

# PrEP Beyond Pills

New Technologies in  
Biomedical HIV Prevention





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**The views expressed are not necessarily those of CDC, HRSA, or the NIH.**

# Objectives

- List three ways in which pre-exposure prophylaxis may be delivered in the future.
- Describe the results of HPTN 083 and what this means for PrEP in the near term.
- Identify the agent currently under investigation as implantable PrEP.
- Explain how broadly neutralizing antibodies work to prevent HIV infections.



@LETSPREPWISC

NDC 61958-0701-1

**Truvada<sup>®</sup>**

(emtricitabine and tenofovir  
disoproxil fumarate)

Tablets

- LIMITED EDITION -  
**PUMPKIN SPICE**

Rx only



GILEAD



# Pregnancy Prevention

## Education & behavior modification

### Condoms



### Rings



### Birth control pill & injection



### “Morning-after pill”



### Spermicide



### Implantable birth control



### Vasectomy/Tubal Ligation

# Pregnancy Prevention

# HIV Prevention

Education & behavior modification

Education & behavior modification

Condoms



Condoms

Rings



Rings

Birth control pill & injection



PrEP (oral & injectable)

“Morning-after pill”



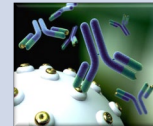
Post-exposure prophylaxis

Spermicide



Topical microbicides

Implantable birth control



Broadly neutralizing Abs  
Implantables

Vasectomy/Tubal Ligation



Vaccination

# Pregnancy Prevention

# HIV Prevention

Education & behavior modification

Education & behavior modification

Condoms



Condoms

Rings



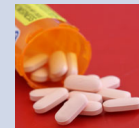
Rings

Birth control pill & injection



PrEP (oral & injectable)

“Morning-after pill”



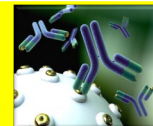
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Broadly neutralizing Abs  
Implantables

Vasectomy/Tubal Ligation



Vaccination

# Rings



# ASPIRE

Monthly dapivirine ring

2629 cis women aged 18-45

Malawi, South Africa, Uganda, Zimbabwe

July 2012 – August 2015



**ASPIRE**

A Study to Prevent Infection  
with a Ring for Extended Use

**27%**

lower  
incidence  
**overall**

71 infections on DPV,  
97 on placebo  
(95%CI: 1, 46)

**56%**

lower incidence  
among  
participants

> 21 years old  
(95%CI: 31, 71)

**61%**

lower incidence  
among  
participants

≥ 25 years old  
(95%CI: 32, 77)

**Younger women didn't adhere**

# The Ring Study

Monthly dapivirine ring

1959 cis women aged 18-45

South Africa and Uganda

April 2012 – December 2016



# 31%

lower  
incidence  
**overall**

77 infections on DPV,  
56 on placebo  
(HR 0.69;  
95%CI: 0.49, 0.99)

# 15%

lower incidence  
among  
participants  
 $\leq 21$  years old

(HR 0.85;  
95%CI: 0.45, 1.60)

# 37%

lower incidence  
among  
participants  
 $> 21$  years old

(HR 0.63;  
95%CI: 0.41, 0.97)

# Open-label extensions

ASPIRE → HOPE

Ring → DREAM

*Placebo incidence is estimated*



39%

lower incidence  
among 1465 open-label  
recipients in HOPE  
(95%CI: 14, 65)

63%

lower incidence  
among 941 open-label  
recipients in DREAM  
(95%CI: 0.86, 2.33)

# Where does dapivirine go from here?



- Positive opinion from European Medicines Agency in **July 2020**
- FDA application anticipated in 2020
- Three-month version in development
- Coformulation with levonorgestrel in development



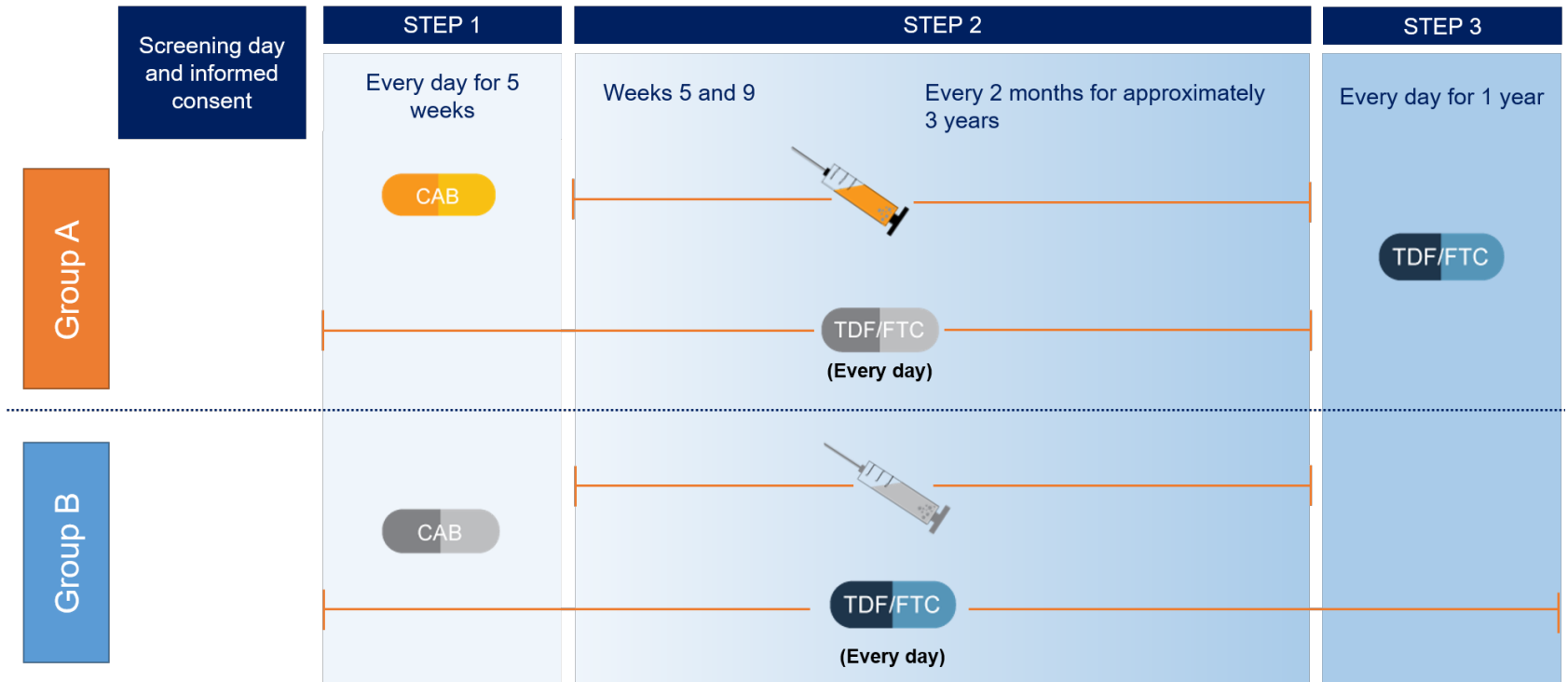
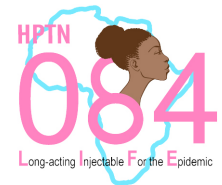


# L A I S



# HPTN 083 & 084

Oral FTC/TDF vs Injectable Cabotegravir-LA  
MSM & TGW (083) and Cisgender Women (084)



- TDF/FTC pill
- Cabotegravir (CAB) injection
- Placebo for TDF/FTC pill
- Placebo for cabotegravir (CAB) injection
- Cabotegravir (CAB) pill
- Placebo for cabotegravir (CAB) pill

# HPTN 083

Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW



## December 2016 – May 2020

# 4566

at-risk persons

(target N = 5000)

87.5% MSM 12.4% TGW

# 50%

daily  
FTC/TDF

(n=2284)

# 50%

long-acting  
injected CAB

(n=2282)

# 37%

from US

(n=1698)

# 49.7%

of US participants  
were Black

(n=844)

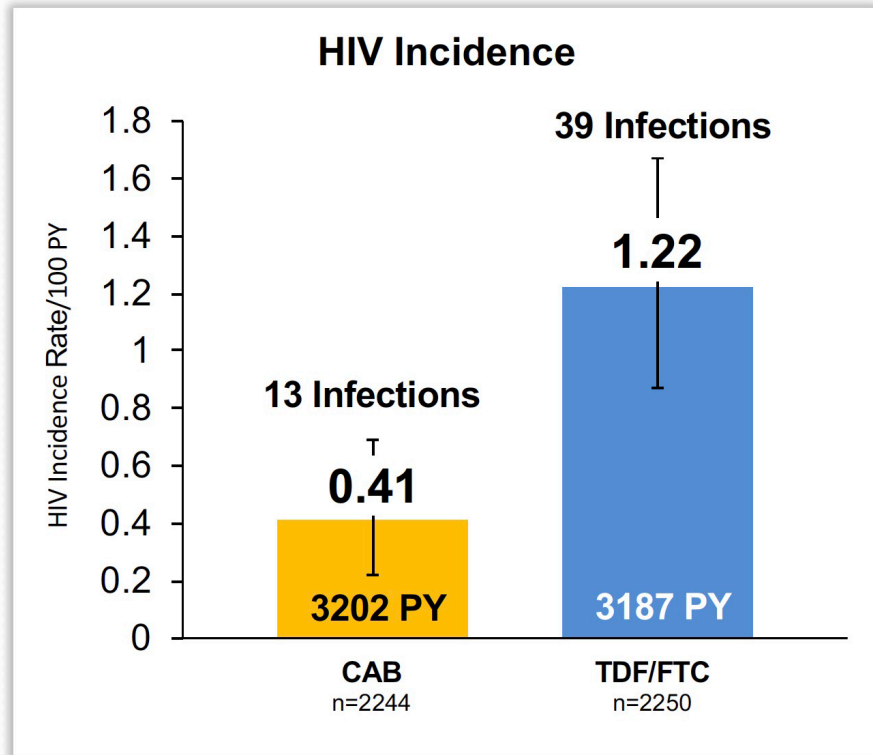
# 26

median age

(IQR 22-32)

