

Advocacy

Access

Scientific

Pharmaco-  
economics

Mechanism

## Science

- To survey the state of microbicide R&D, identify intellectual or resource gaps, and specify how to best fill these gaps

## Pharmaco-economics

- To estimate the market potential, returns to investment and public benefits of microbicides

*Goal: to accelerate dramatically the development of safe, effective, available and affordable microbicides*

**BASIC RESEARCH  
DISCOVERY**

**Pre-clinical**

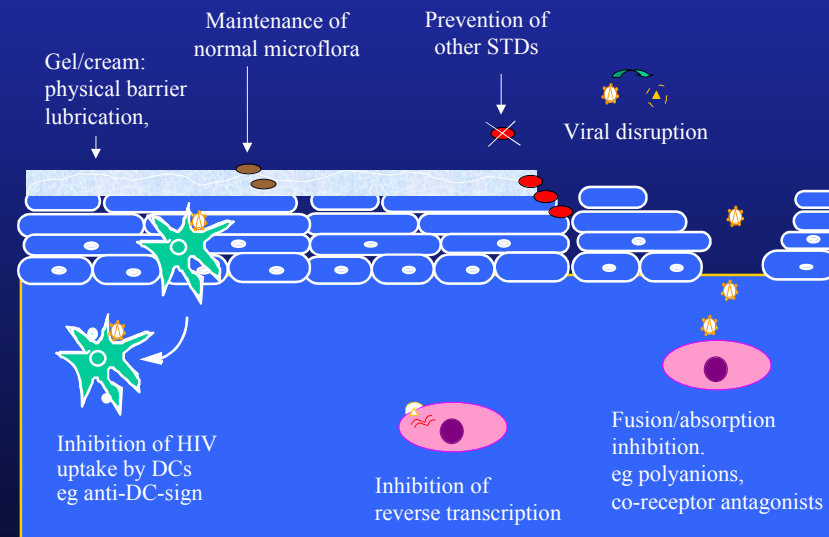
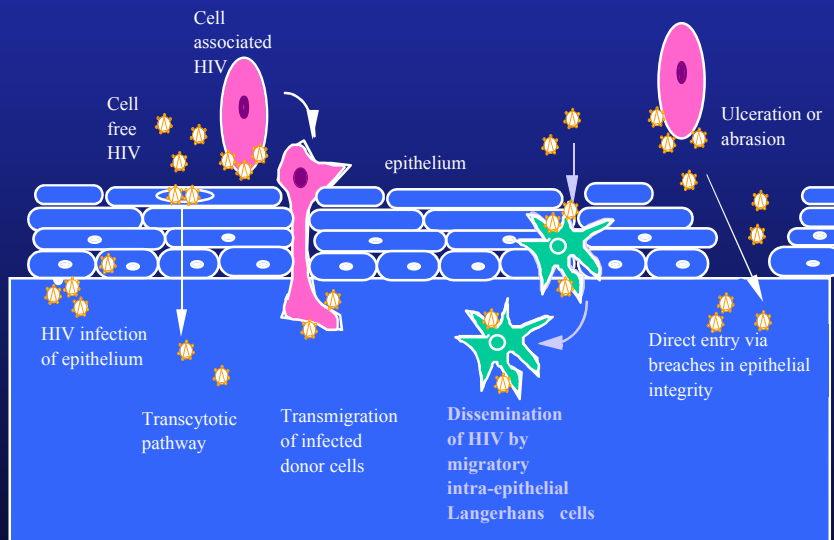
**Clinical  
Regulatory**

