

# **DMID/NIAID Priorities in STI Research**

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**National Institutes of Health**

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# Topics I will cover today

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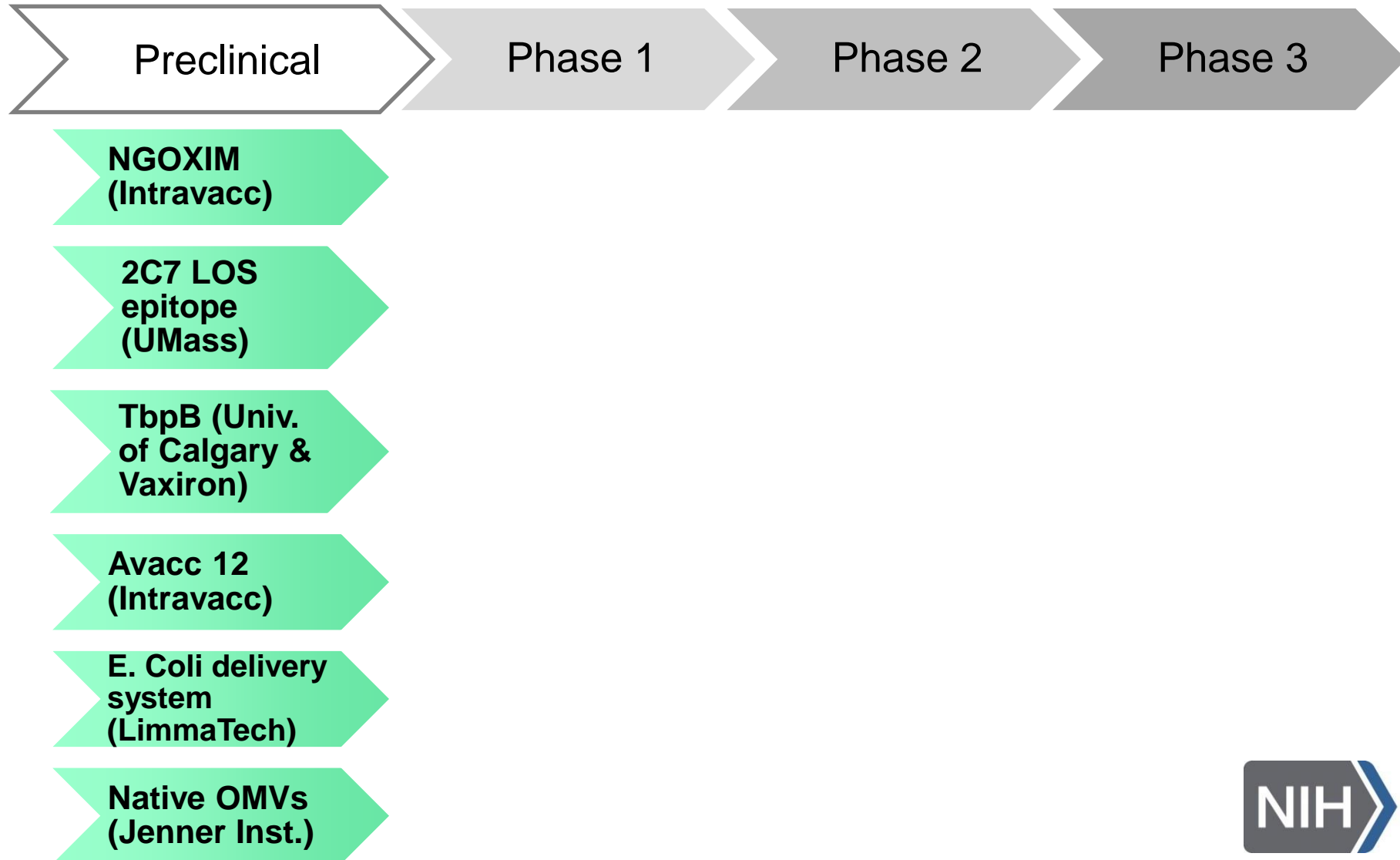
- Vaccines for gonorrhea, chlamydia and syphilis
- Alternative therapeutics for syphilis
- Select diagnostics for STIs
- Miscellaneous

