

Overview of Products in Development-Topical

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The MTN Priorities

- Safe and effective vaginal microbicides
- Safe and effective rectal microbicides
- Combination hormonal contraceptive and antiretroviral vaginal ring
- Special populations
 - Pregnancy
 - Adolescents
 - Post menopausal women
 - MSM and transgender women



New Products & Formulations

□ Candidates

- Griffithsin
- 5P12-RANTES
- MIV-150
- IQP-0528
- Tenofovir
disoproxil
fumarate ring

□ Formulations

- Intravaginal rings
 - Combination
- Films
- Suppositories
- Gels

How is the microbicide pipeline prioritized and progressed?

What is available:

- Many API; Often same or similar mode of action and/or phys-chem properties
 - Most are early stage
- Multiple dosage form options and device technologies
- Combinations of API and dosage forms
- Intra-organizational prioritization in the absence of field wide prioritization

Consequences to pipeline:

- Independent development of similar or duplicative products
 - Several individual API in multiple dosage form products
 - Independent but similar API in the same dosage forms
- Dilution of resources

Is this an appropriate and feasible approach to the microbicide pipeline?

Identifying Least Risk/Highest Impact Products in Current Context?

One Extreme...

- HIV Only
- Early stage API in applicator based gel
- Similar MoA/equal potency to advanced products
- Vaginal only
- Minimal pre-clinical tox/pharmacology
- Minimal CMC
- Expensive
- No human experience
- Manufacturing unknown
- No Regulatory input
- Lengthy timeline to market

Never this clear!

Standard application of conventional criteria is of limited utility

...or the Other

- HIV + Other Indication(s)
- Later stage API in known high adherence formulation
- Significantly more potent/Distinct MoA
- Achieves vaginal & rectal protection
- Advanced CMC/PreClin packages
- Cheap
- Established manufacturing
- Strong clinical package
- Clear, positive Regulatory input
- Short timeline to market