**Commercial**

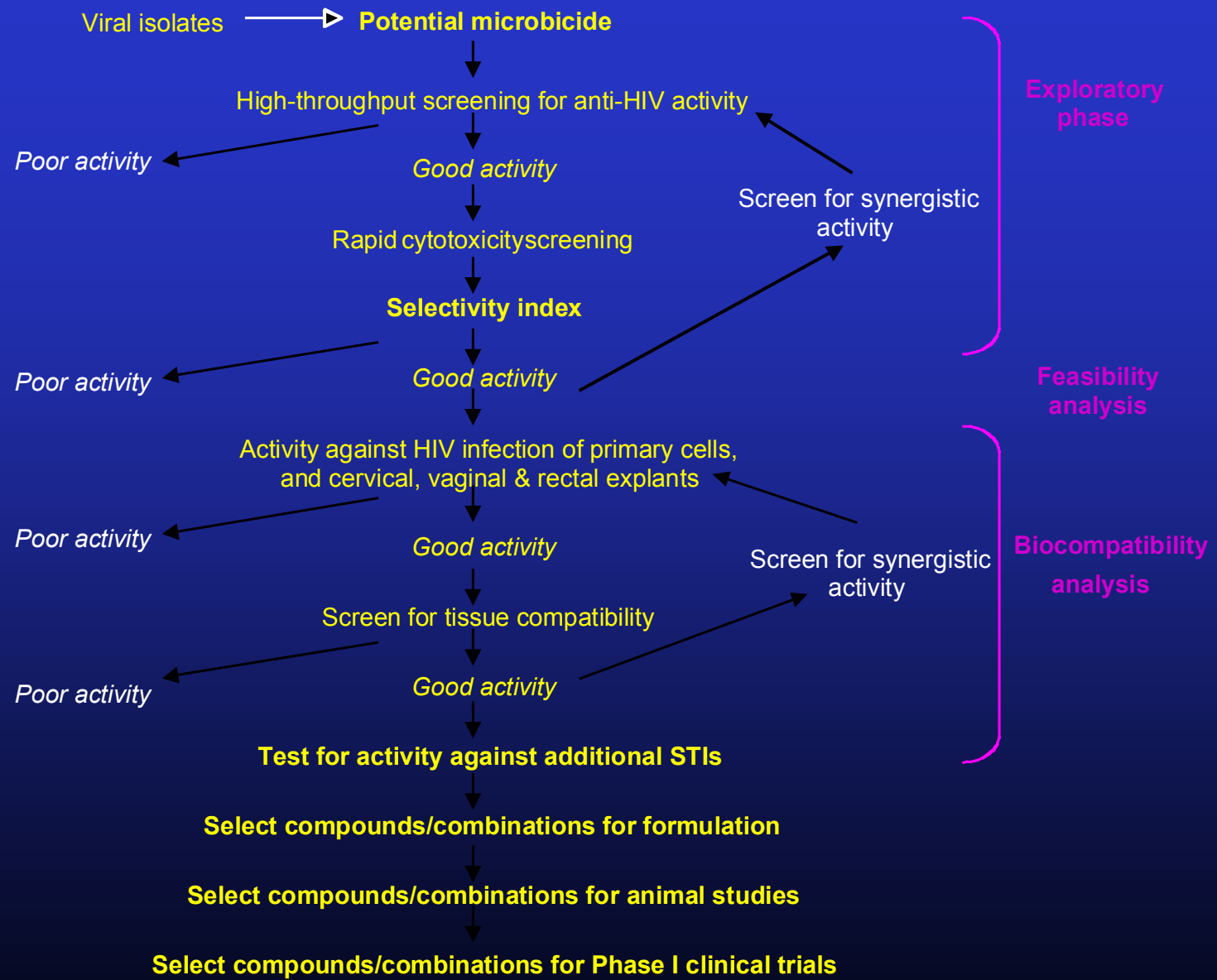
## Significant progress... Manageable challenges

