# International Partnership for Microbicides

## *Current Progress and Future Directions in Microbicide Research and Development*

**Nairobi, Kenya**

**Dr. Zeda F. Rosenberg**

***2 July 2007***

# What is a Microbicide?

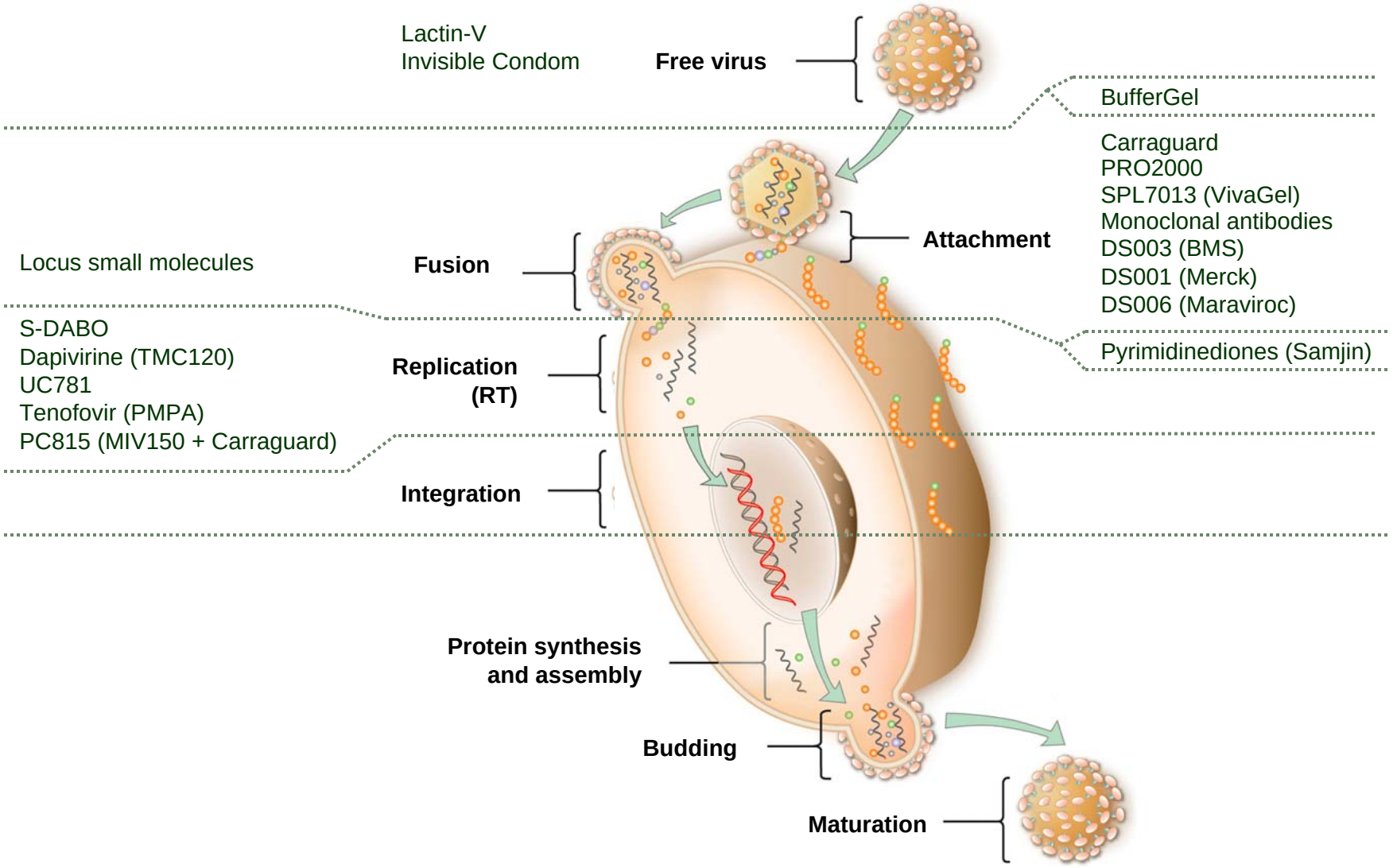
- Vaginally applied substance that prevents or reduces transmission of HIV
- Could potentially be delivered in many forms:
  - gel
  - intravaginal ring
  - vaginal tablet
  - film
  - sponge
  - diaphragm