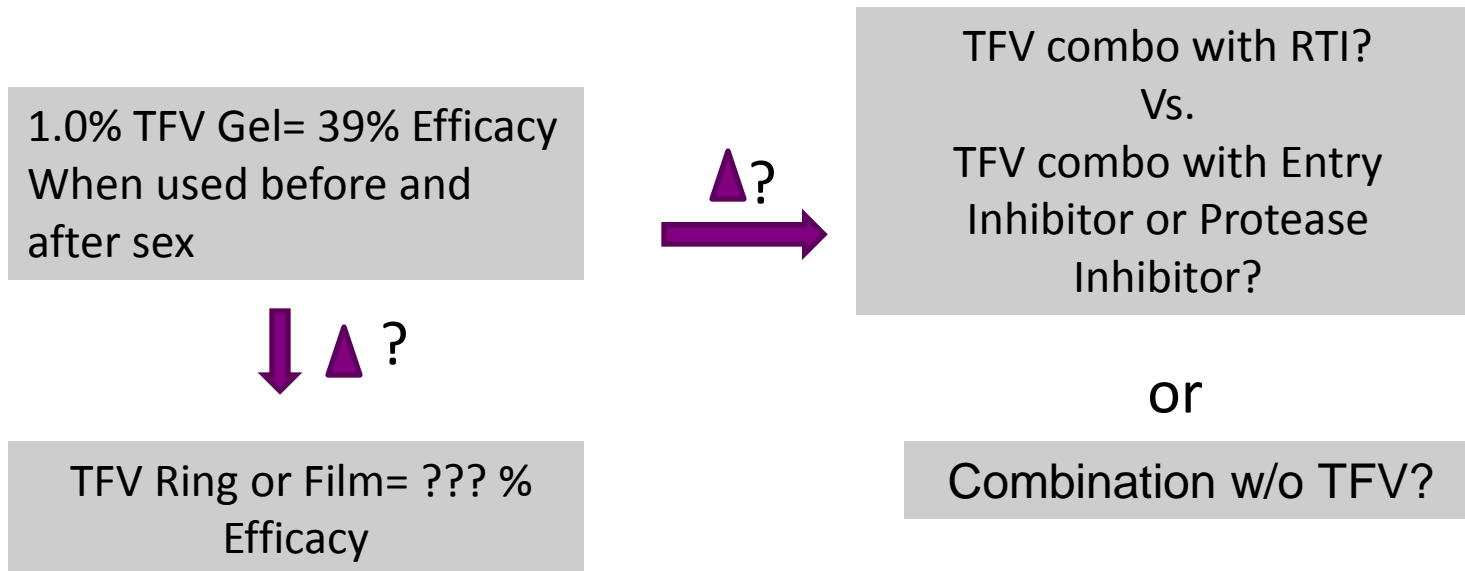


Critical Pipeline Questions

1. How likely is it that a candidate product will achieve a meaningfully higher level of effectiveness than what is currently available?
2. Can a single product be developed for both vaginal and rectal use?
3. Is a product a “me too” version of an alternative product that is later stage?
4. Does a product address other user needs, such as contraception or the prevention of other STI’s?
5. Does a product option provide distinct advantages from an access perspective?
6. How amenable is a product to achieving licensure, particularly in a post-placebo controlled efficacy study regulatory environment, by means of innovative trial designs and strategies?

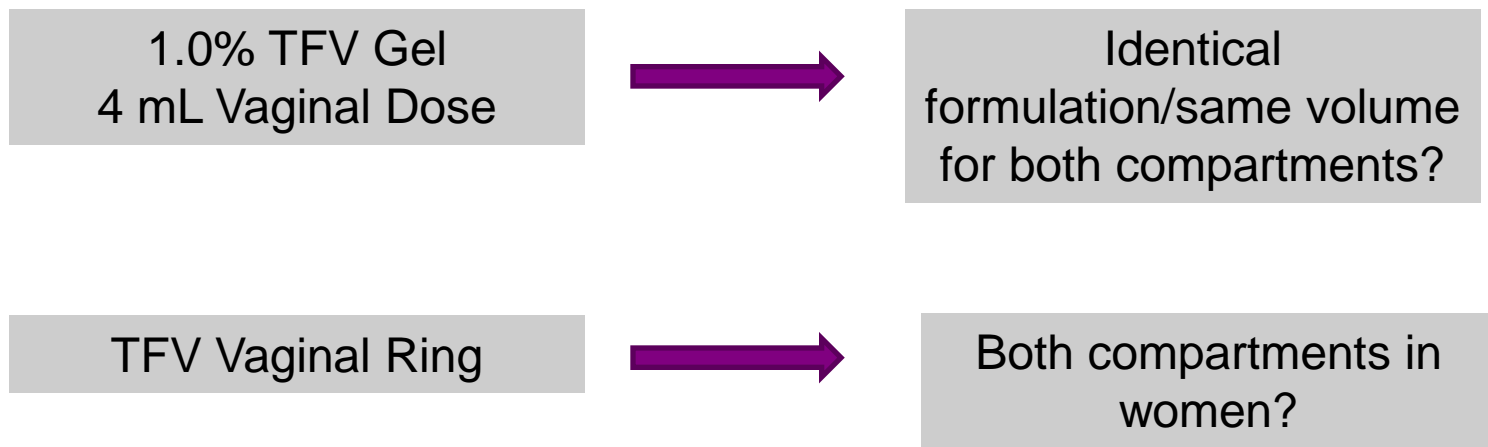
How Can You Achieve a Higher Level of Effectiveness?

- Higher potency drug?
- Broader spectrum (combination of drugs)?
- Greater adherence or acceptability in at risk populations, thereby increasing effectiveness?