# Phase 2 Clinical Trial: Testing 4CMenB as a Gonococcal Vaccine

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- Collaboration between NIAID (sponsor), Uniformed Services University, WRAIR/AFRIMS and GSK
- Phase II, randomized, observer-blind, placebo-controlled, multi-site trial of the FDA licensed vaccine, 4CMenB (Bexsero)
- Objective: To demonstrate efficacy in prevention of urogenital and/or anorectal gonococcal infection <https://clinicaltrials.gov/ct2/show/NCT04350138>
- Approximately 2,200 participants are to be enrolled to achieve at least 202 evaluable cases. Participants: Men (MSW and MSM) and women
- 7 sites in the United States, 2 sites in Bangkok, Thailand, site in Lilongwe, Malawi
  - Atlanta, Birmingham, New Orleans, UCLA, San Francisco, Chicago, New York

# Gonorrhea Vaccines in Preclinical Development



# Gonococcal Vaccines in Early Clinical Development

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## NIAID Funded

- Intravacc (BAA): NGOXIM
  - *N. gonorrhoeae* OMV & microencapsulated IL-12
- UMass (BAA): 2C7 LOS epitope
  - Peptide mimetic
- University of Calgary & Vaxiron (Partnership R01): TbpB
  - Cocktail of recombinant TbpB that are unable to bind transferrin

## CARB-X Sponsored

- Intravacc: Avacc 12
  - *N. meningitidis* OMV expressing gonococcal antigens
- LimmaTech Biologics AG
  - *E. coli* delivery system expressing gonococcal antigens
- Jenner Institute
  - Native gonococcal OMVs

# Intravacc: Intranasal Gonorrhea Vaccine

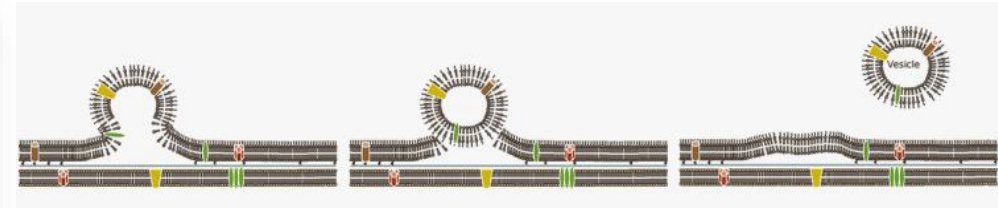


## Press Release

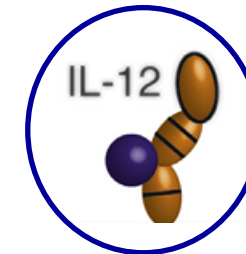
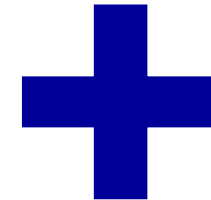
### Intravacc Announces Favorable Preclinical Data for its Candidate Intranasal Gonorrhea Vaccine Avacc 11®

- Pre-clinical data of Avacc 11® demonstrated protection against gonorrhea infection
- Global incidence rate of this sexual transmitted disease is at 87 million infections per year
- OMV technology is a powerful tool to induce protective systemic and mucosal immunity
- Data published in the peer reviewed journal MSphere of the [American Society of Microbiology](#)

**Bilthoven, The Netherlands, 16 January 2023** – [Intravacc](#), a world leader in translational research and development of preventive and therapeutic vaccines, today announced favorable pre-clinical data for Avacc 11®, the prophylactic intranasal gonorrhea candidate vaccine Intravacc develops in partnership with [Therapyx inc.](#) The results of the candidate, a proprietary outer membrane vesicle (OMV) platform-based gonorrhea vaccine combined with encapsulated IL-12, showed protection against subsequent infection with *Neisseria gonorrhoeae* (NG). Results were published in the peer reviewed journal MSphere of the [American Society of Microbiology](#). In October 2022, Intravacc was awarded a \$14.6 Million [NIH/NIAID contract](#) to further develop this intranasal candidate gonorrhea vaccine.