Vaginal applicator

Vaginal ring

- Ideally safe, effective, low cost and user-friendly

# Microbicides in Product Development



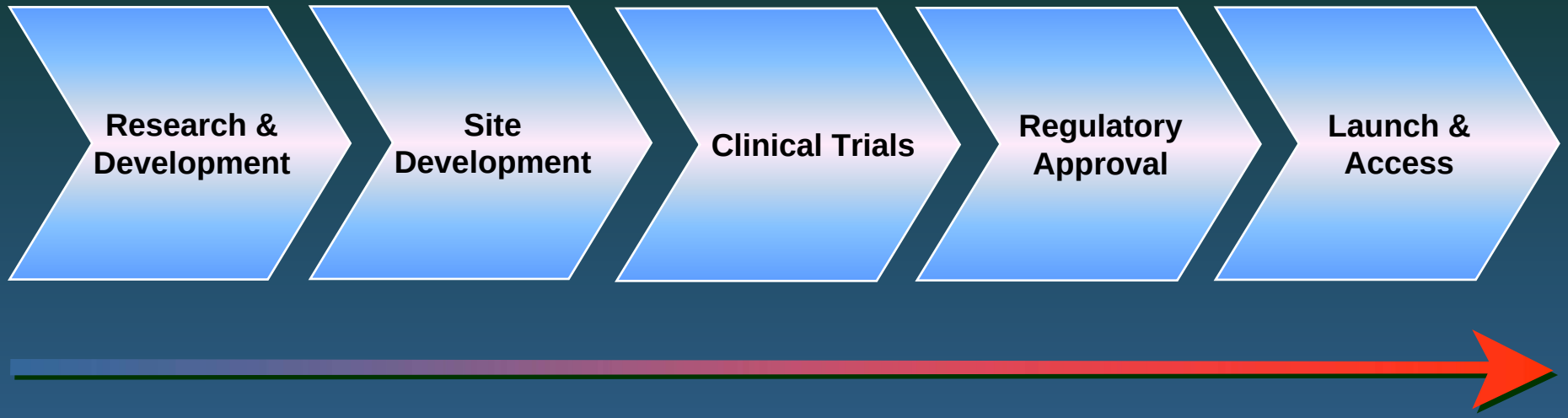
# Early-Generation Microbicides

- Products that non-specifically block HIV from interacting with target cells
- In efficacy trials
- Partial, low or no effectiveness
- Short-acting (used near time of sex)

# Next-Generation Microbicides

- Based on antiretroviral drugs used to treat HIV
  - Highly potent and HIV-specific
  - Small molecules
- Delivery mechanisms for sustained protection
  - Once a day or less
  - Gels and intravaginal rings
  - Vaginal tablets and others
- Developed as single drugs and in combination
- Phase 2B trial of tenofovir gel (South Africa)
  - Initiated May 2007 (CAPRISA, CONRAD, USAID)

# Microbicide Development Process




- Pipeline
- Basic research
- Pre-clinical tests
- Lead selection

- Community engagement
- Site selection
- Site preparation
- Site monitoring
- Incidence studies

