



ASPR
ASSISTANT SECRETARY FOR
PREPAREDNESS AND RESPONSE

OVERVIEW: ZIKA VACCINES IN DEVELOPMENT

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Atlanta, GA

Prevention of ZIKV Infection

There is currently no licensed ZIKV vaccine available, however...

- Vaccines for other flaviviruses have been developed and used for over 70 years
- Active development programs for Dengue and West Nile vaccines have been ongoing for over 30 years; however, knowledge of Zika virus was limited at the outset of the epidemic
- Past experience is being leveraged for ZIKV vaccine development
- Zika R&D efforts accelerated greatly by NIAID, WRAIR, and BARDA
- A coordinated, interagency portfolio management team was established to oversee and accelerate vaccine development



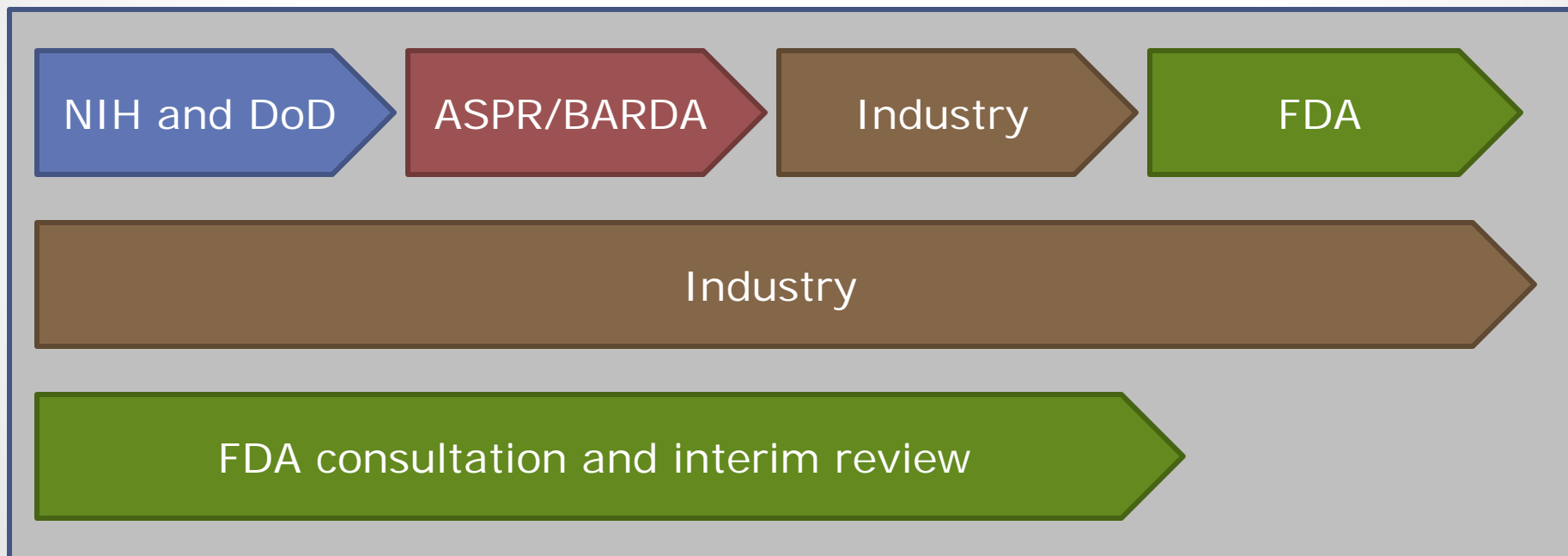
Product Development Pipeline

**Early Concept
and Product
Development**

**Advanced
Product
Development**

**Commercial
Manufacturing
and Licensure**






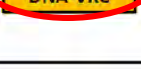

**Regulatory
Review**



Adapted from AS Fauci/NIAID



Vaccine Landscape Feb 2016

Platform	Research & Discovery	Preclinical	Phase 1
Recombinant or Subunit	 		
Live Attenuated	 		
Whole Virus Inactivated			
Nucleic Acid	 		
Viral Vector			
Other			