OMVs isolated from genetically-modified *N. gonorrhoeae* (Intravacc)



Micro-encapsulated IL-12

(Glassman et al. 2021)



National Institute of Allergy and Infectious Diseases

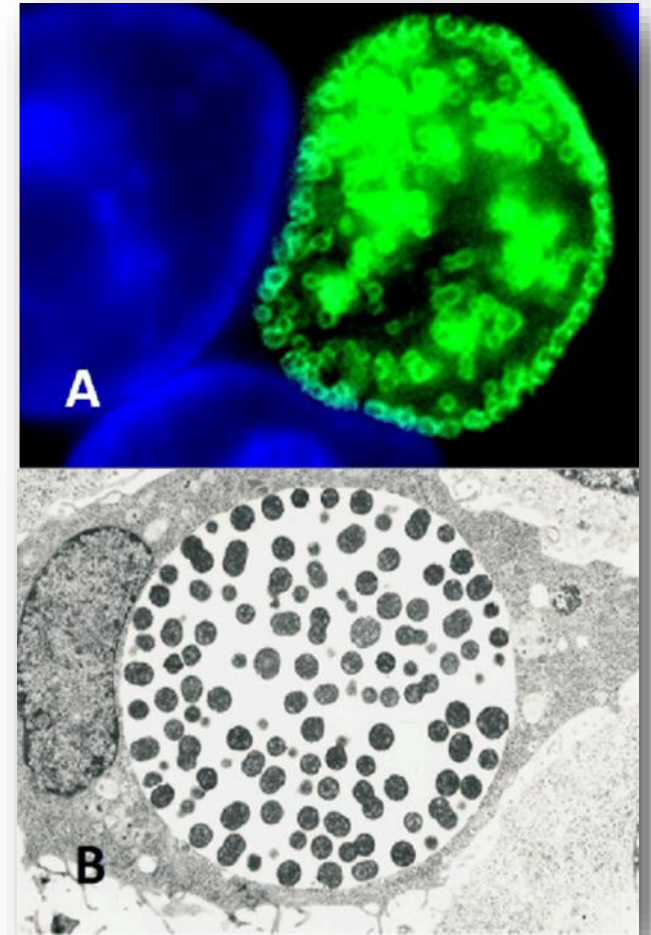
For media and investors only

# GSK receives US FDA Fast Track designation for investigational vaccine against gonorrhoea

- Fast track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier.