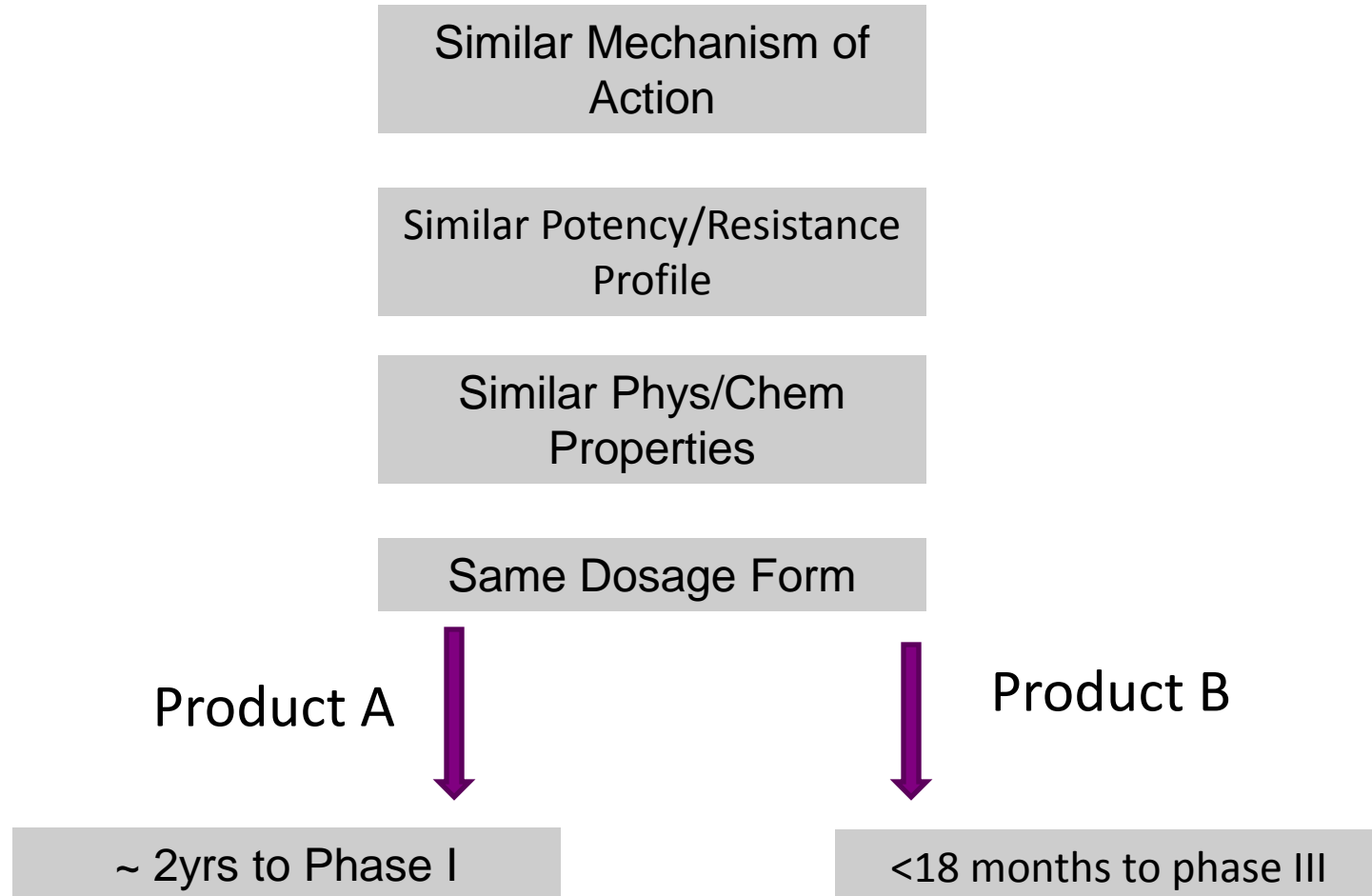


Expanding effectiveness by protecting more sites of HIV exposure

What is the magnitude of development difference required to achieve use in both compartments?



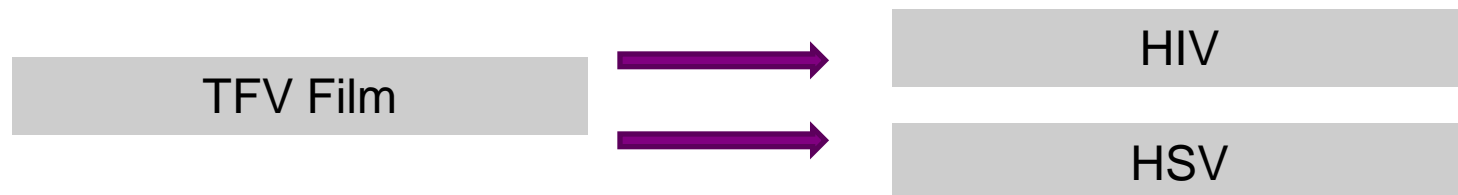
Is a product a “me too” version of an alternative product that is later stage?



Other Factors to Consider Regarding the Pipeline

4. Does a product address other user needs, such as contraception or the prevention of other STI's (particularly those serving as cofactors for HIV infection)?
5. Does a product option, in addition to satisfying the efficacy standards set by current products, also provide distinct advantages from an access perspective?

e.g. Stability, cost, easier to ship, easier to store, easier to manufacture and package, less waste generating, etc



Critical View of the Microbicide Pipeline

6. How amenable is a product to achieving licensure, particularly in a post-placebo controlled efficacy study regulatory environment, by means of innovative trial designs and strategies?