USG
Funded



US Zika Vaccine Goals

2016-2018

Aim #1: Evaluate available vaccine candidates to assess safety, efficacy, and immunogenicity and identify protective immune correlates during the time of highest disease incidence

By 2018

Aim #2: Deploy an available vaccine under an appropriate regulatory mechanism to US populations at high risk of exposure

By 2020

Aim #3: Work with industry partners to commercialize vaccine(s) for broad distribution



General Considerations on Vaccine Technologies

Technology	Pros	Cons	Licensed Human Flavivirus Vaccines
Nucleic Acid (DNA, mRNA)	Simple process development/mfg. Potential for rapid response capability.	No DNA or mRNA vaccines licensed for human use. Limited experience at commercial scale.	No
Whole Virus Inactivated	Commercial platforms exist. Inactivated vaccines approved for other indications.	May need several doses and adjuvant. Need large production requirement.	Japanese Encephalitis, Tick Borne Encephalitis
Live Attenuated (including flavi-chimeras)	Commercial platforms exist.	Generally contraindicated in pregnant women and very young children.	Yellow fever, Dengue, Japanese Encephalitis
Viral Vectors	Viral-vectored vaccines in advanced trials for other diseases. Commercial platforms exist.	Safety concerns in pregnant women, depending on replication competency.	No
Recombinant/ Subunit	Low risk. Several commercial platforms exist.	Some difficulty depending on the platform, e.g. protein folding. Use of adjuvants may increase concerns.	No

Alignment of USG Candidates

Primary Aim	Current USG Candidates			
Aim #1: Evaluation of candidates to obtain correlate	DNA <i>VRC, Partner TBD</i>	mRNA <i>VRC, BARDA, Moderna</i>	PIV <i>WRAIR, NIAID, BARDA</i>	
Aim #2: Deploy vaccine to "at risk" US population	DNA <i>VRC, Partner TBD</i>	mRNA <i>BARDA, Moderna</i>		
Aim #3: Commercialization of global, durable vaccine	PIV <i>WRAIR, NIAID, BARDA, Sanofi</i>	PIV <i>BARDA, Takeda</i>	mRNA <i>BARDA, Moderna</i>	Live Attenuated Zika Chimera <i>LID, Butantan</i>
Additional Candidates In Development	VSV Vecteded Vaccine <i>NIAID, Harvard, No Partner</i>	Chimera <i>CDC, No Partner</i>	VLP <i>CDC, No Partner</i>	
	mRNA <i>VRC, GSK</i>	PIV <i>BARDA, Butantan</i>		
<i>Other candidates are in early development</i>				

Note: Candidates from Aim 2 can be used to address Aim 3



Nucleic Acid Vaccines

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News Release

NIH Begins Testing Investigational Zika Vaccine in Humans

- DNA vaccine developed by VRC
- Phase I trial to enroll 80 vols ages 18-35 yo
- Initial results expected by the end of 2016



AS Fauci/NIAID

Accelerated Planning: Phase 2/2b

Zika DNA Vaccine Candidate

A Phase 2b, Randomized, Placebo-Controlled Trial to Evaluate the Safety and Immunogenicity of a Zika Virus DNA Vaccine
Healthy Volunteers Ages 15-35



30+ sites in the US, Caribbean, Central and South America

REVISED VRC 705 Injection Schema

Part A

Group	Subjects	Total Dose	Divided over Number of Injections	Location of Vaccination: Number of Limbs	Day 0	Week 4	Week 8
1	30	4 mg	2	2 limbs (both arms)	DNA	DNA	DNA
2	30	4 mg	4	4 limbs (both arms and legs)	DNA	DNA	DNA
3	30	8 mg	4	4 limbs (both arms and legs)	DNA	DNA	DNA
Total	90	Injections are administered IM by needleless injection device.					