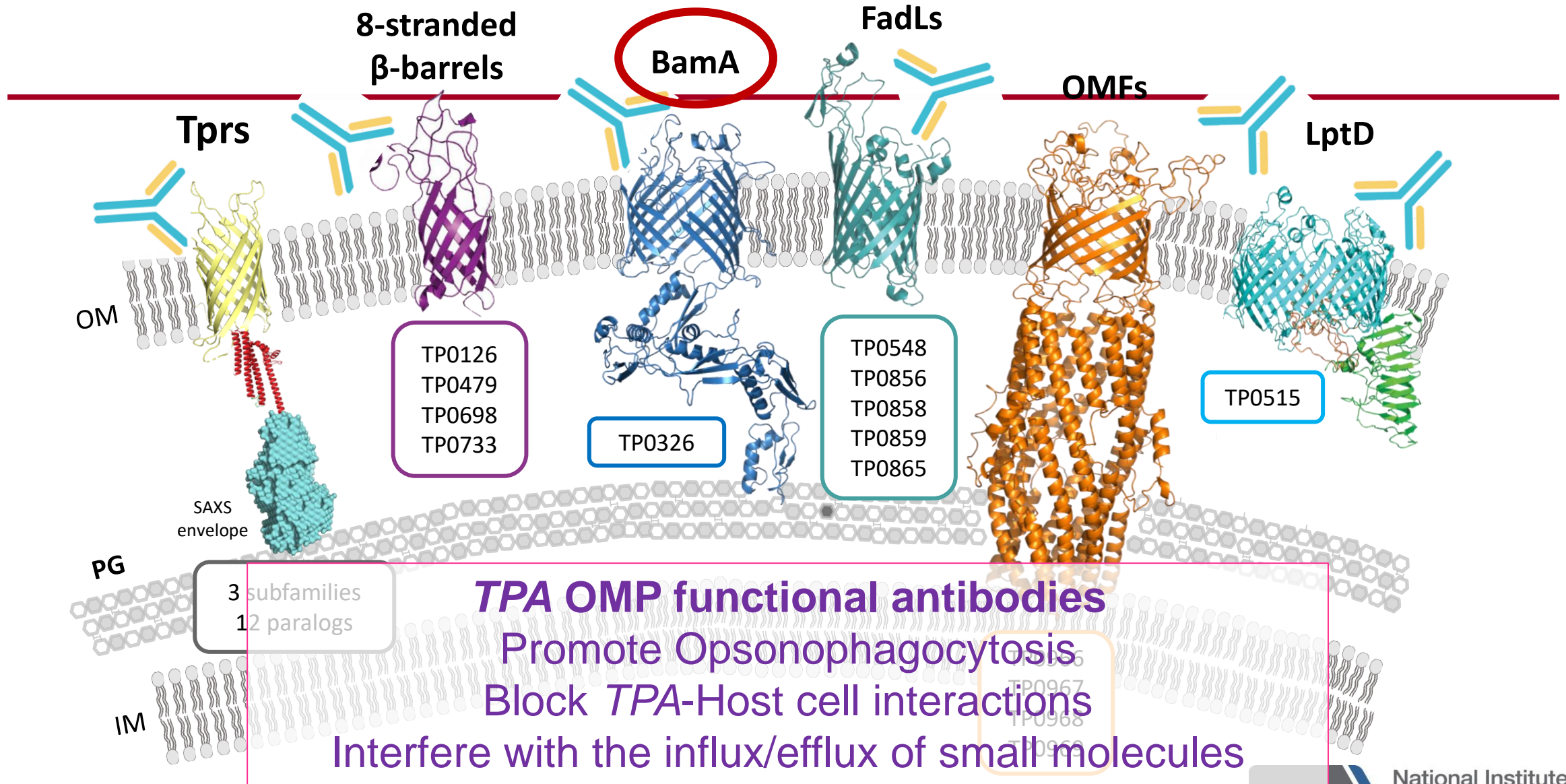
# Basic Research & Pre-clinical Chlamydia Vaccine Development

- Toni Darville (UNC):
  - Cellular vaccine designed to induce antigen-specific CD4 Th1 or Th1/Th17 cells producing IFN $\gamma$
  - Antigen: chlamydia protease activity factor (CPAF) (additional antigens may be added)
  - Currently investigating adjuvants, formulation and production
- Matthew Coleman (Lawrence Livermore National Laboratory):
  - Recombinant major outer membrane protein (MOMP) in nanolipoprotein disks
- Guangming Zhong (UT San Antonio):
  - Live-attenuated *Chlamydia muridarum* vaccine delivered orally to induce “transmucosal” response to *C. trachomatis*
- Statens Serum Institut Ct vaccine in Phase 1 trial





