Director of Antiviral Research, AbbVie
Machelle Sanders, MHA, Vice President, Manufacturing & General Biogen Idec Inc.
Jonathan "JZ" Zalevsky, PhD, Head, Immunology Research, Takeda Pharmaceuticals U.S.A., Inc.

Ex officio (PHRMA): Bill Chin-Executive VP: Scientific and Regulatory Affairs

Sanofi and PHRMA Ebola Activities

- Participated in Hever Group Ebola Medicines Day
  - **November 24, 2014**
  - **Pharma, biotech and government representatives developed a Global Call for clinical compounds to be tested in the NIH and USAMRIID Ebola Screening Cascades**
- Reviewed External Requests for Support of Discovery Programs

Sanofi Contributions

- 136 compounds identified for screening at USAMRIID

- 5 Biotech/Academic groups referred to USAMRIID for further testing.

Policy and Regulatory Concerns

Indemnification

Vaccines/Prevention

Anti-Viral Therapy

Clinical Trials

Specific for TPP's

POC in humans

Efficacy Studies (Placebo Controlled, Adaptive)

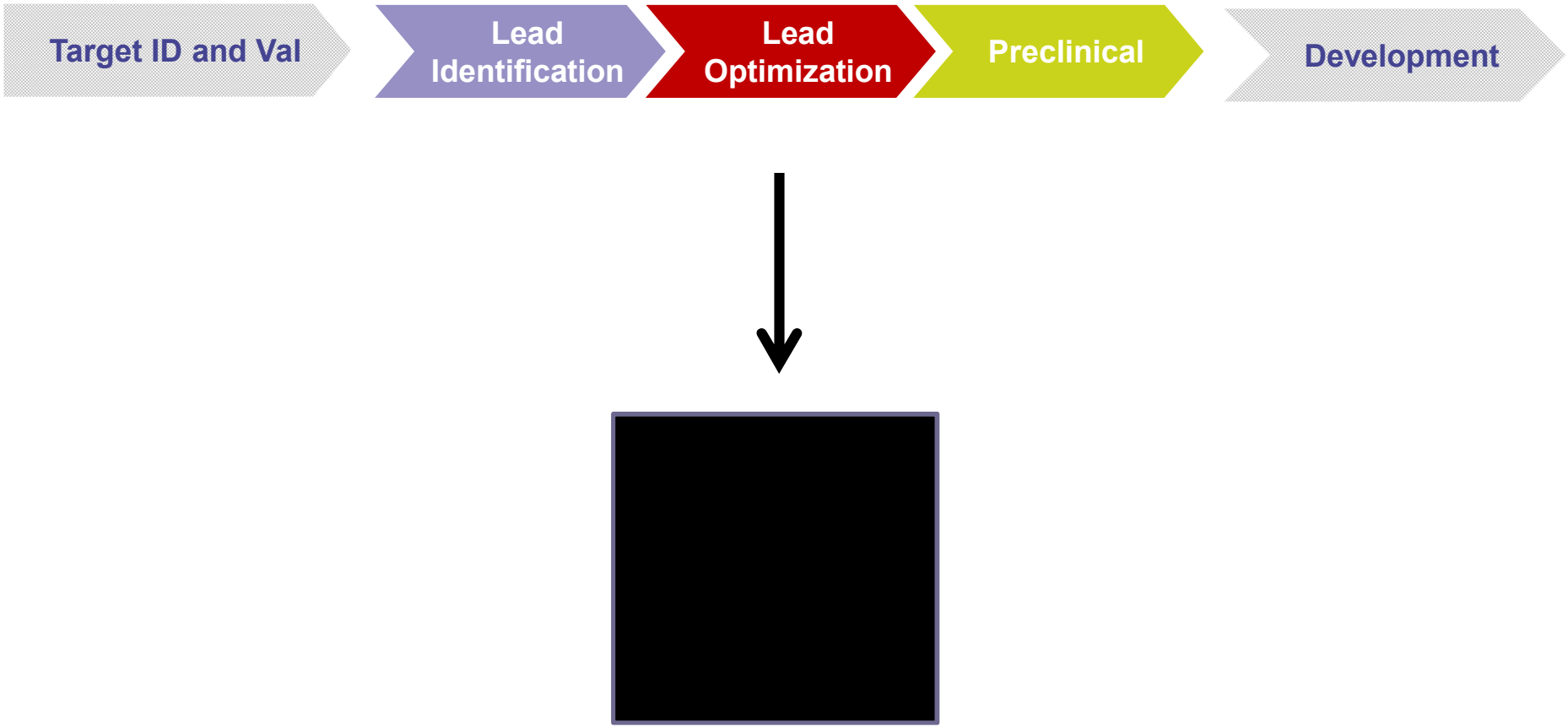
Licensure Requirements

Ethics

Ethical Review Committees

Informal Consent

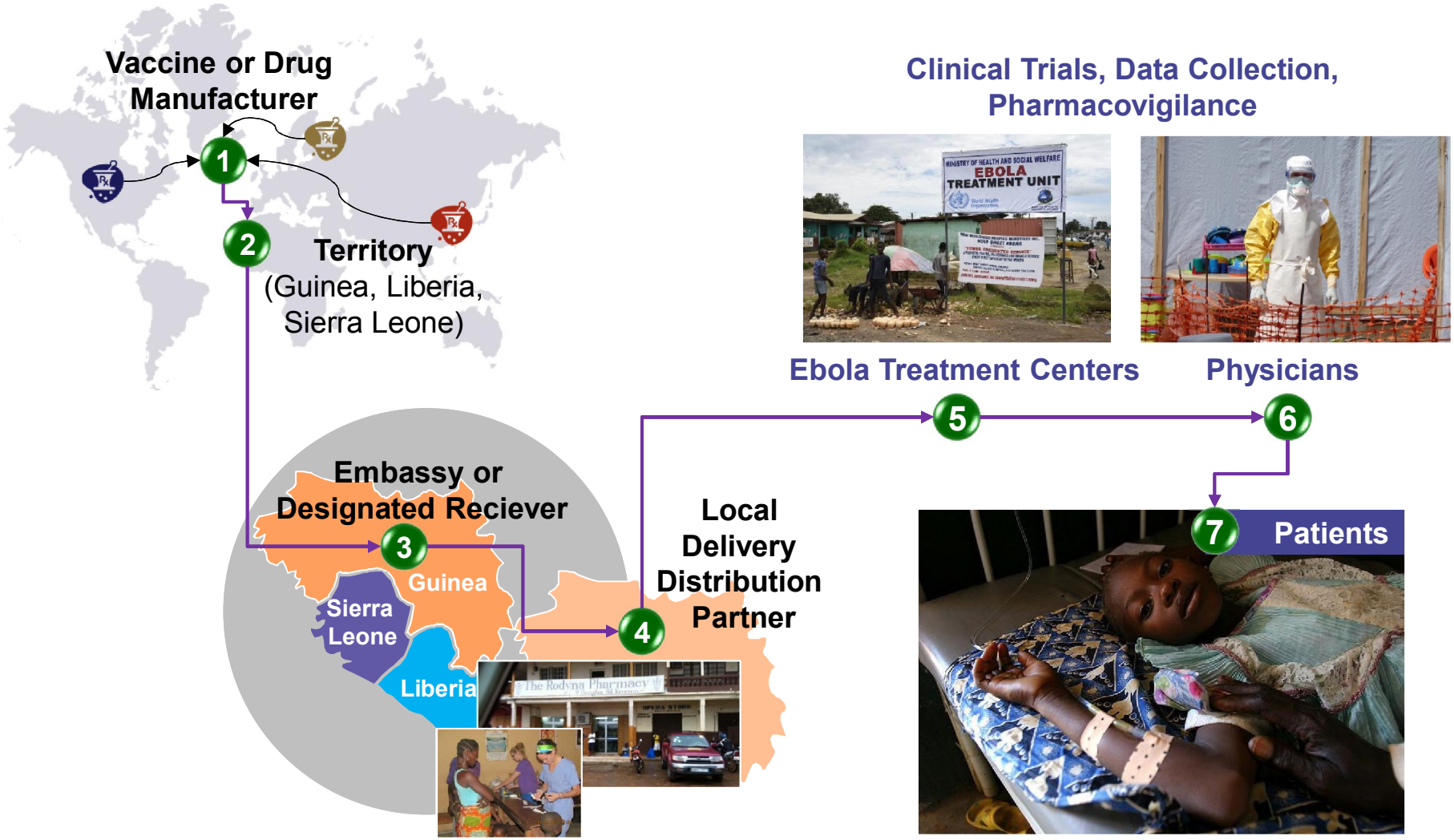
Licensure is only one step in combating disease



Manufacturing

- Production Capacity
- Reagents for Testing and Lot Release
- Formulation
- Delivery Strategies

Managing the Flow of Ebola Drugs or Vaccines to Patients



Galaxies Colliding: Countering Emerging Infectious Diseases

Public Health Impact

Sustainable Funding/Commitment

The challenge facing countermeasures for emerging pathogens

21

Summary

1. Ebola virus is a prototypic filovirus with high lethality that is readily spread by human contact during active infection.

2. Ebola mortality is multifactorial, driven by viral cytopathicity for hepatocyte, reticuloendothelial, and endothelial cells whose damage ultimately causes septic shock.

3. It is possible to generate protective immunity to Ebola by vaccination. The cellular immune response plays a critical role in mediating protection. The antibody response correlates but is not responsible for immunity.

4. Two vaccine candidates are progressing in clinical trials. Antiviral therapies, including antibody (ZMapp) and anti-sense oligonucleotides, are in evaluation but are yet unproven in humans.

5. In the interim, barrier precautions and containment represent the key public health tools to control Ebola virus spread.