Part B

(To begin accrual following analysis of preliminary data from Part A)

Group	Subjects	Total Dose	Divided over Number of Injections	Location of Vaccination: Number of Limbs	Day 0	Week 4	Week 8
4	1200	TBD	TBD	TBD	DNA	DNA	DNA
5	1200	TBD	TBD	TBD	Placebo	Placebo	Placebo
Total	2400*	Injections are administered IM by needleless injection device.					

*Accrual up to a total of 5000 subjects (randomized 1:1 into Groups 4 and 5) is permitted if additional subjects are necessary for safety and efficacy evaluations.

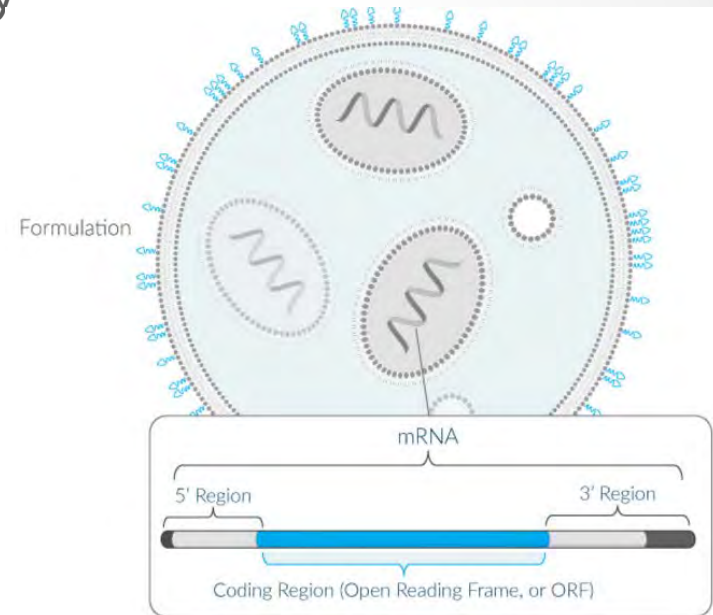
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mRNA Vaccine

Moderna Therapeutics

- Synthetic mRNAs used to deliver virtually any gene
- “Plug and play” technology
- Novel chemistry enables mRNA to elude intracellular innate immune responses
- Once in cell, acts like a native mRNA to express foreign gene
- Robust, protective immunological responses in animal models
- Simple needle and syringe delivery
- Phase I initiated in December 2016 – currently enrolling



Purified Inactivated Vaccines

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Zika Purified Inactivated Vaccines (ZPIV)

- Two candidates in advanced development: Sanofi Pasteur and Takeda
- Formalin-inactivated Zika virus, alum-adjuvanted
- “Proof-of-concept” lot manufactured by WRAIR based on technology used for JEV vaccine
- Vaccine is fully protective in mice and NHP models
- NIAID and WRAIR conducting Phase I clinical trials to evaluate safety, immunogenicity, regimen, dose-sparing, prior flavivirus immunity
- WRAIR transferring technology to Sanofi Pasteur – accelerating development
- BARDA awarded large development contracts to Sanofi and Takeda to manufacture and license ZPIV vaccines