# *T. pallidum* Nichols OMPeome



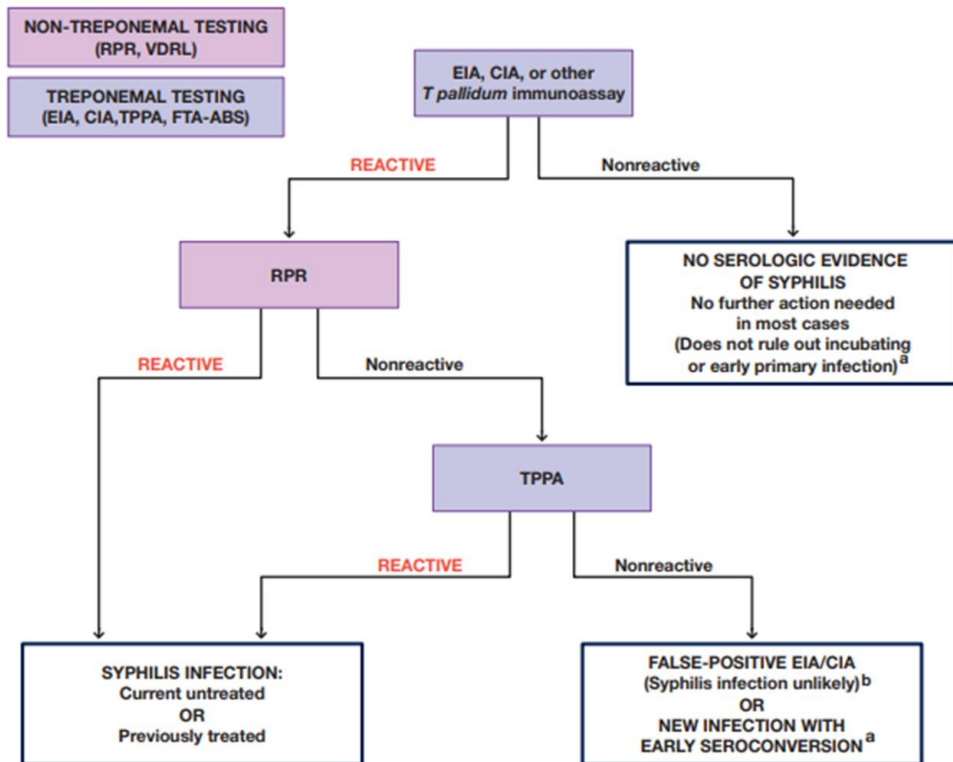
# Syphilis Vaccines in Preclinical Development

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- Tony Moody (Duke):
  - Identification of immunogenic extracellular loops of putative *T. pallidum* outer membrane proteins
  - mRNA and VLP platforms to be explored
  - Loops from BamA are lead antigen candidates
- Caroline Cameron (U. of Victoria):
  - Use of an immunogenic *T. pallidum* surface protein (Tp0751) as a scaffold to present protective *T. pallidum* repeat (Tpr) polypeptides (“chimeric syphilis vaccine”)
  - Adjuvant selection, formulation and scale up/process development

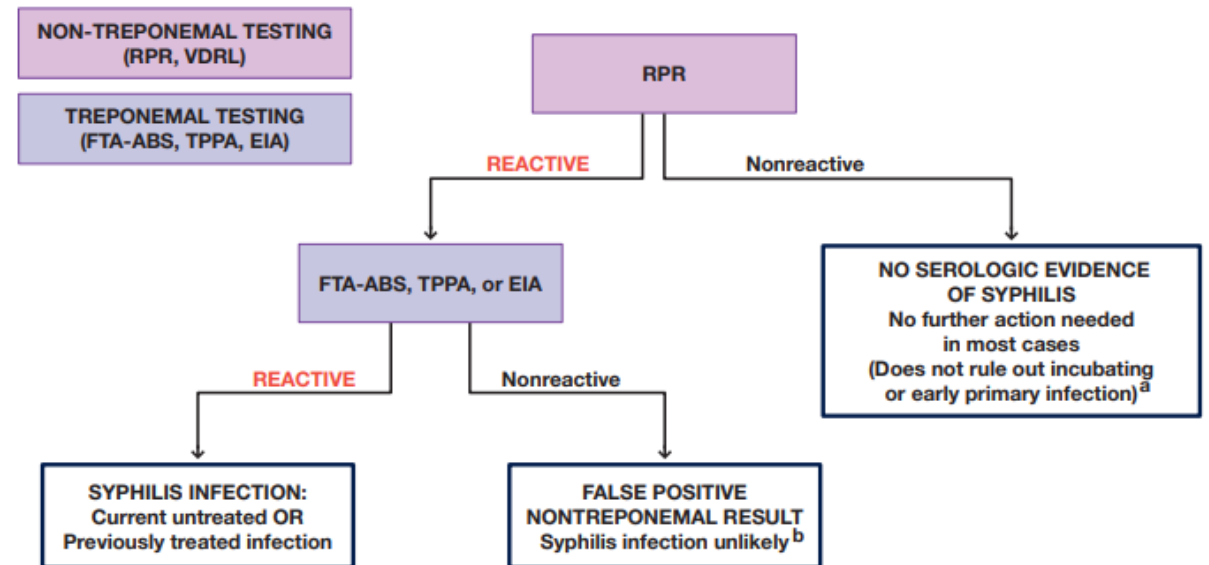
# Syphilis Diagnostics: A Picture Is Worth 1000 Words!