- Pharmacokinetic
- Safety
- Efficacy
- Acceptability

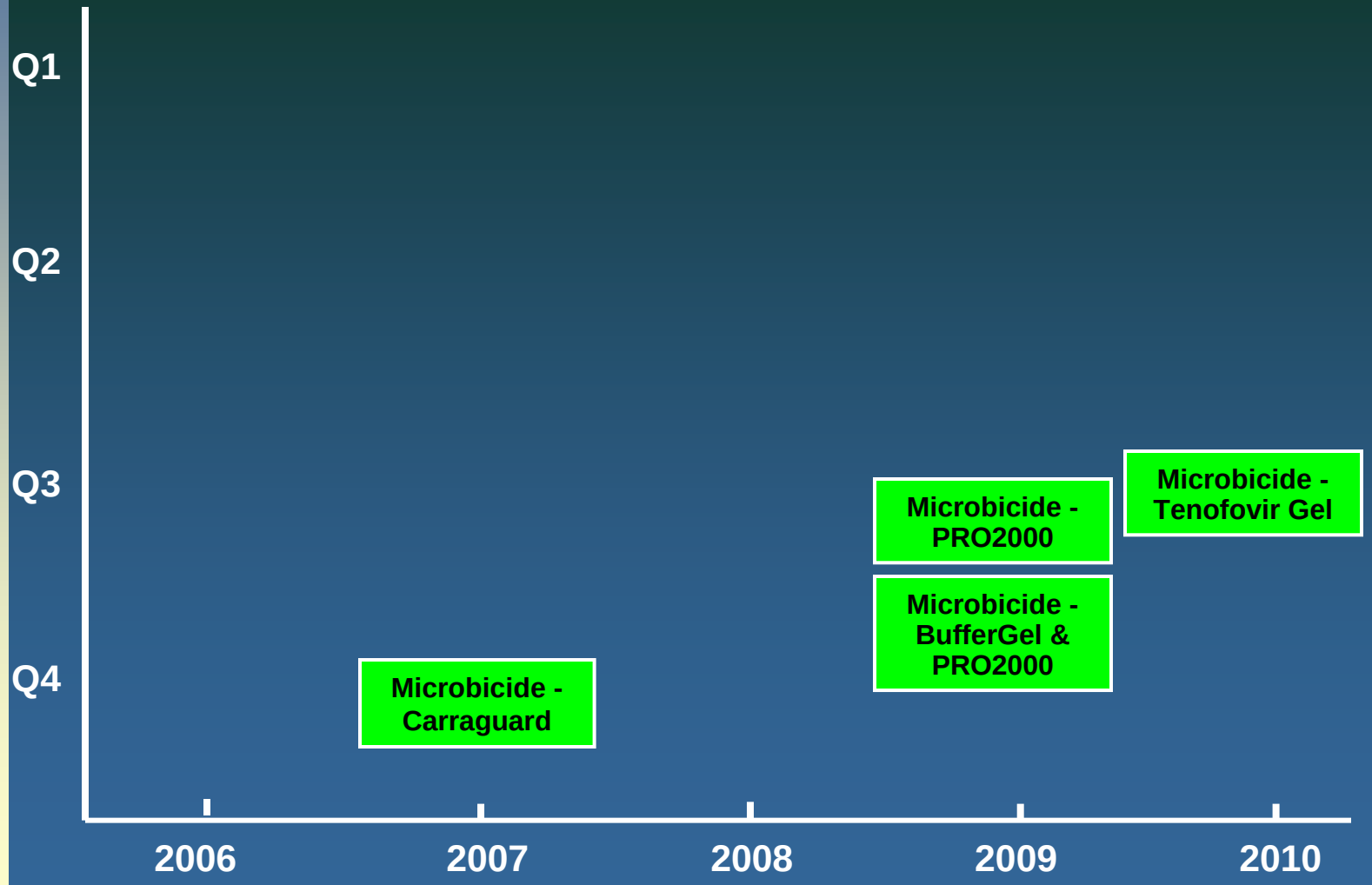
- Clinical trials
- Licensure
- Post-licensure studies

- Manufacturing
- Service delivery
- Marketing

# Early-Generation Efficacy Trials

| Candidate Microbicide | Phase | Mechanism of Action | Sponsor/Developer | Trial Location |
|---|---|---|---|---|
| Carraguard | 3 | Entry Inhibitor | Gates, USAID / Population Council | South Africa – Cape Town, Durban, Medunsa |
| PRO2000 | 3 | Entry Inhibitor | UK Medical Research Council, DFID / MDP | South Africa – Mtubatuba, Durban, Johannesburg<br>Uganda – Masaka<br>Tanzania – Mwanza<br>Zambia – Mazabuka |
| PRO2000 & BufferGel | 2/2B | Entry Inhibitor & Vaginal Defense Enhancer | NIAID / HPTN (MTN) | Zimbabwe – Harare, Chitungwiza<br>Zambia – Lusaka<br>Malawi – Blantyre, Lilongwe<br>South Africa – Durban, Hlabisa<br>United States – Philadelphia |