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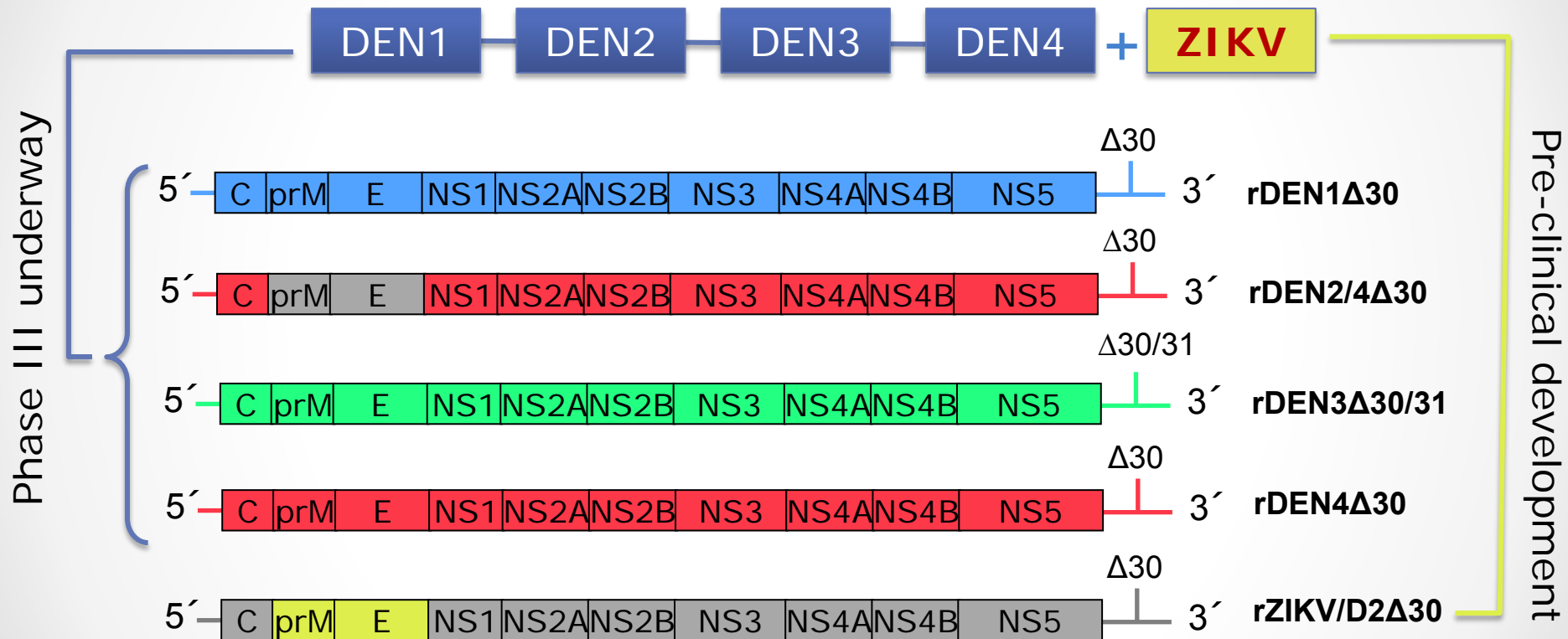
Live Attenuated/Chimeric Vaccine

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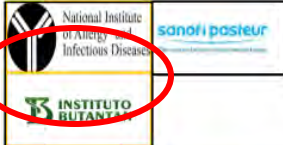










Live Attenuated DV/ZIKV Vaccine

(NIAID Laboratory of Infectious Diseases)



- Addition of this ZIKV component provides an immunological advantage for DENV
- ZIKV component may also be suitable as stand-alone vaccine