## Reverse-Sequence Algorithm



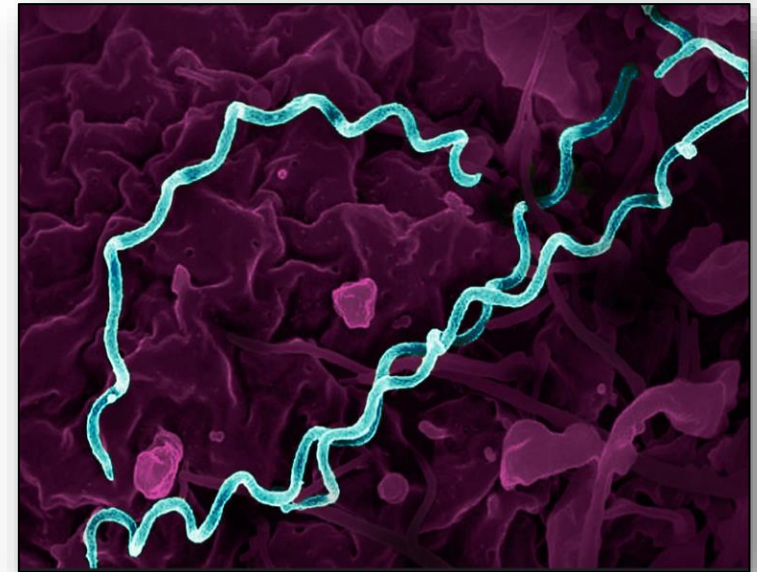
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## Traditional Algorithm