# HPTN 083

Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW

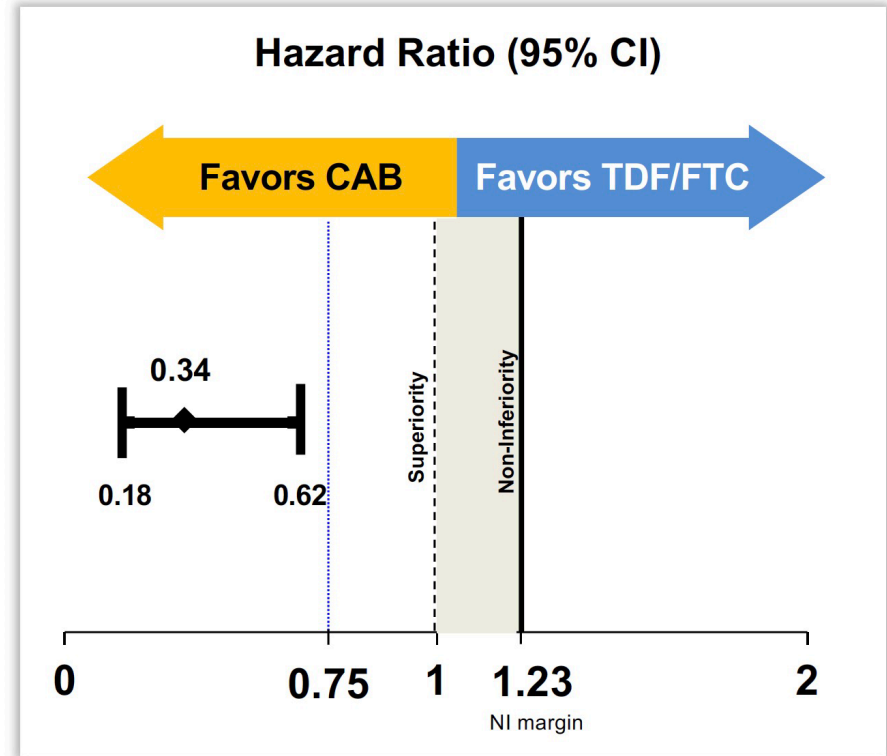
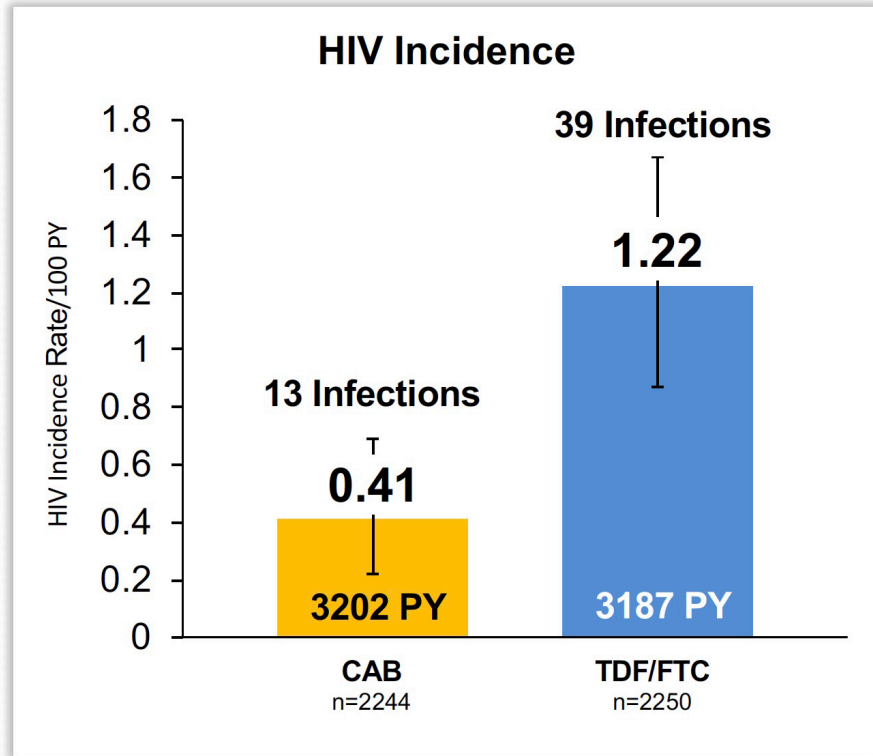


CI, confidence interval

52 infections  
6389 PY of follow-up

# HPTN 083

Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW



CI, confidence interval

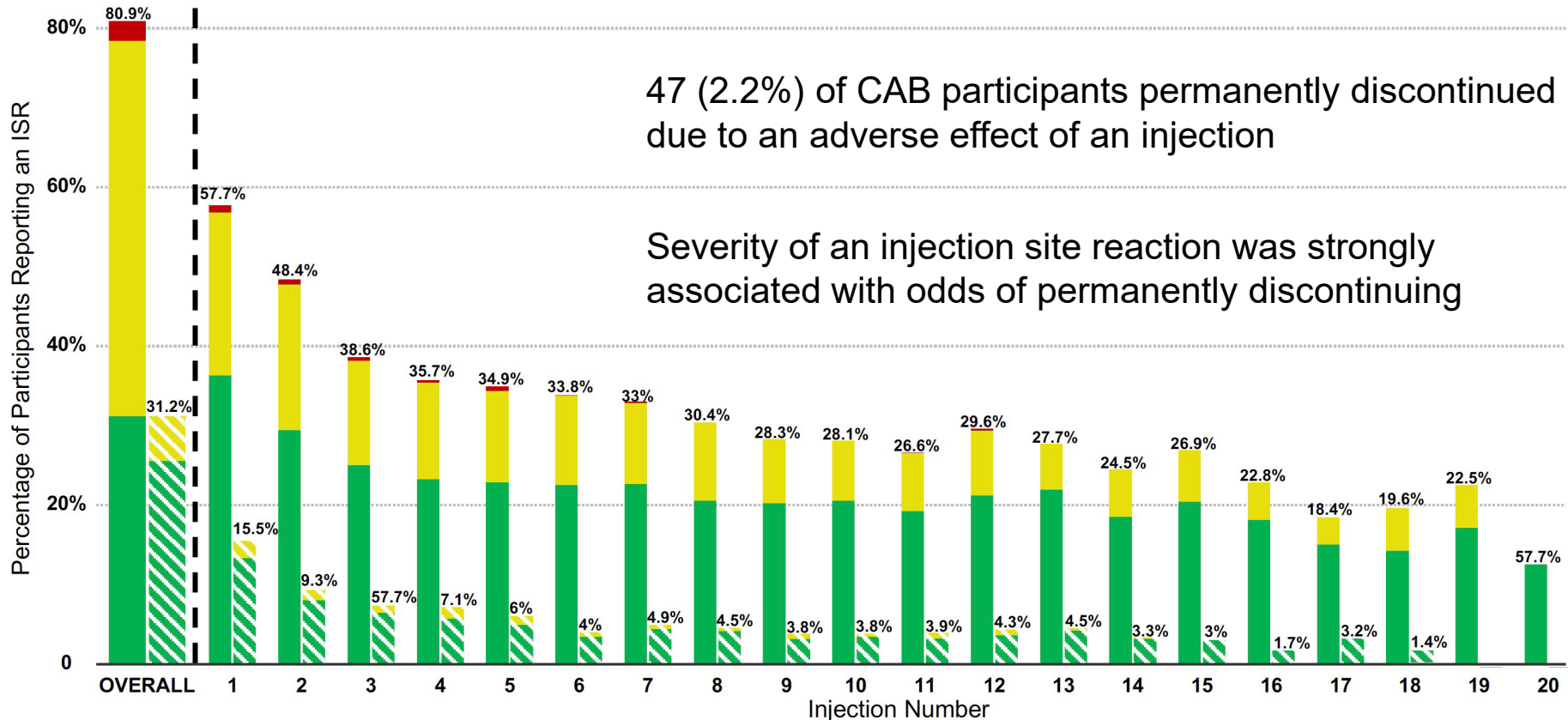
52 infections  
6389 PY of follow-up

# 66%

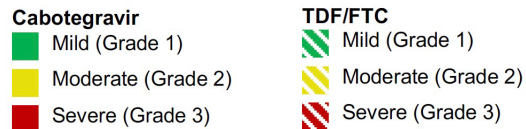
reduced hazard of HIV among CAB recipients,  
compared with FTC/TDF  
(95%CI: 18%, 62%; p=0.0005)