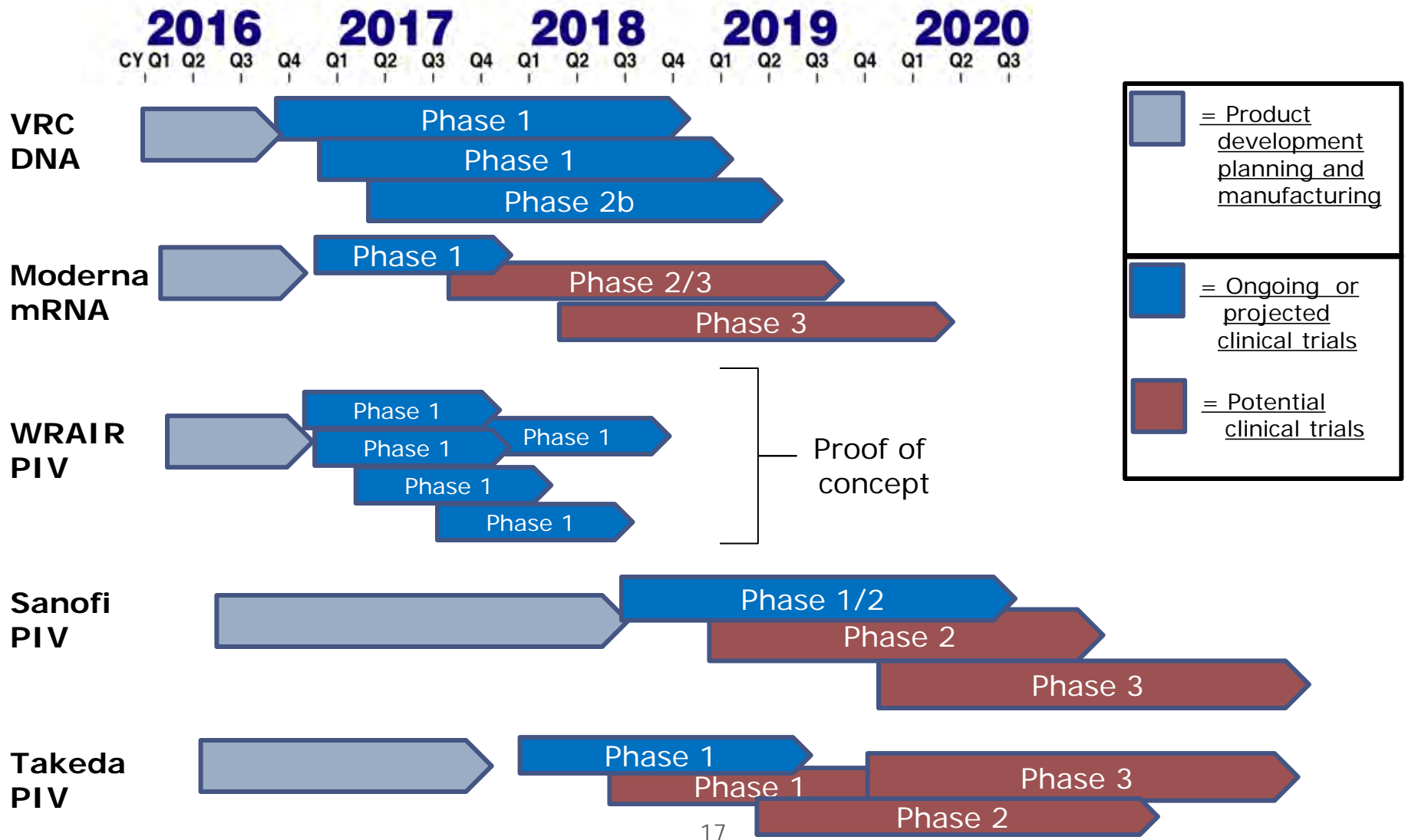
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USG Zika Vaccines Trials



Key Challenges/Questions

- Regulatory/Clinical
 - Will future disease incidence support evaluation of vaccine efficacy?
 - Which regulatory path will be most feasible?
 - Will human challenge and/or accelerated approval (correlate of protection) facilitate/accelerate evaluation?
 - Will an animal model(s) provide us with sufficient data to support efficacy determinations in humans?
 - Will pre-immunity to other flaviviruses affect Zika vaccine take, and/or vice versa?
- Manufacturing
 - Will manufacturers be able to develop a vaccine fast enough to impact the epidemic?
 - Will previous flavivirus vaccine platforms work well enough to prevent congenital infections?
 - Will the market sustain more than one vaccine?



FOR MORE INFORMATION CONTACT BARDA

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