

NEXT GENERATION 3D PRINTED INTRAVAGINAL RINGS FOR PREVENTION OF HIV AND UNINTENDED PREGNANCY

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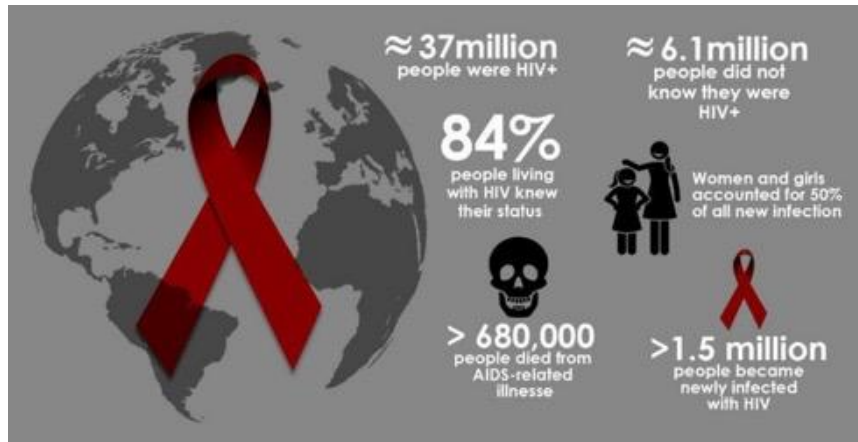
Disclosures

Author S. Rahima Benhabbour of this presentation is the Founder and Director of Anelleo, Inc. and has equity ownership in Anelleo, Inc. to which the following technologies used or evaluated in this presentation have been or could be licensed: 3D Printed IVRs.

Author S. Rahima Benhabbour is inventor of the ISFI and PSI technologies and could receive royalties.

Global HIV and Unplanned Pregnancy Prevalence

HIV



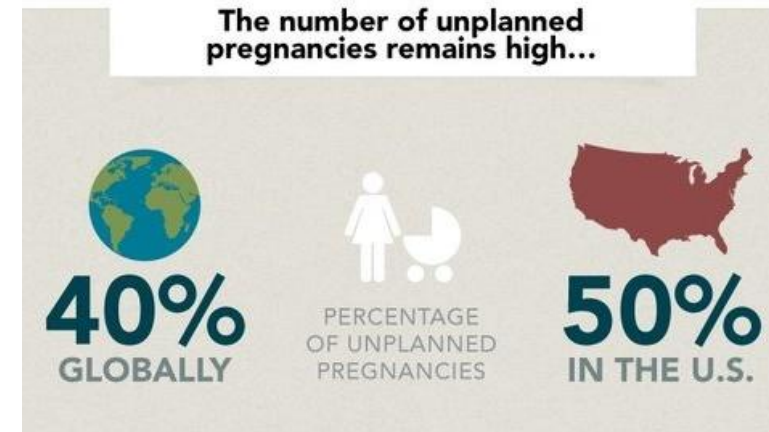
38 million people are living with HIV

1.5 million people became newly infected in 2021

19.2 million women are living with HIV

Sub-Saharan Africa accounts for 68% of global HIV infections

Unplanned Pregnancy



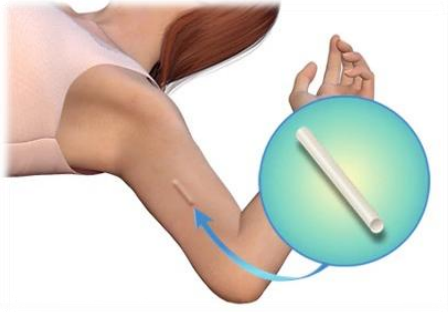
120 million unplanned pregnancies each year