# HPTN 083

## Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW

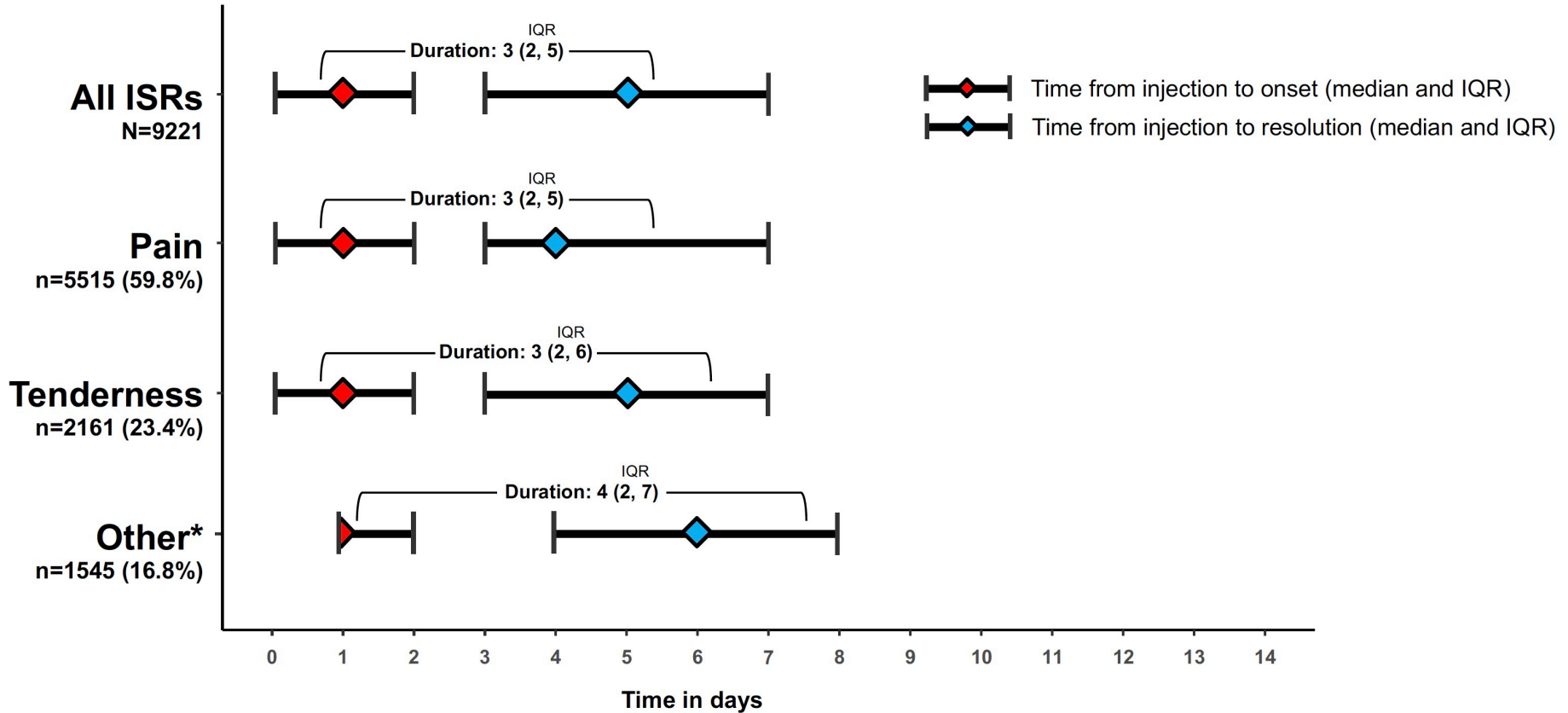


<b>Cabotegravir, n</b>	2117	2117	2037	1938	1872	1761	1620	1464	1360	1200	1034	877	744	604	465	372	298	234	168	111	8
<b>TDF/FTC, n</b>	2081	2081	2014	1940	1869	1760	1606	1463	1355	1193	1037	903	760	596	482	370	288	220	146	89	6



# HPTN 083

## Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW



\*Other injection site reactions include induration, nodule, hematoma, bruising, discoloration, swelling, erythema, itching, warmth, anesthesia, hemorrhage, and abscess

# Unanswered questions

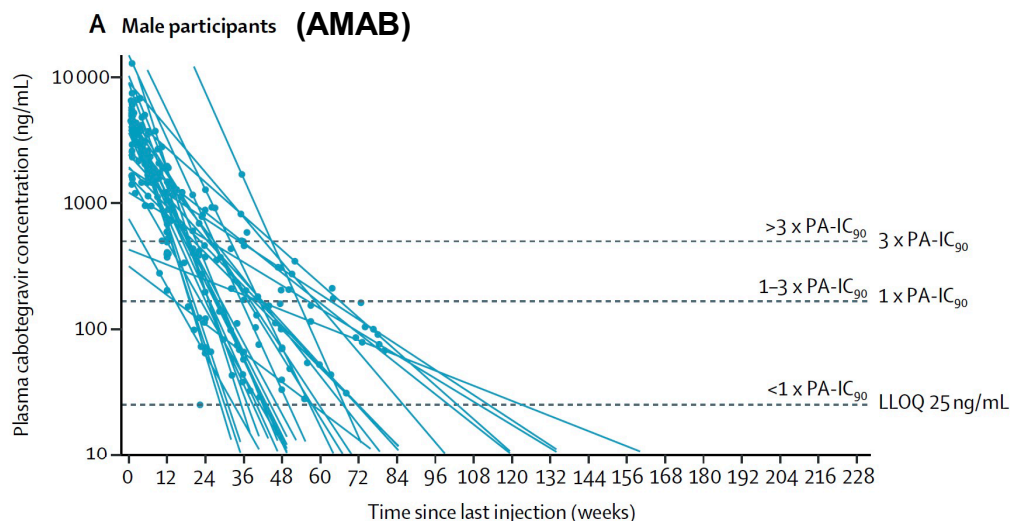
## Is an oral “lead-in” really necessary?

	TOTAL (n=4566)	TDF-FTC (n=2284)	CAB (n=2282)	p-value
<b>Participants with grade 3+ AEs, n (%)</b>	1490 (32.7%)	766/2282 (33.6%)	724/2280 (31.8%)	
CPK increased	633 (13.9%)	309 (13.5%)	324 (14.2%)	0.51
Creatinine clearance decreased	348 (7.6%)	190 (8.3%)	158 (6.9%)	0.08
Lipase increased	152 (3.3%)	76 (3.3%)	76 (3.3%)	0.99
Creatinine increased	152 (3.3%)	75 (3.3%)	77 (3.4%)	0.87
AST/SGOT increased	122 (2.7%)	69 (3.0%)	53 (2.3%)	0.14
<b>Participants with EAEs and SAEs, n (%)</b>	240 (5.3%)	122 (5.4%)	118 (5.2%)	
<b>Participant deaths, n (%)</b>	11 (0.24%)	7 (0.3%)	4 (0.2%)	



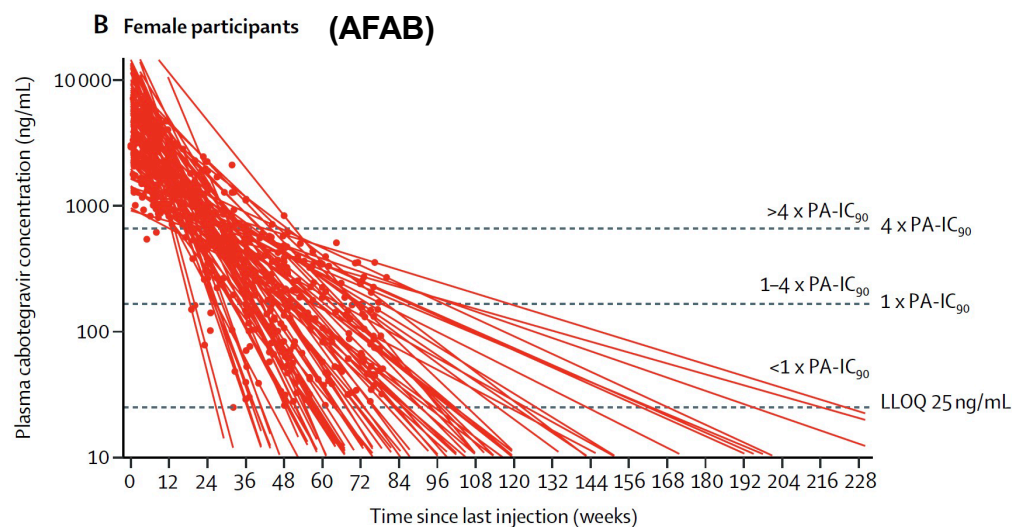
# Unanswered questions

## What about covering the “tail”?



CAB dropped below LLOQ  
after a median of  
**10 months**  
among participants  
assigned male at birth

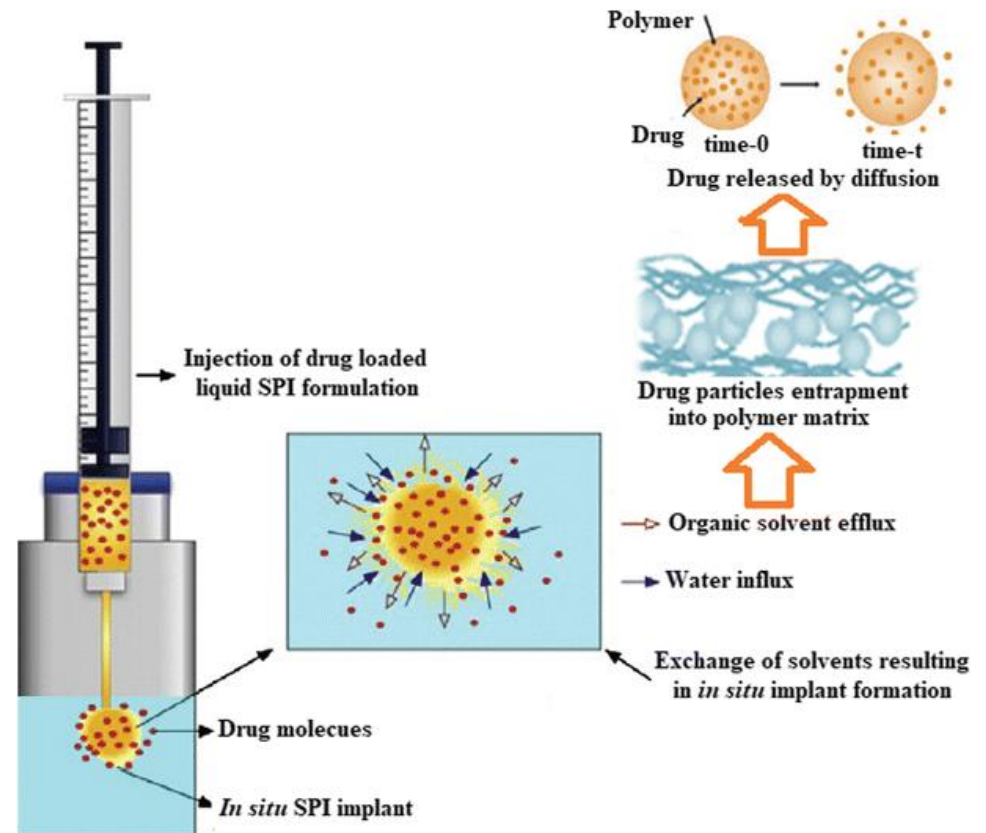
**15.5 months**  
among participants  
assigned female at birth