# Expected Efficacy Trial Results



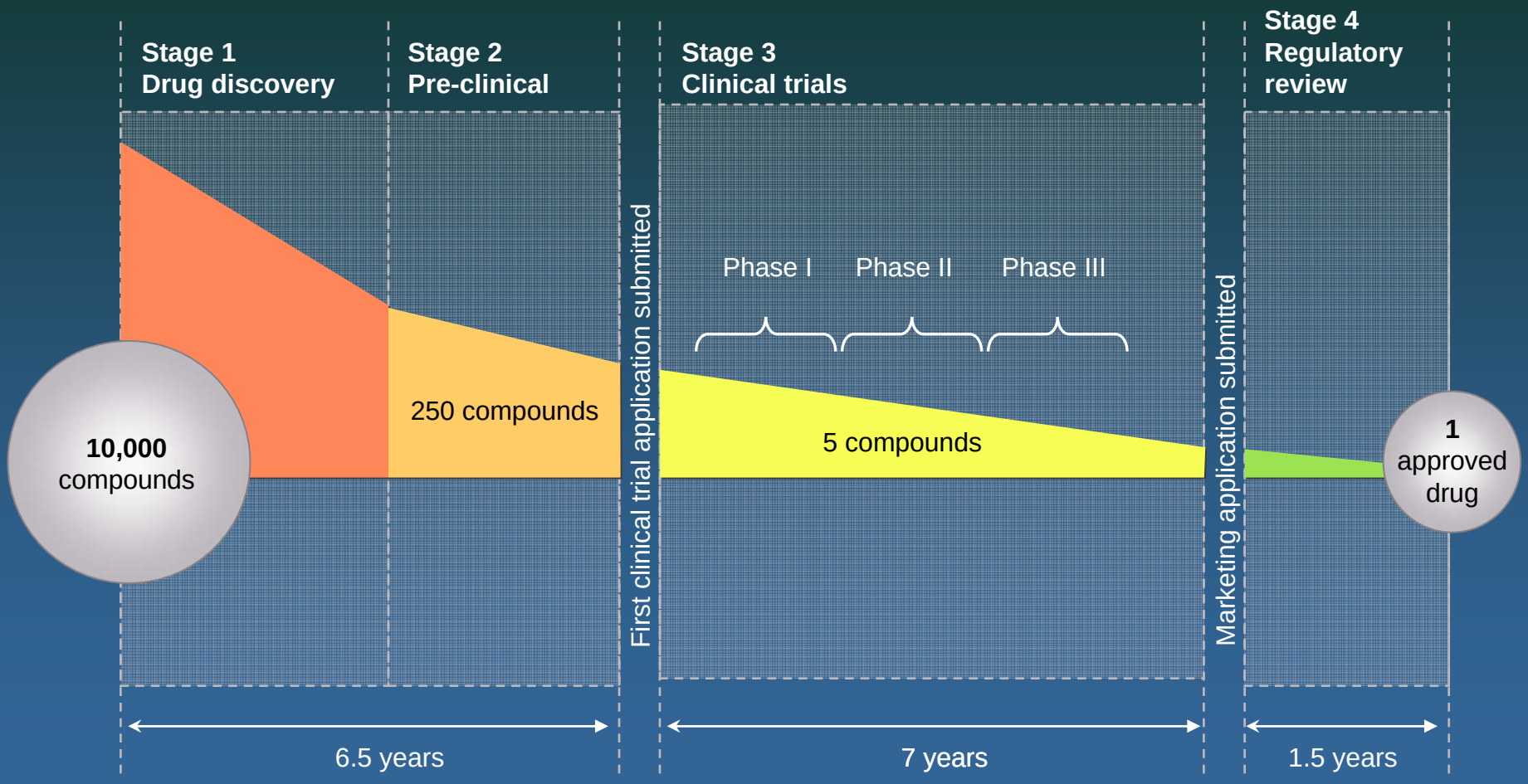
# Challenges in Microbicide Efficacy Trials

- Relatively low incidence in trial settings
  - Savvy, cellulose sulfate (FHI)
  - Large trials
  - Few endpoints
- Lack of surrogate markers
- Relatively high pregnancy rates
- Level of adherence to study regimen
- Unclear regulatory pathways
- Limited clinical trial capacity