65% of unplanned pregnancies arise from nonuse of contraceptive methods

14 million unplanned pregnancies in Sub-Saharan Africa

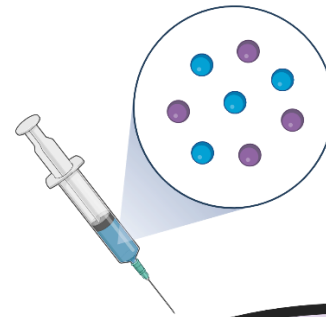
41% women discontinue short-acting birth control methods

Ultra-Long-Acting Multipurpose Prevention Technologies

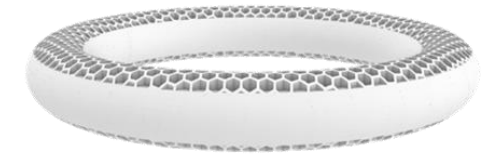


U.S. PCT/US20/16061

MPT ISFI for HIV prevention & contraception

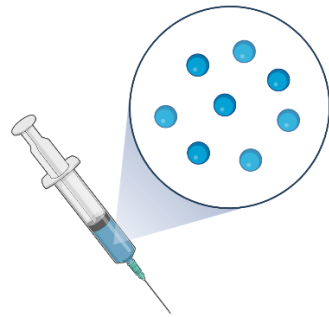


ARV (CAB or DTG)
Hormone (ENG or MPA)



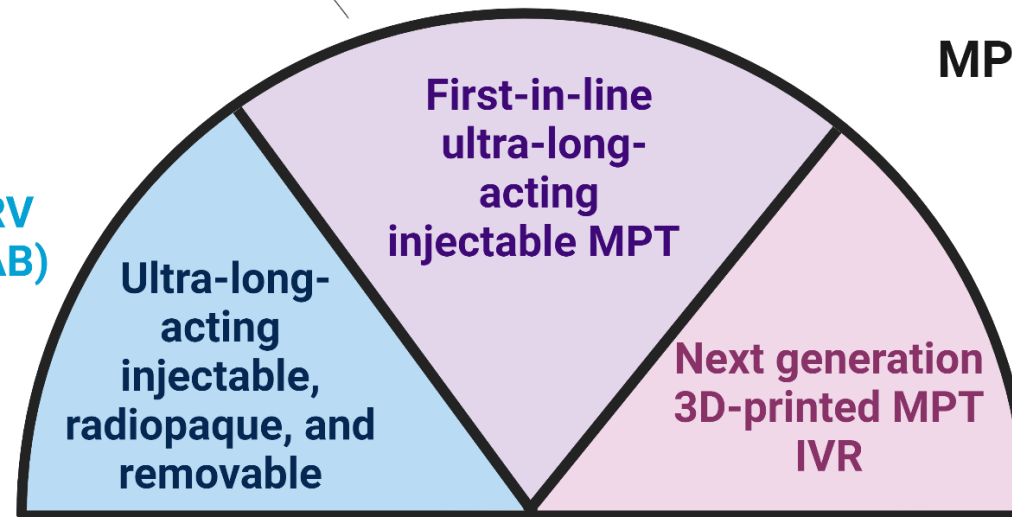
US PTO 11,219,595 B2
U.S. PCT/US21/50949

CAB ISFI for HIV prevention

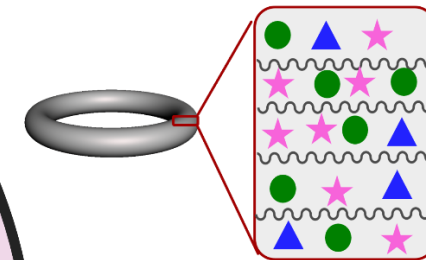


ARV (CAB)