# What if you could just remove it?



S. Rahima Benhabbour, PhD  
and Martina Kovarova, PhD



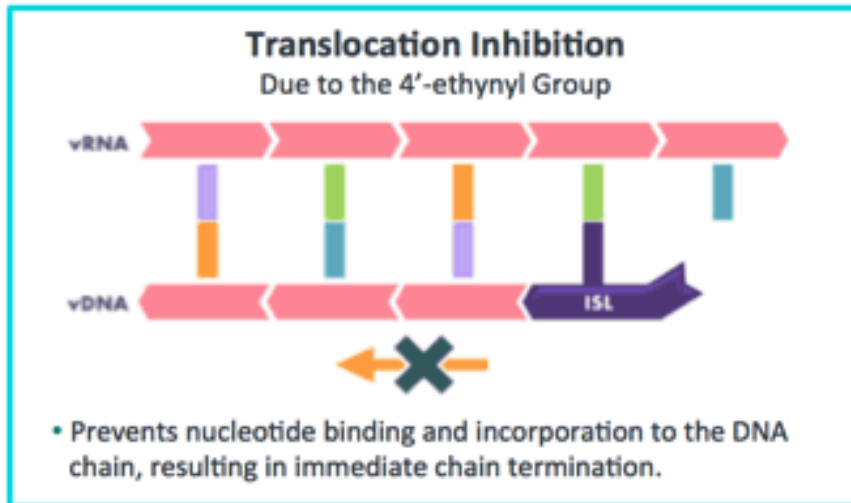
# Implant s



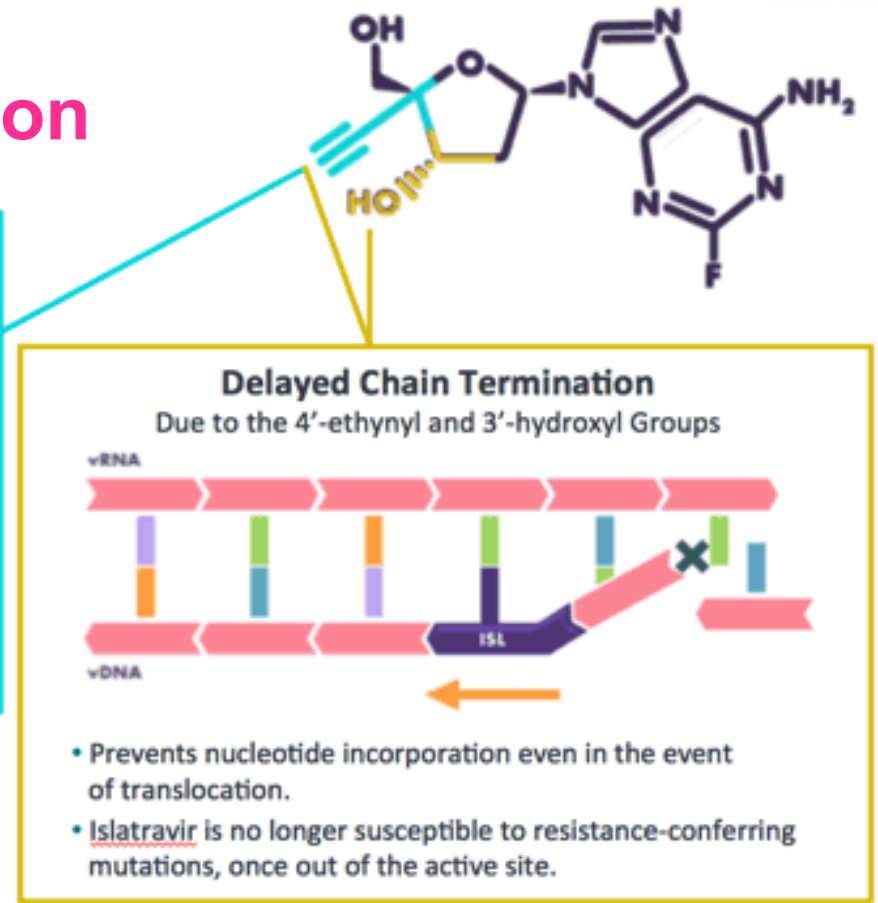
# Islatravir

First-in-class nucleoside reverse transcriptase **translocation** inhibitor <sup>NRTTI</sup>  
Formerly known as MK-8591 or EFdA

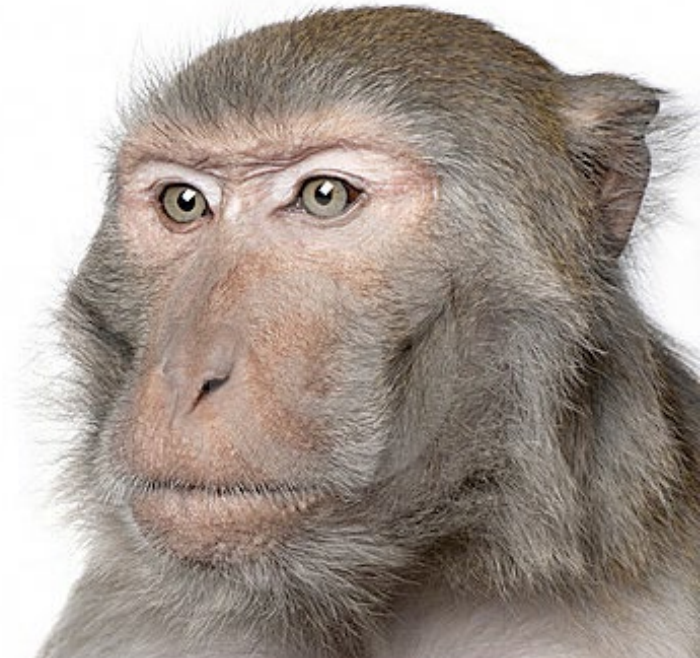
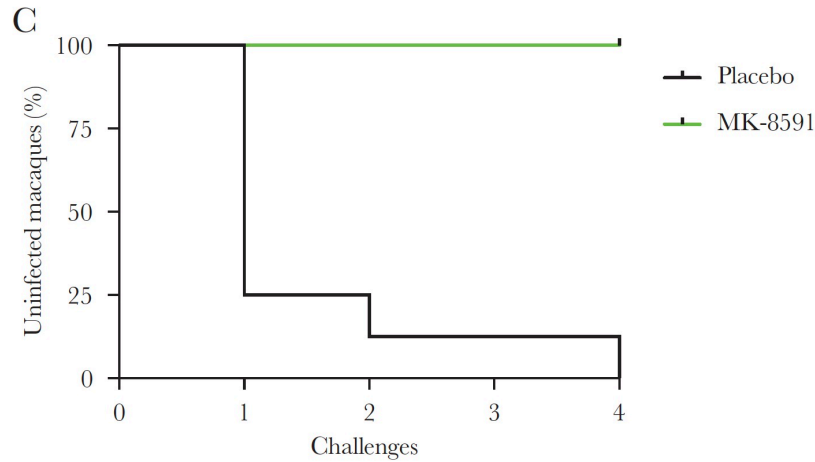
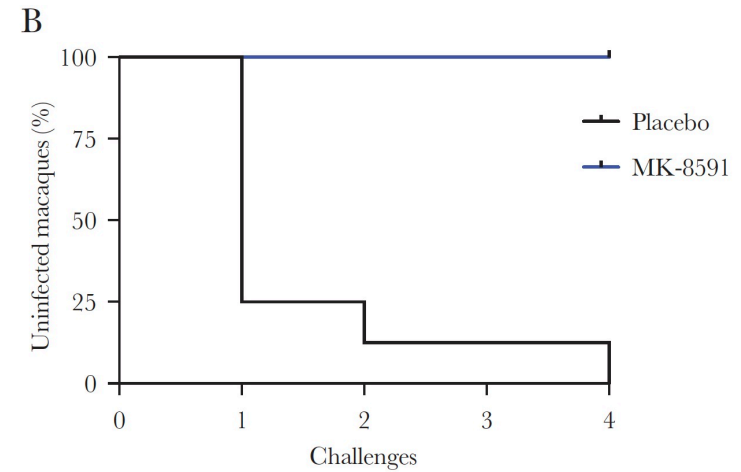
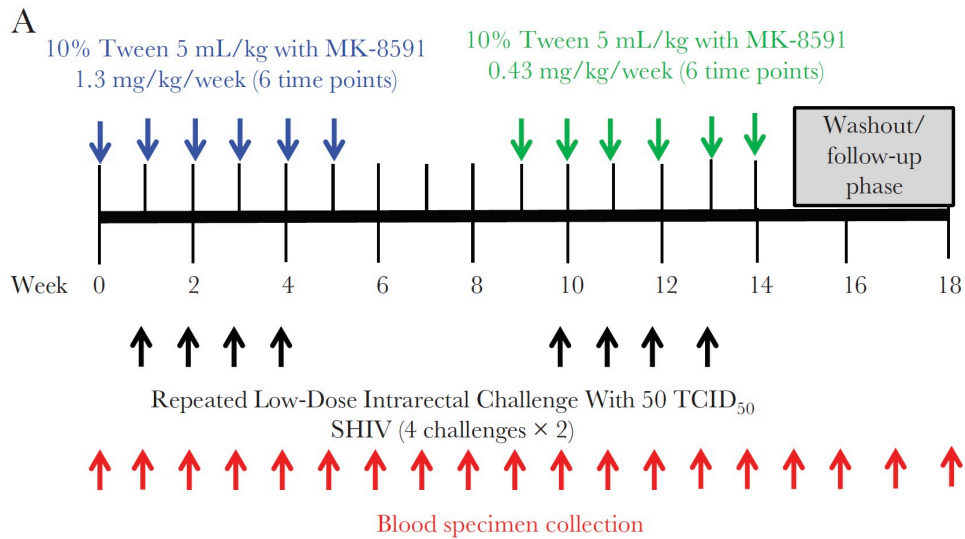
## Two mechanisms of action



Essentially, it's "sticky" and once incorporated, it keeps the entire RT "machine" from ratcheting forward (strong interaction with dNTP binding site of RT)