# Cellulose Sulfate: Closure of Efficacy Trials

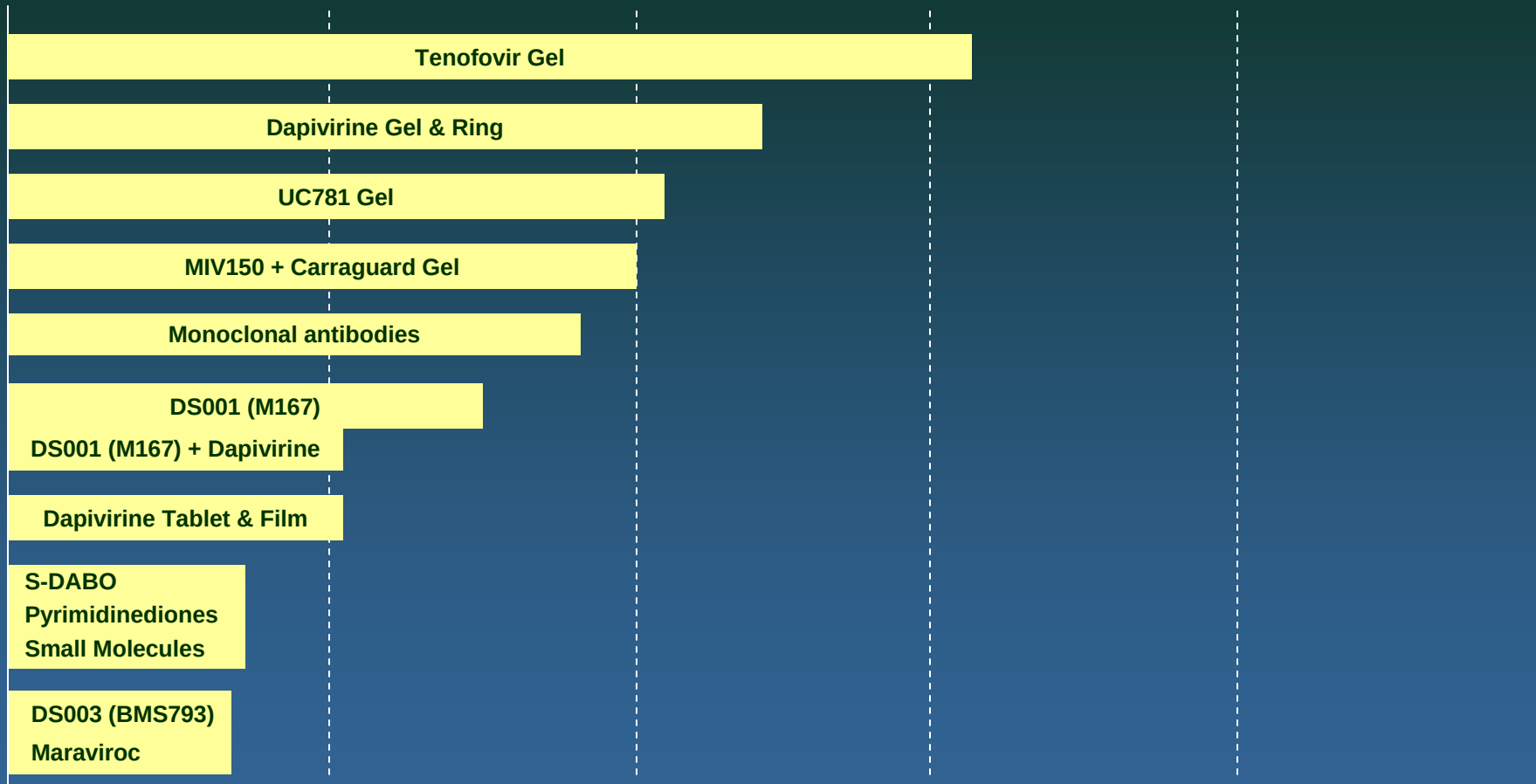
- Phase 3 trials in South Africa, Benin, Uganda, India (CONRAD) and Nigeria (FHI)
- Preliminary data indicated a potential 'increased risk of HIV infection in women who use the product' at CONRAD sites
- FHI data inconsistent with CONRAD findings
- Participant safety prioritized
  - Decision to close trials with preliminary results
  - Commitment to high standard of care for participants
- Sponsor now analysing data