**Multiple targets identified**

**Over 60 compounds under consideration as microbicides acting through multiple mechanisms**



stroma



Basic Research  
Discovery

PRE-CLINICAL

Clinical  
Regulatory

Commercial

Improved in vitro testing  
Appropriate animal models

... BUT not validated pending POC

*NEED TO:*

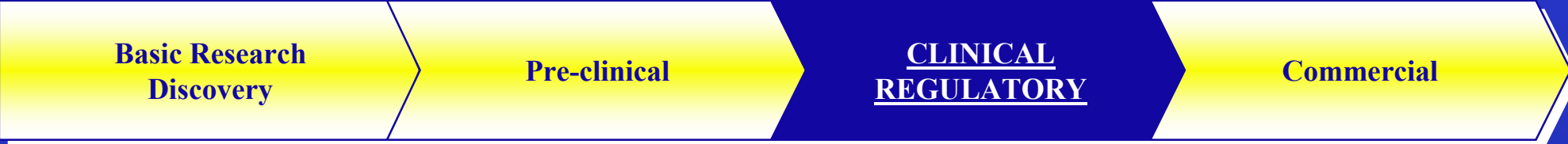
*Standardize and improve comparability of in vitro and animal models*

*Increase development & use of tissue explants and cell culture*

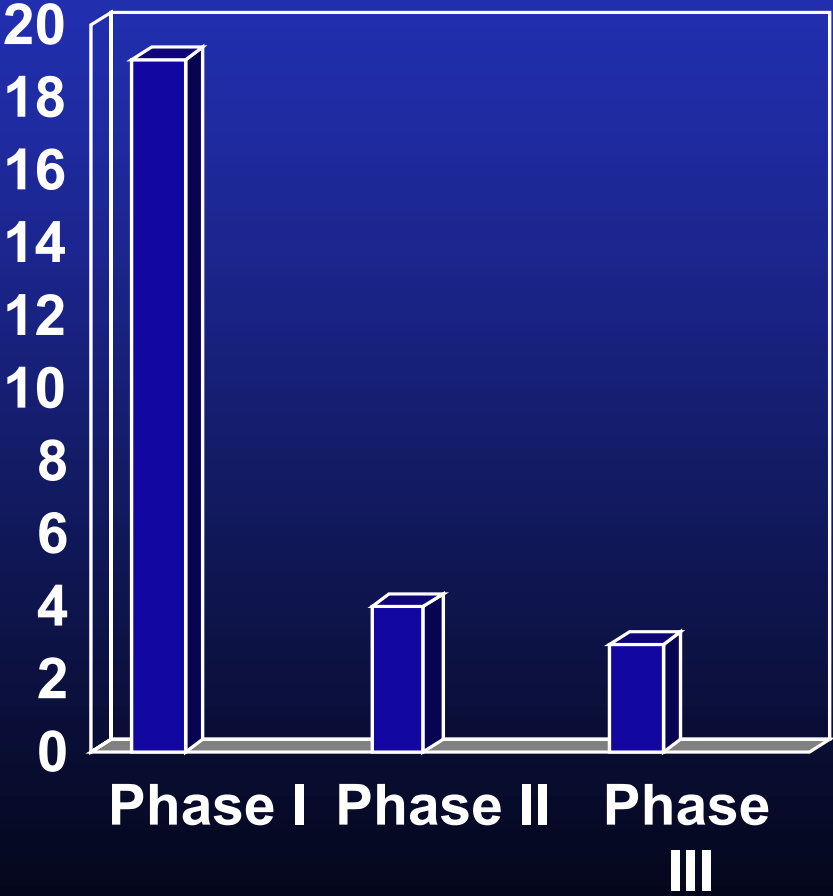
*techniques to screen compound activity*

*Better manage & invest more into toxicology and pharmacodynamics*

*Improve access to evaluation assays*



## Significant progress... Manageable challenges



Over 25 compounds in clinical stage of development

However, time from compound discovery to entry into trials is long

Investment required to shorten time lines

# Proving Effectiveness is Generally Difficult...

Large Phase III trials

Vast majority of resources required in late stage development

... Especially difficult for microbicides

- To prevent an infection with relatively low incidence after counseling about safe sex practices
- Requires thousands of participants willing to use the product with every sex act