# Islatravir PO once weekly protects macaques

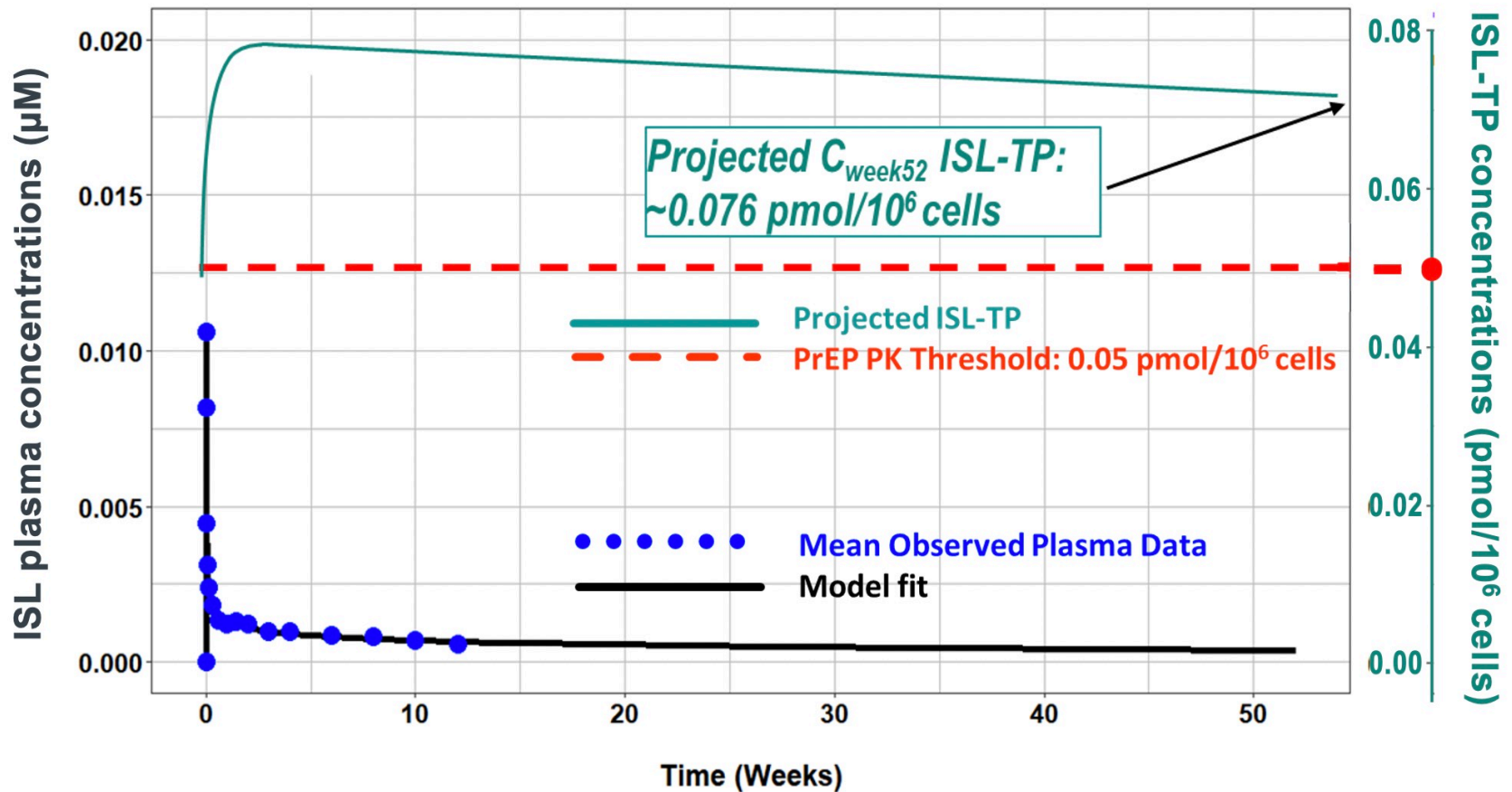




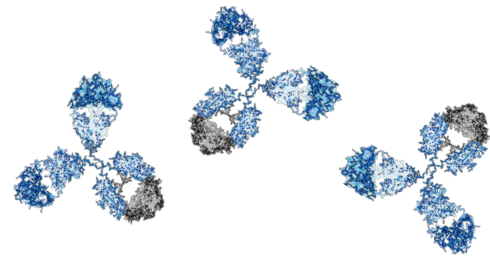
# Islatravir prototype similar to Nexplanon



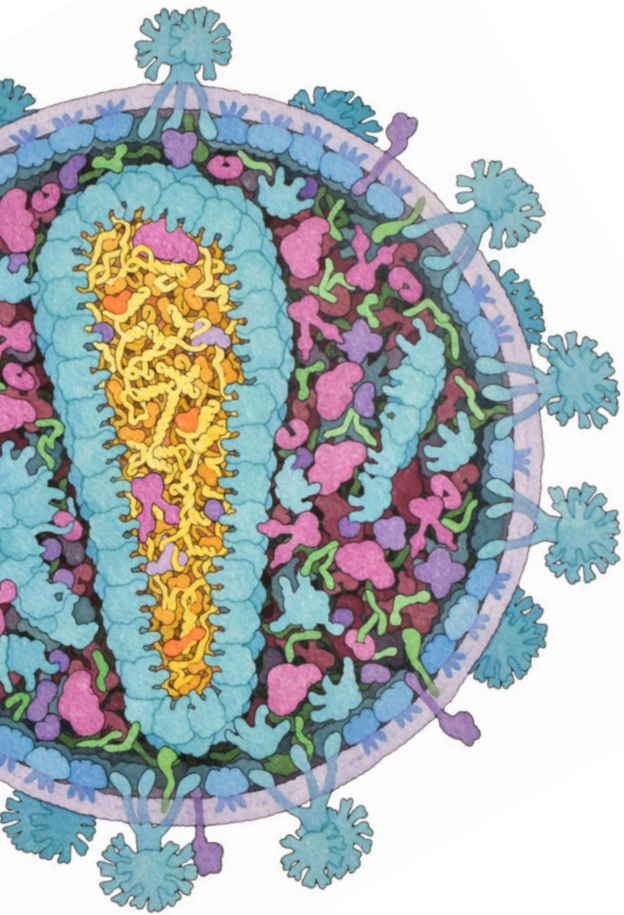
# Islatravir levels predicted to last 1 year