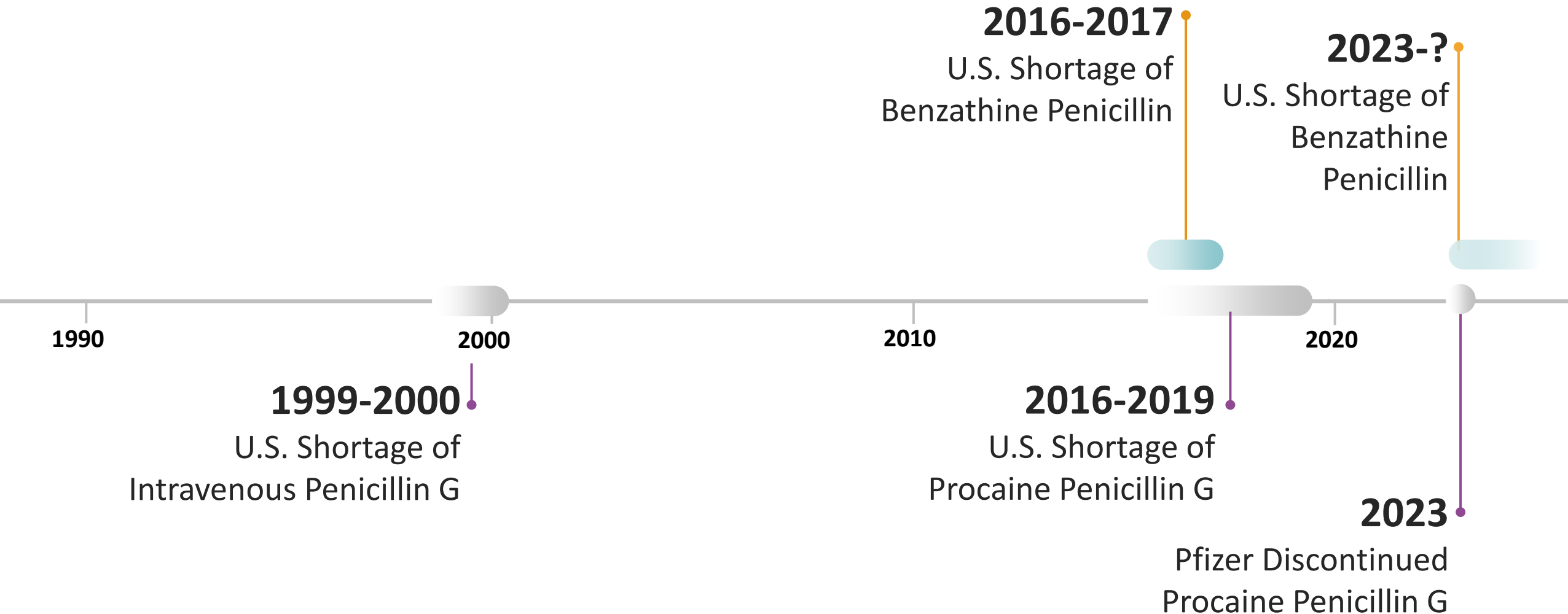
# NIAID Syphilis Workshop: Alternative Therapies

- In February 2024, NIAID convened a workshop on alternative therapies to BPG for the treatment of adult syphilis, neurosyphilis, and syphilis in pregnant persons and infants.
- Topics included preclinical evaluation of candidate drugs, the potential need for studies on how candidate drugs are processed in the body during pregnancy, and how to approach clinical trials of treatment for congenital syphilis.



Colorized electron micrograph of *Treponema pallidum*. Credit: NIAID

# Penicillin Shortages Have Been More Common in Recent Years






# Repurposing Drugs for Treatment of Syphilis: Clinical Trials

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- **Linezolid vs BPG for treatment of early syphilis:** (PI: Oriol Mitja Villar)
  - Study Completion estimated: December 2025
- **Clinical Efficacy of Cefixime for Treatment of Early Syphilis in Women:** (PI: Melanie Taylor)
  - Currently enrolling
- **Doxycycline compared to penicillin for treatment of neurosyphilis and ocular syphilis** (PI: Matt Golden and Ken Mayer)
  - Protocol in development
- **Other concepts under discussion:** Amoxicillin +/- probenecid for early stage syphilis; BPG for high titer latent syphilis of unknown duration (vs BPG x 3 sequential doses)

# National Institute of Biomedical Imaging and Bioengineering (NIBIB) Solicitation

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ITAP FOR MPOX  
DIAGNOSTIC LESION PANEL

Independent Test Assessment Program (ITAP) for Diagnostic Mpox Lesion  
Panel Test Validation and Regulatory Authorization

- NIAID participates in the Trans-NIH Point of Care Testing Research Network coordinated by NIBIB
- Multiplex tests for the direct detection of mpox virus (MPXV), HSV 1/2, *Treponema pallidum* and varicella-zoster (VZV) in lesion swab specimens.

# Other Efforts That May Benefit From DAIDS/DMID Collaborations

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- Hepatitis C vaccine
- HSV-2 (1/2) vaccine
- HSV-2 mAb's





Eye Syphilis is Serious

**freeSTDcheck.org**

AHF