Clinical trial infrastructure largely insufficient

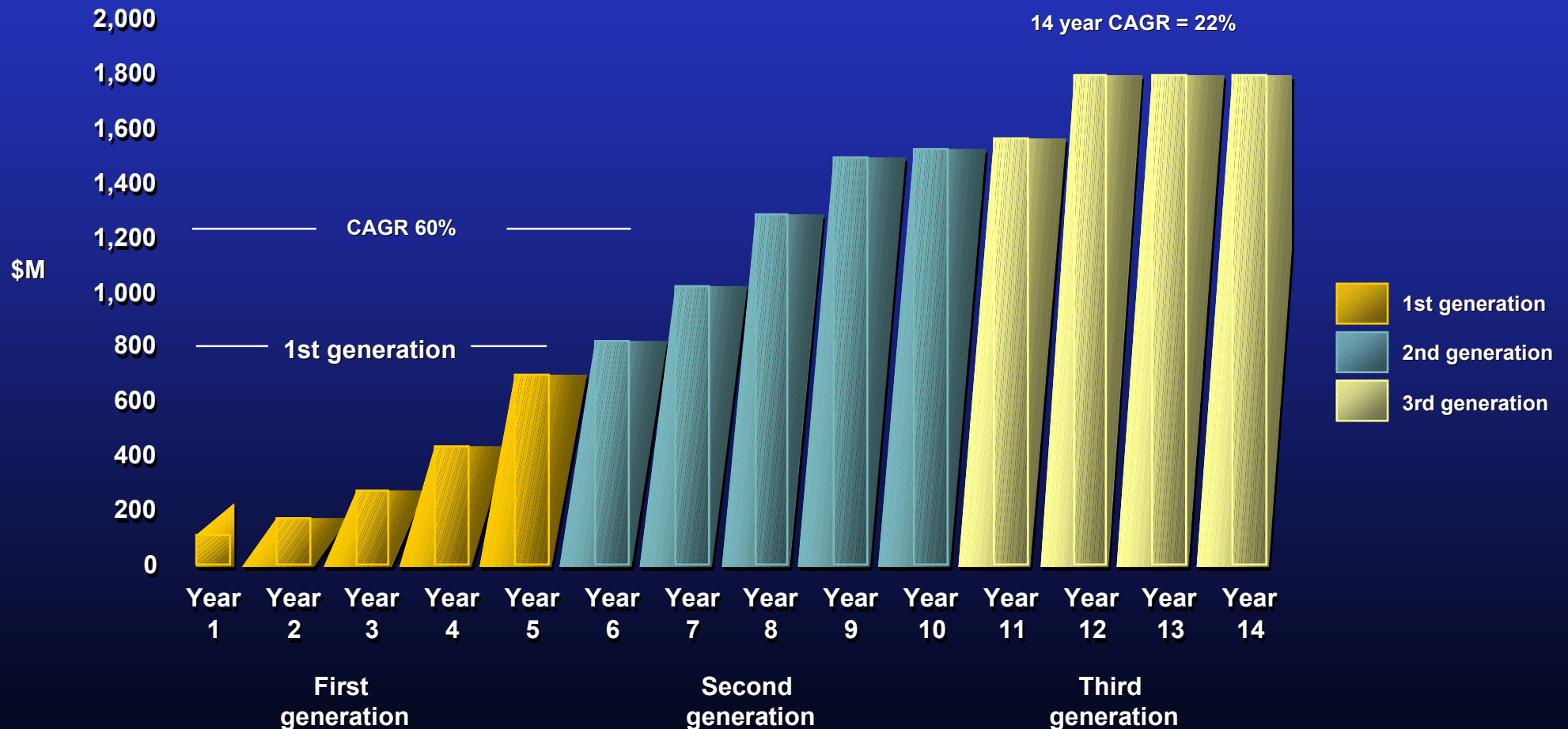
## Conclusion (1)

### Priorities and opportunities for investment

- Funding prospective clinical trials
- Improving clinical trials infrastructure
- Promoting shared resources in formulation, manufacturing & packaging
- Funding toxicology & pharmacodynamic validation
- Funding to leverage the coordination & standardization of animal and in vitro models
- Funding to provide equal access to animal and in vitro models