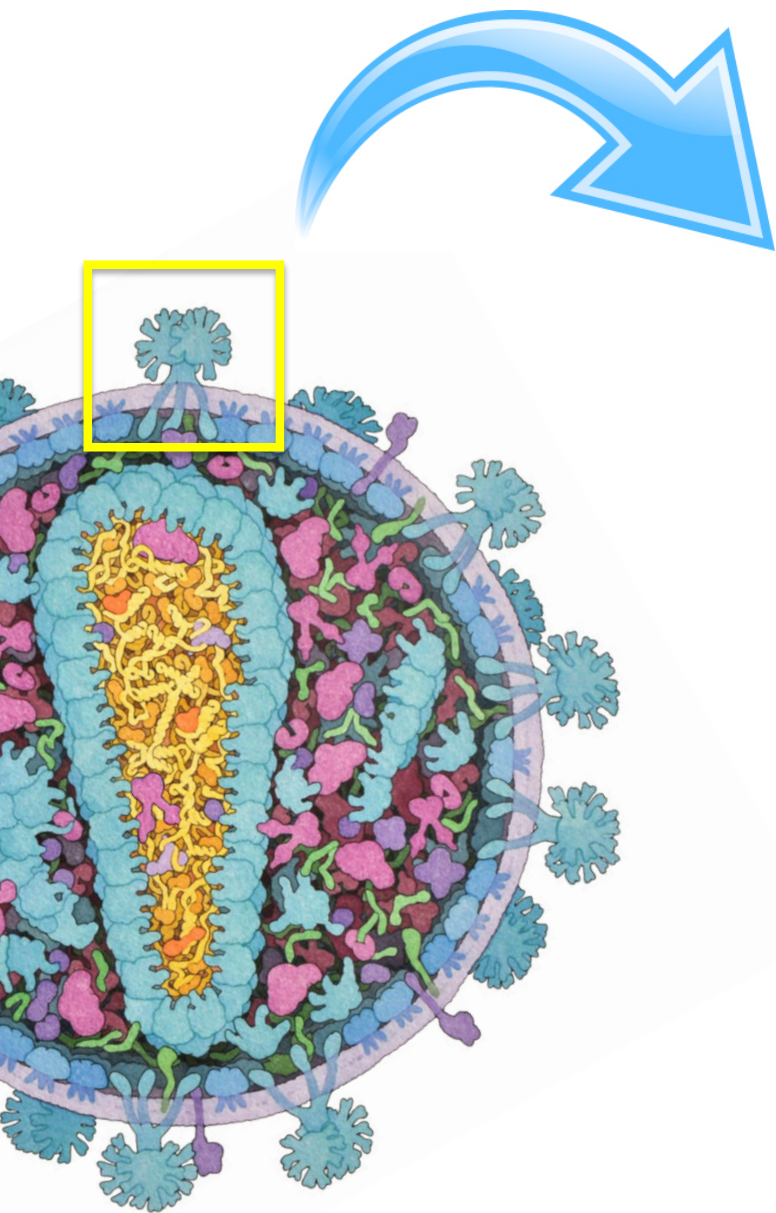


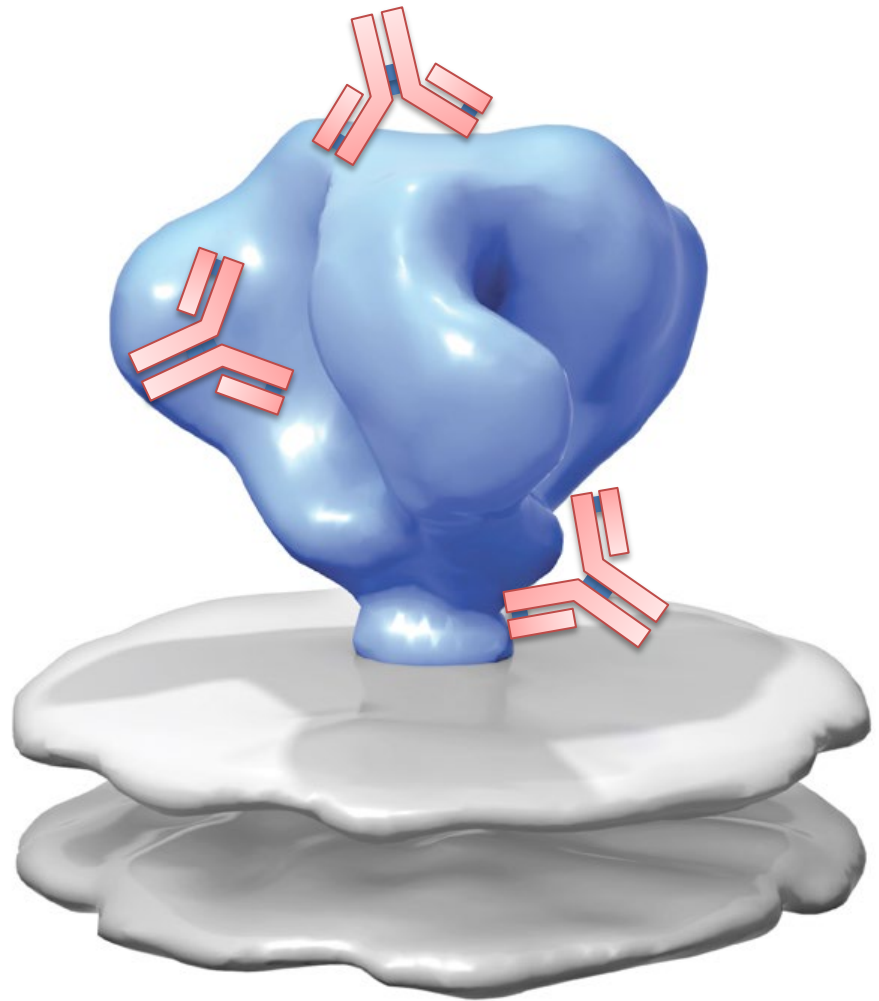
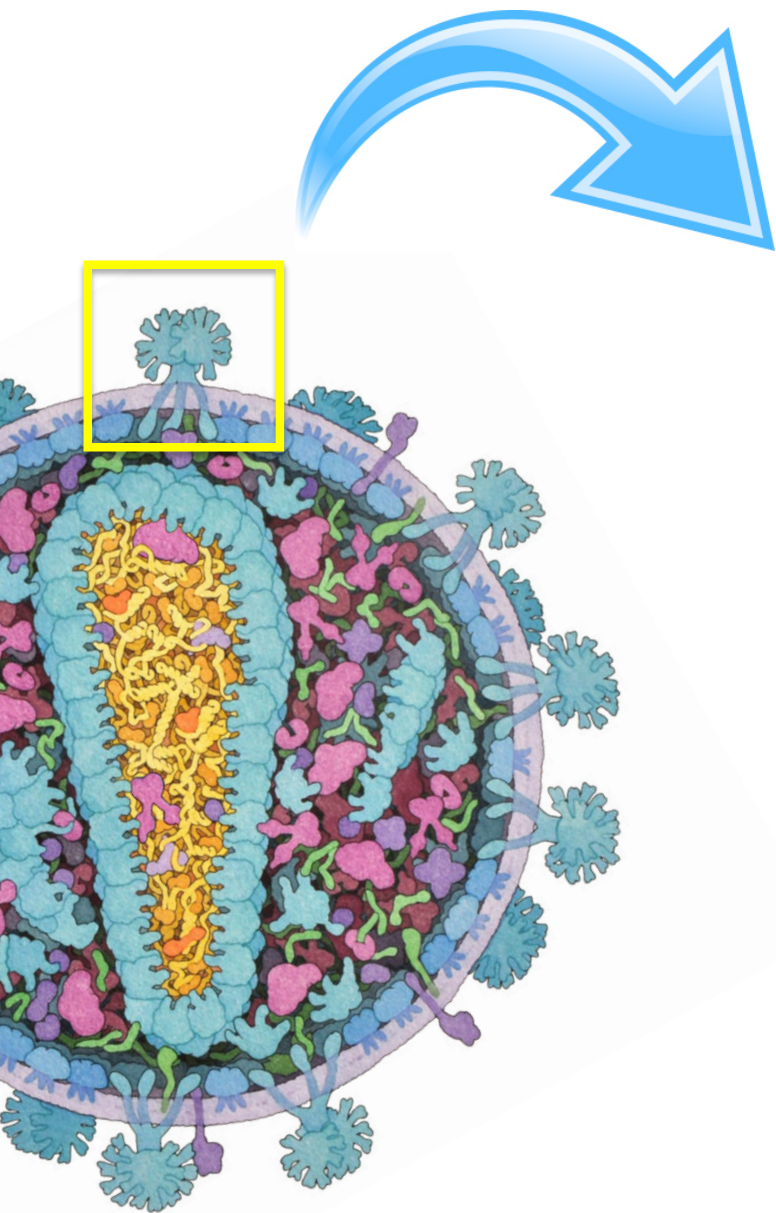
# bnAbs