Approved TFV Gel



Approvable TFV Film

The MTN Portfolio

Study	Product	Formulation	Population	Phase	N	2013	2014	2015	2016	2017	2018	2019	2020
MTN-015	N/A	N/A	Seroconverters	N/A	N/A								
MTN-016	N/A	N/A	Pregnancy and infants	N/A	N/A								
MTN-020 (ASPIRE)	Dapivirine	Ring	Women	3	3476								
MTN-018 (CHOICE)	Truvada	Oral	Women	3B	TBD								
MTN-017	Truvada and TFV	Oral / Rectal Gel	MSM TG	2	186								
MTN-026	Maraviroc	Rectal Gel	Men/Women	1	45								
MTN-027	TFV	Rectal Gel	Men/Women	1	45								
MTN-028	MIV-150	Vaginal Gel / Ring	Women	1	45								
MTN-029	MIV-150	Rectal Gel	Men/Women	1	45								
MTN-030	TFV	Rectal Gel	MSM/TG	3	5000								
MTN-031	HC/ART	Ring	Women	1	45								
MTN-032	IQP-0528	Vaginal Gel	Women	1	45								
MTN-033	5P12-RANTES	Rectal Gel	Men/Women	1	45								
MTN-034	Dapivirine	Film	Women	1	45								
MTN-035/HVTN 117	HIV Vaccine/TFV	Oral/Rectal Gel	Men/Women	1	120								
MTN-036	TBD	Rectal Gel	Men/Women	1	45								
MTN-037	HC/ART	Ring	Women	2	200								
MTN-038	Griffithsin	Vaginal Gel	HIV+ Women	1	45								
MTN-039	Dapivirine	Film	Women	2	200								
MTN-040	Dapivirine	Film	Pregnancy	1	45								
MTN-041	HC/ART	Ring	Women	3	5000								
MTN-042	TDF	Ring	Women	2	200								
MTN-043	IQP-0528	Ring	Women	1	45								
MTN-044	Griffithsin	Rectal Gel	Men/Women	1	45								
MTN-045	Dapivirine	Film	Adolescent girls	1	45								
MTN-046	HC/ART	Ring	Lactating women	1	45								

Vaginal Microbicides

Study	Phase	Population	Product(s)	N
MTN-028	1	Women	MIV-150 gel/ring	45
MTN-032	1	Women	IQP-0528 gel	45
MTN-034	1	Women	DPV film	45
MTN-038	1	HIV + Women	Griffithsin gel	45
MTN-039	2	Women	DPV film	200
MTN-040	1	Pregnancy	DPV film	45
MTN-042	2	Women	TDF ring	200
MTN-043	1	Women	IQP-0528 ring	45
MTN-045	1	Adolescents	DPV film	45
MTN-046	1	Lactation	HC/ARV	45

Rectal Microbicides

Study	Phase	Population	Product(s)	N
CHARM-03 / MTN-026	1	Men/Women	MVC gel	45
MTN-027	1	Men/Women	TFV gel	45
MTN-029	1	Men/Women	MIV-150	45
MTN-030	2B/3	MSM and Transgender women	TFV gel	5,000
MTN-033	1	Men/Women	5P12-RANTES	45
MTN-035 HVTN 117	1	MSM and Transgender women	Oral TDF/FTC TFV gel HIV vaccine	120
MTN-036	1	Men/Women	TBD	45
MTN-044	1	Men/Women	Griffithsin	45

Combination Rings

Dual Protection VR	Indications	Status	Developer
TFV + LNG	HIV + pregnancy (+ HSV)	Preclinical	CONRAD
MIV-150+ZN acetate + LNG	HI + pregnancy + HSV (+HPV)		Population Council
DPV + HC (TBD)	HIV + pregnancy		IPM
TDF + progestin type HC	HIV + pregnancy		AECOM, U Utah
AZT + ferrous gluconate	HIV + pregnancy		Weill COM, Cornell
AZT + l-ascorbic acid	HIV + pregnancy		Weill COM, Cornell
Nuvaring + ARV (TBD)	HIV + pregnancy		Merck

Proposed Ring Studies

Study	Phase	Population	Product(s)	N
MTN-031	1	Women	HC/ARV ring	45
MTN-037	2	Women	HC/ARV ring	200
MTN-041	3	Women	HC/ARV ring	5,000



Summary

- Development of safe and effective microbicides remains a critical focus for HIV prevention research; more critical prioritization and coordination is critical
- Increased emphasis on sustained delivery products
- Parallel vaginal and rectal microbicide development critical important
- “Best” microbicide product may be cheapest to manufacture and/or sustained delivery and/or “multipurpose” rather than most potent ARV

MTN Partners



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