# CONSERVATIVE ASSESSMENT SUGGESTS ANNUAL GLOBAL MARKET COULD APPROACH \$2B

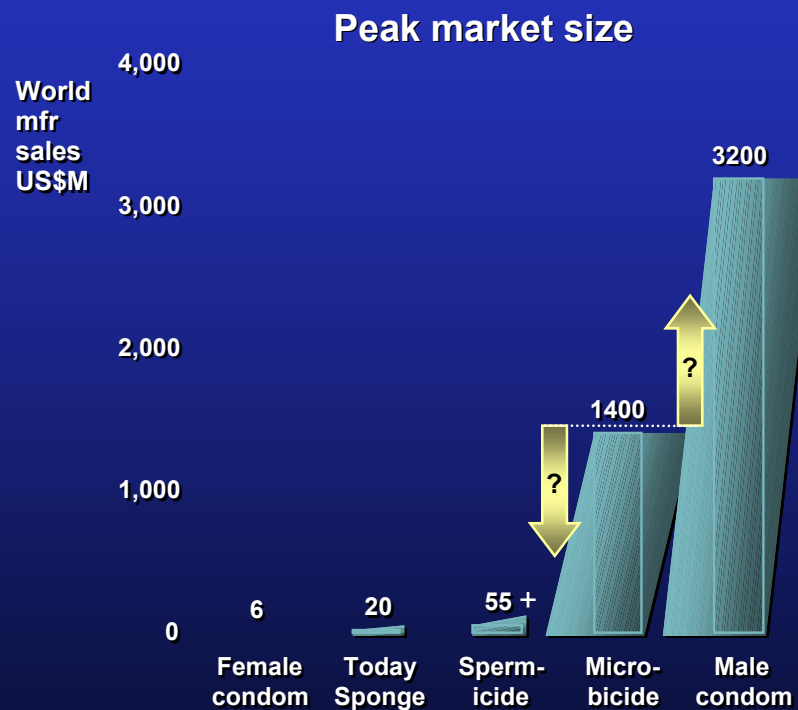
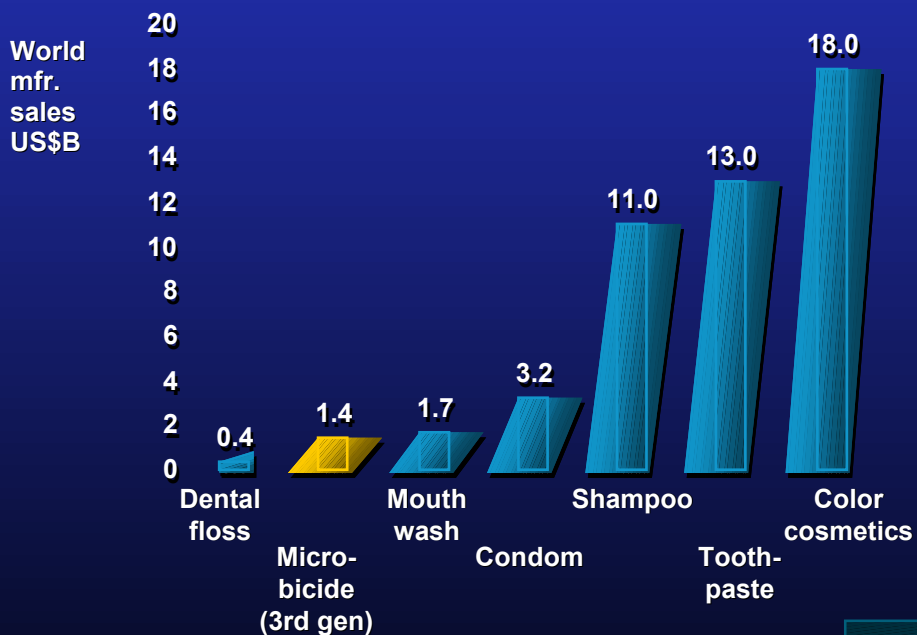
Estimate of market penetration



Microbicide market could be much larger...