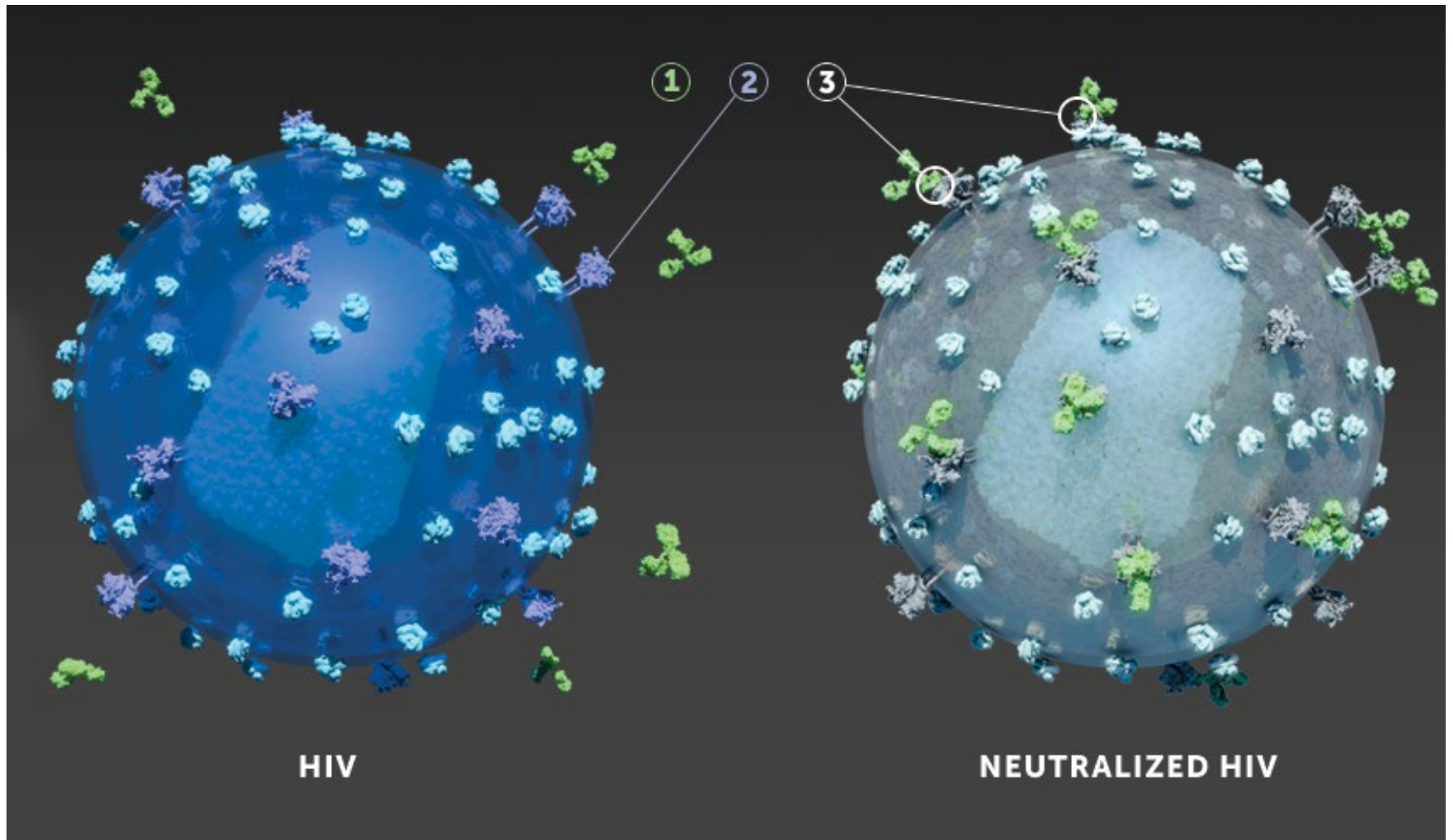


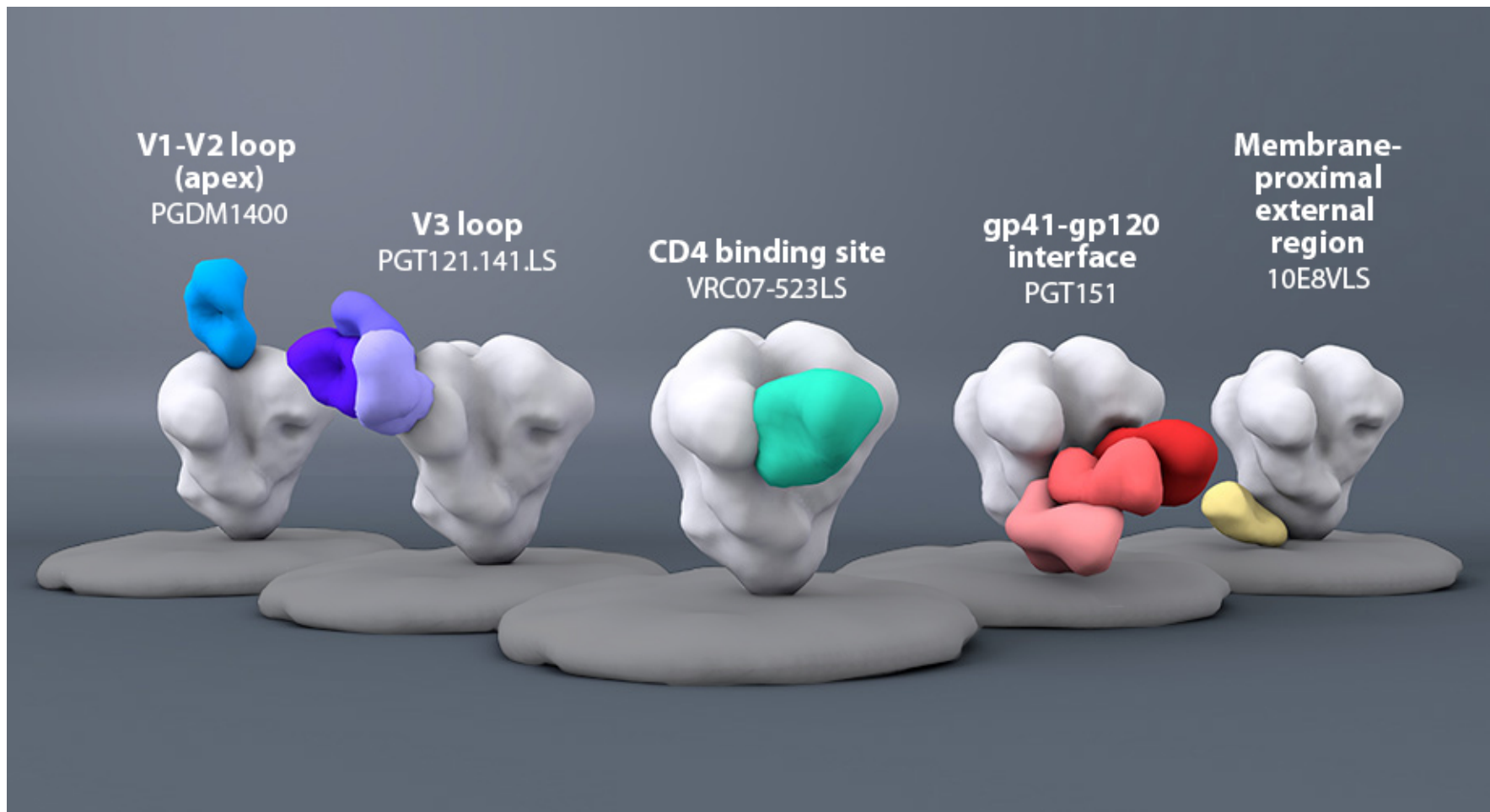


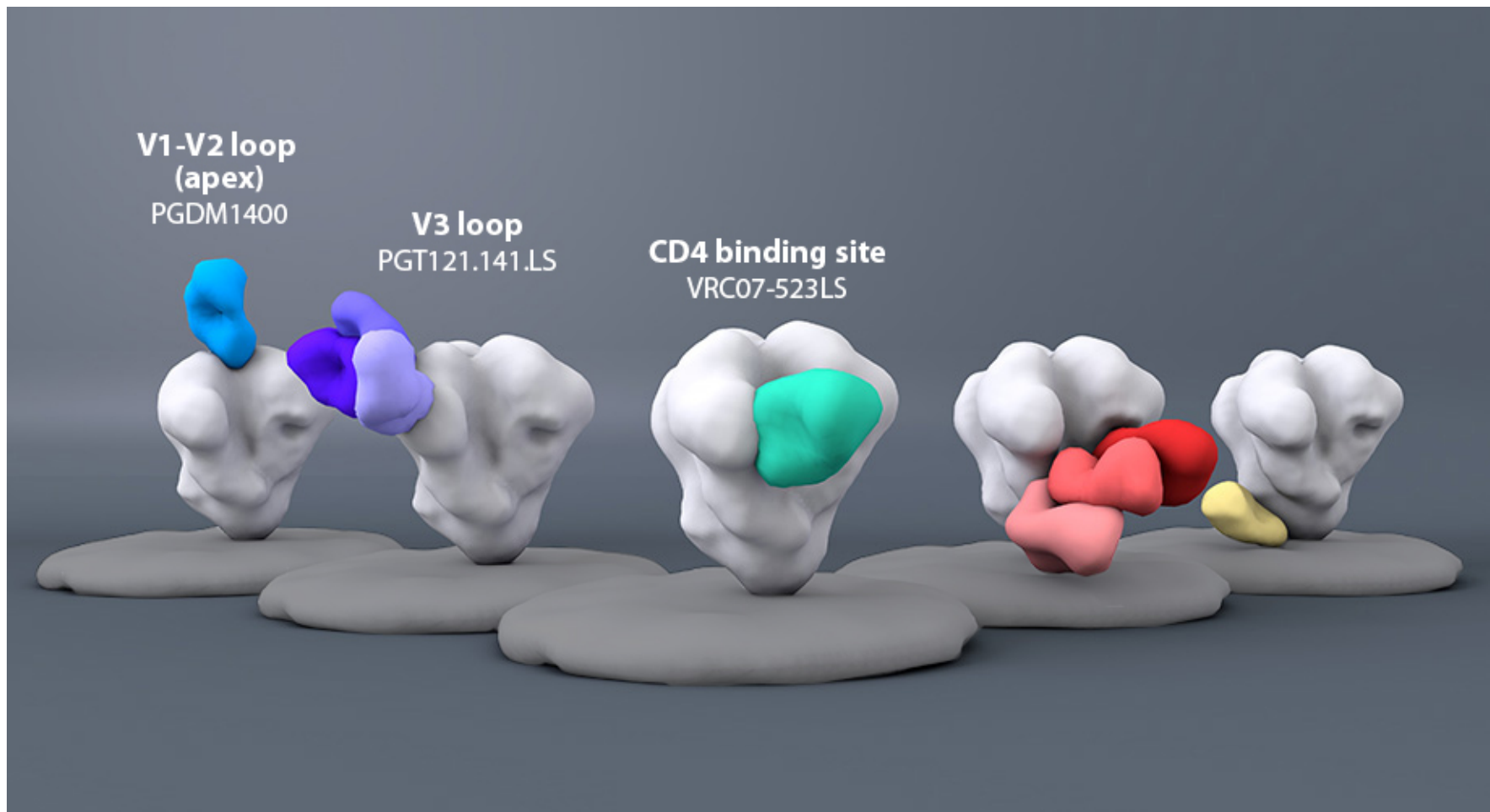






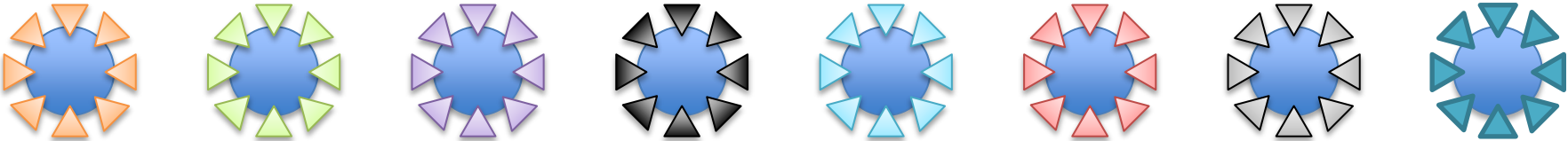






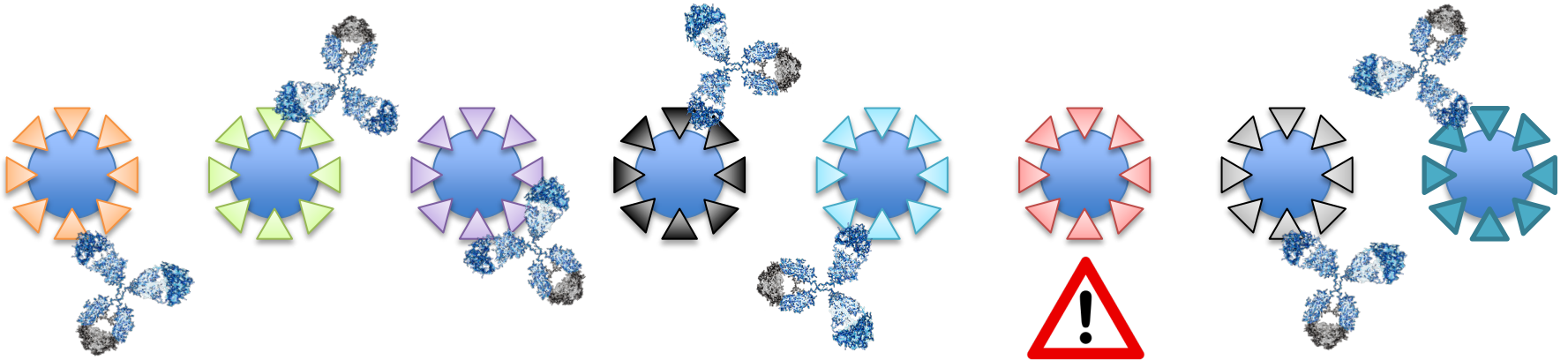
# Breadth & potency of bnAbs are important

How many viruses circulating in transmission networks will the antibody neutralize?



# Breadth & potency of bnAbs are important

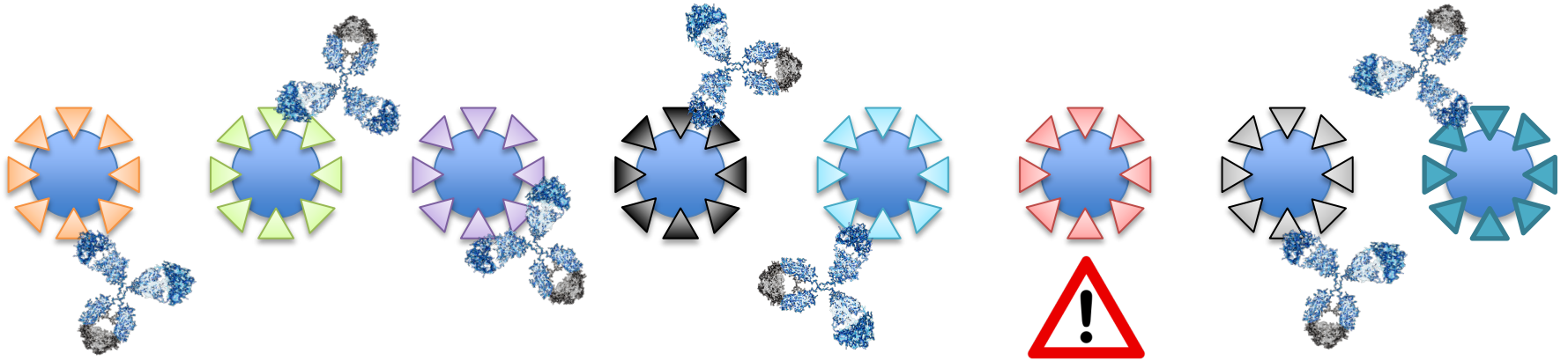
How many viruses circulating in transmission networks will the antibody neutralize?