# Drug Discovery, Development and Review Process

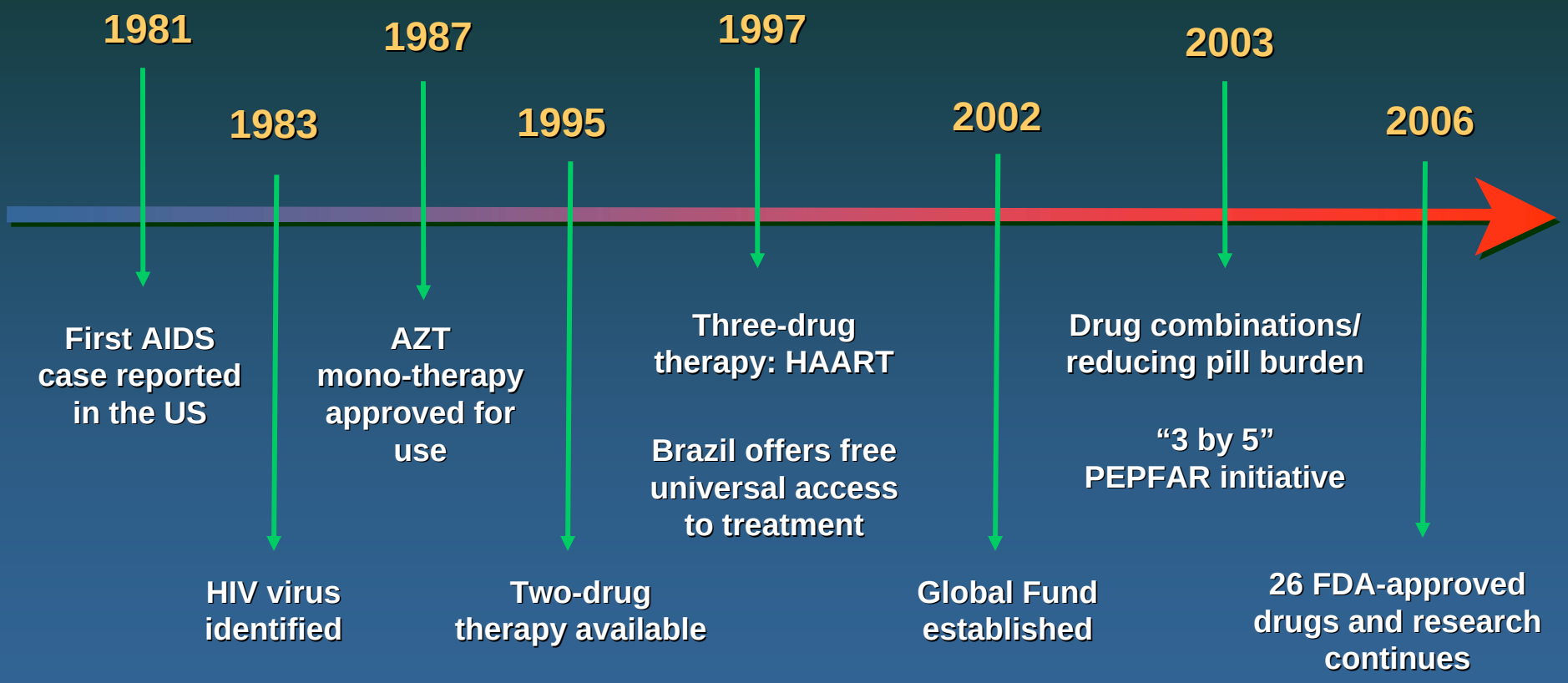



Adapted from: Pharmaceutical Research and Manufacturers of America, 2006

# Next-Generation Product Development



# Realistic Expectations



# Development Summary

- Data on Carraguard imminent
- PRO2000 and BufferGel report 2009
- First next-generation efficacy study initiated
- Additional next-generation products in safety
  - Several possible formulations
- Future focus on combination products

# Development Summary

- Currently unclear:
  - Which, when and where first product licensed
    - RSA currently involved in all efficacy trials
  - License designation (prescription most likely)
  - Which formulation or delivery mechanism
  - Product and program costs