If women used it more often

Or smaller....if market evolves more like women's OTC contraceptives

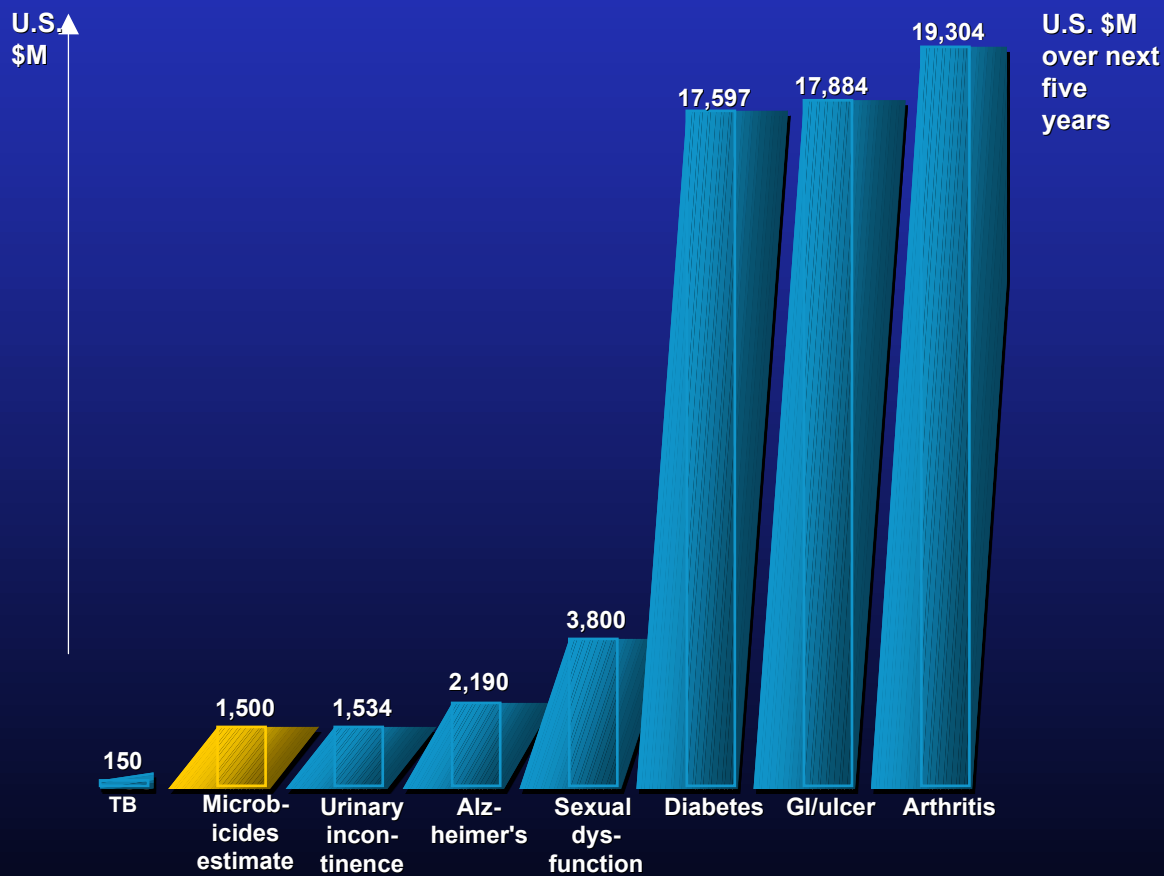