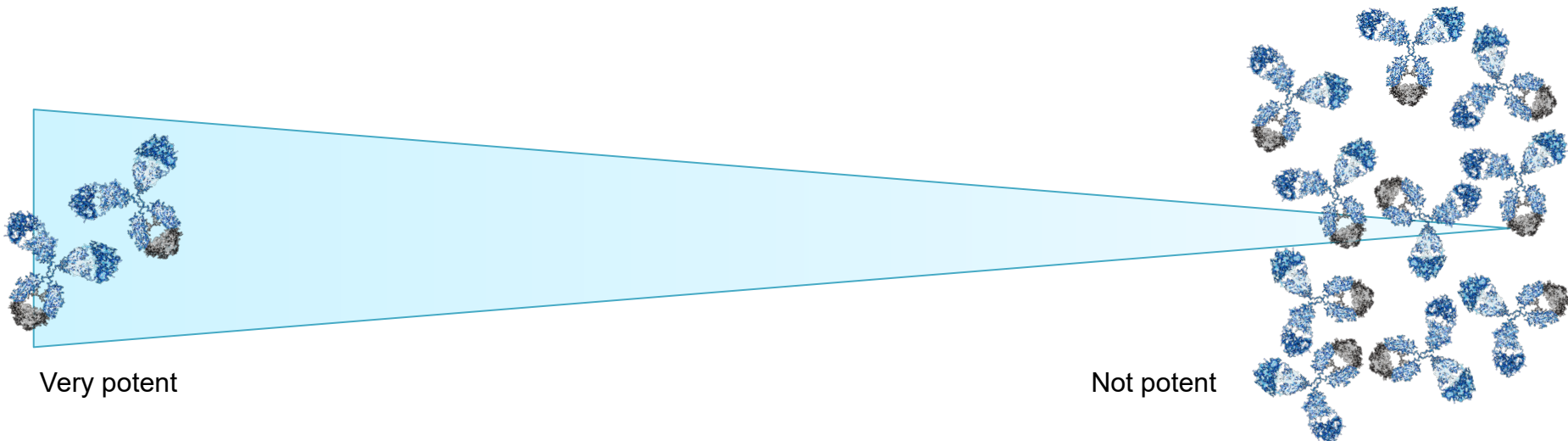


# Breadth & potency of bnAbs are important

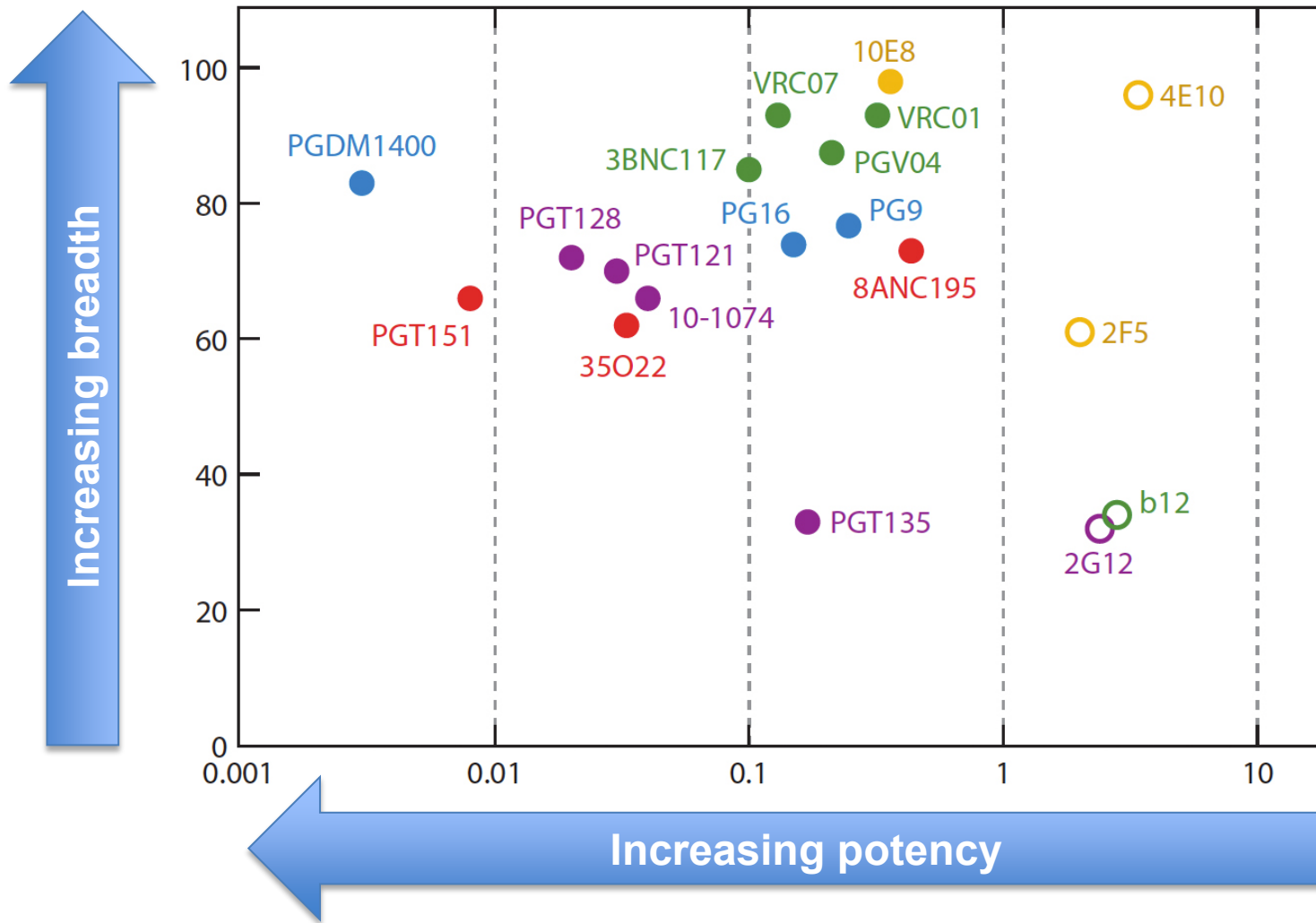
How many viruses circulating in transmission networks will the antibody neutralize?



How much of an antibody “dose” is required to neutralize viruses?



# Breadth & potency of bnAbs are important

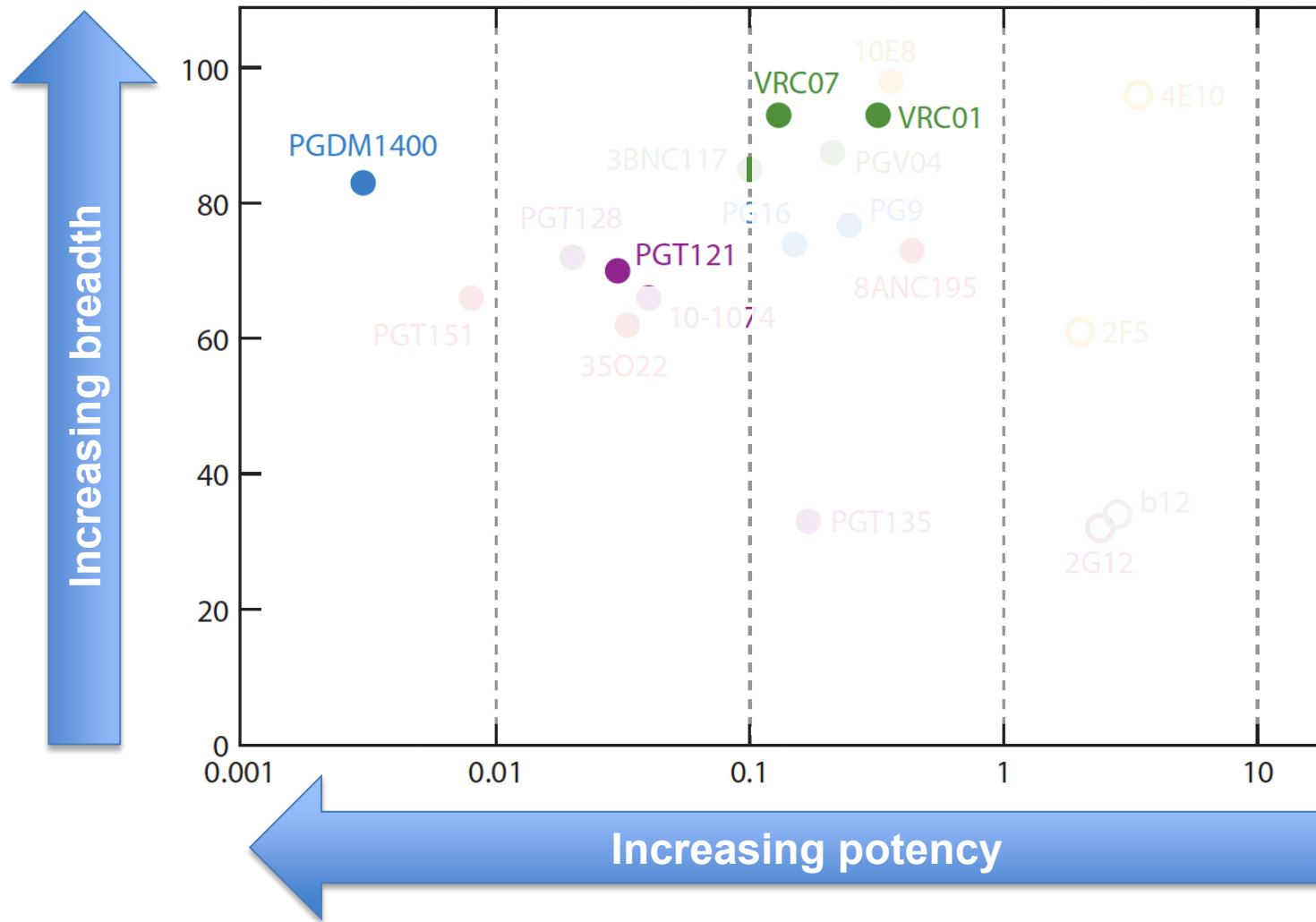


Open circle: 1st generation mAb  
 Filled circle: 2nd generation mAb

CD4 binding site  
 Apex-specific

High-mannose patch  
 gp120-gp140 interface  
 Membrane proximal external region (MPER)

# Four bnAbs are the focus of current studies



Open circle: 1st generation mAb  
 Filled circle: 2nd generation mAb

CD4 binding site  
 Apex-specific

High-mannose patch  
 gp120-gp140 interface  
 Membrane proximal external region (MPER)

# Antibody-Mediated Prevention Study (VRC01)



**COMING SOON**



**STOP AIDS**

**Questions?**

Please email me!

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