The standard for product acceptability is high

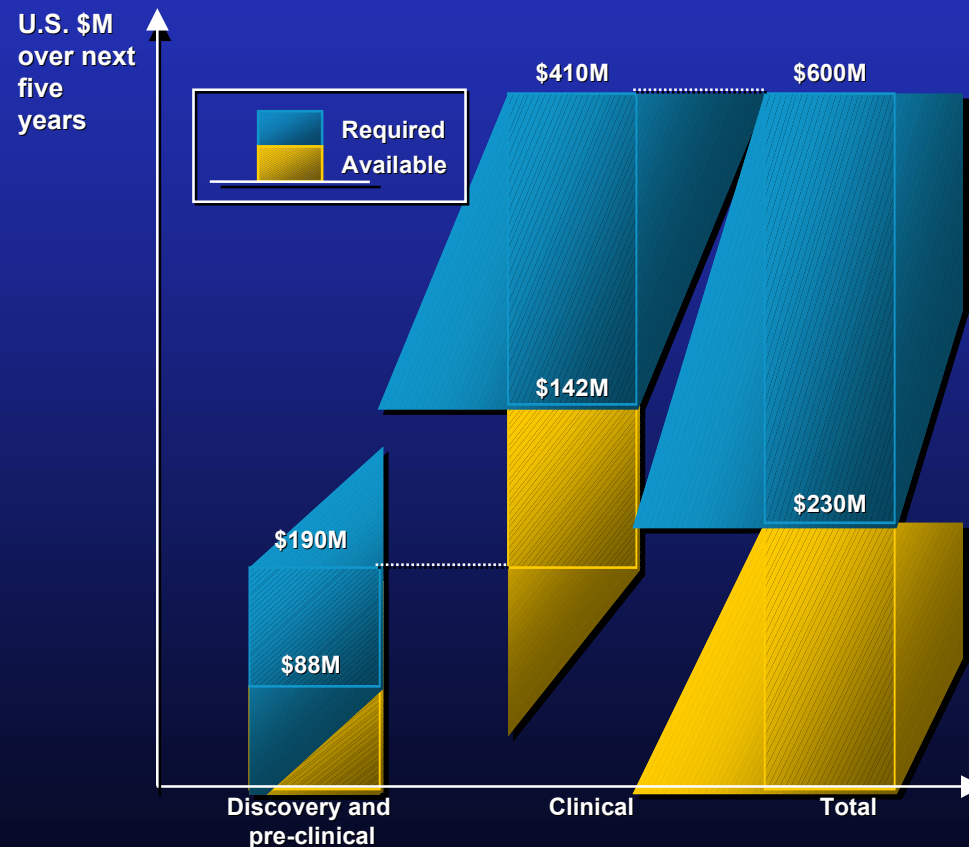
- However, magnitude of AIDS epidemic may speed acceptance of an effective preventative

# ...BUT, DESPITE SOME SIGNIFICANT MARKET POTENTIAL, COMMITTED RESOURCES CURRENTLY INADEQUATE...

Projected annual therapeutic area sales



Required versus available microbicide product development funding

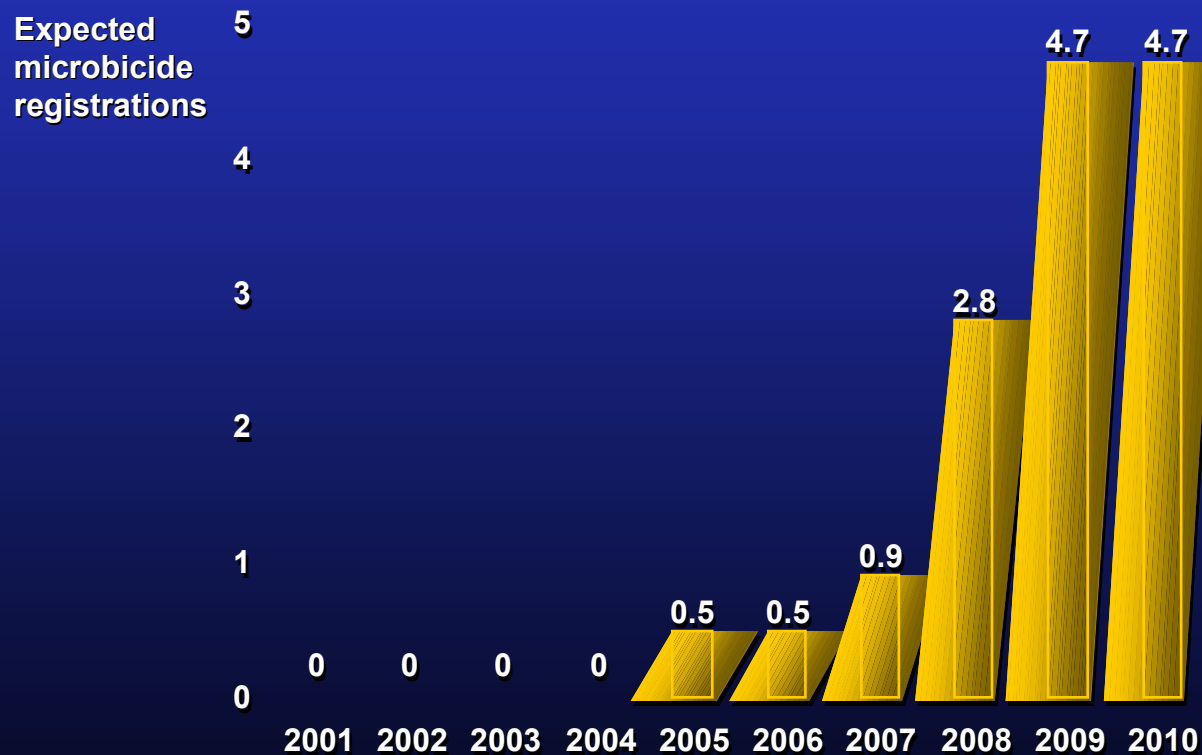


Source: SG Cowen; Pharmaco-economics team analysis; BCG probabilistic portfolio model; BCG interviews

# CURRENT MICROBICIDE DEVELOPMENT EFFORTS ARE PROMISING...

...May Produce a Product in Next 5 to 10 Years  
(If All Products Developed On Schedule)

Expected number of product registrations:  
full portfolio scenario



# 1<sup>st</sup> GENERATION MICROBICIDES REQUIRE SUBSIDY

## Later Generations Have Chance of Creating Economic Value

Example: For 25% chance of developing a microbicide, at a discount rate of 12.5%

	Pessimistic case "Niche product"	Expected case "Widely acceptable product"	Optimistic case "Regular hygiene product <sup>(1)</sup> "
<b>1st generation</b> • launch 2007 • 8 yr lifecycle • 100% share	Market <b>\$20M</b> NPV = (\$65M) IRR = N/A	Market <b>\$900M</b> NPV = (\$27M) IRR = 7%	Unlikely scenario
<b>2nd generation</b> • launch 2012 • 15 yr lifecycle • 50% share	Market <b>\$40M</b> NPV = (\$56M) IRR = N/A	Market <b>\$1500M</b> NPV = \$37M IRR = 18%	Market <b>\$3000M</b> NPV = \$122M IRR = 24%
<b>3rd generation</b> • launch 2017 • 33% share • 3% growing perpetuity	Market <b>\$100M</b> NPV = (\$49M) <i>(of which terminal value=\$6M)</i> IRR = N/A	Market <b>\$1800M</b> NPV = \$117M <i>(of which terminal value=\$112M)</i> IRR = 14%	Market <b>\$5000M</b> NPV = \$428M <i>(of which terminal value=\$307M)</i> IRR = 26%

Negative NPV at 12.5% cost of capital
  Positive NPV at 12.5% cost of capital

Knowledge and certainty about market will increase with each generation

(1) Unlikely that first generation product would become a daily hygiene product because it will have relatively low effectiveness and limited set of indications.

## Conclusion 2

- For a first generation microbicide, the expected returns are unlikely to cover developmental costs
- Donor support critical through phase 3 of 1<sup>st</sup> generation
- If 1<sup>st</sup> gen does well, subsequent generations may well be self-supporting.

## Conclusion (3)

Significant **OPPORTUNITY** to bring development to the next step

- 1st generation microbicide commercialized
- Proven proof of concept → Pharmaceutical interest

Requires increased **INVESTMENT** and **COORDINATION**

- **Public sector & private foundation leadership and resources**
- **Coordinated portfolio management**