U.S. PCT/US22/35713

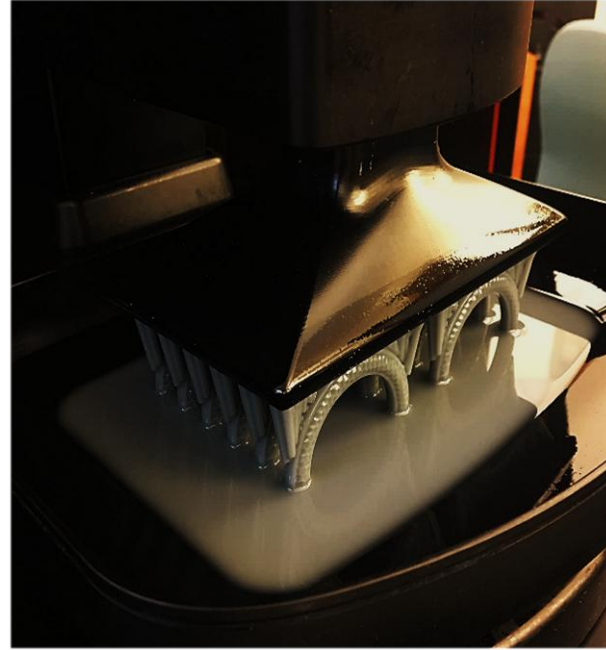
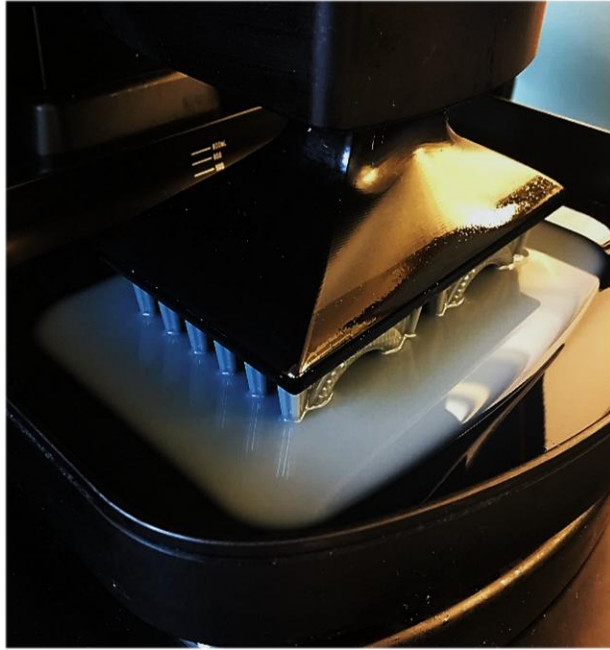


MPT IVR for HIV prevention & contraception



Hormone (ENG/EE)
ARV (ISL)

Expand preventative options, bring choice and empowerment to women and girls, and make a global impact in women's sexual and reproductive health



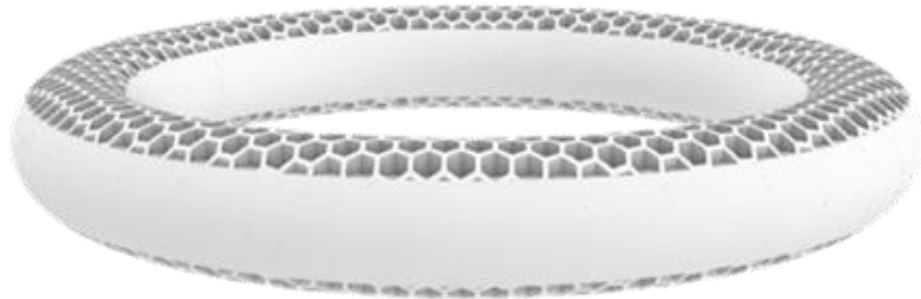
Fabrication of 3D Printed Intravaginal Rings for Controlled Drug Release Innovative MPT



US PTO 11,219,595 B2 / European Patent
3432889 / Canadian Patent No.
3,018,148 / US PCT/US21/50949 / U.S.
Provisional Patent No. 63/762,296

Spinoff Company – AnelleO, Inc.

Sustained delivery of progesterone over 30 days



Eunice Kennedy Shriver
National Institute of
Child Health and
Human Development

Anelleo, Inc. (AnelleO) ; www.anelleo.com

AnelleO PRO

New Advancement in
A.R.T.



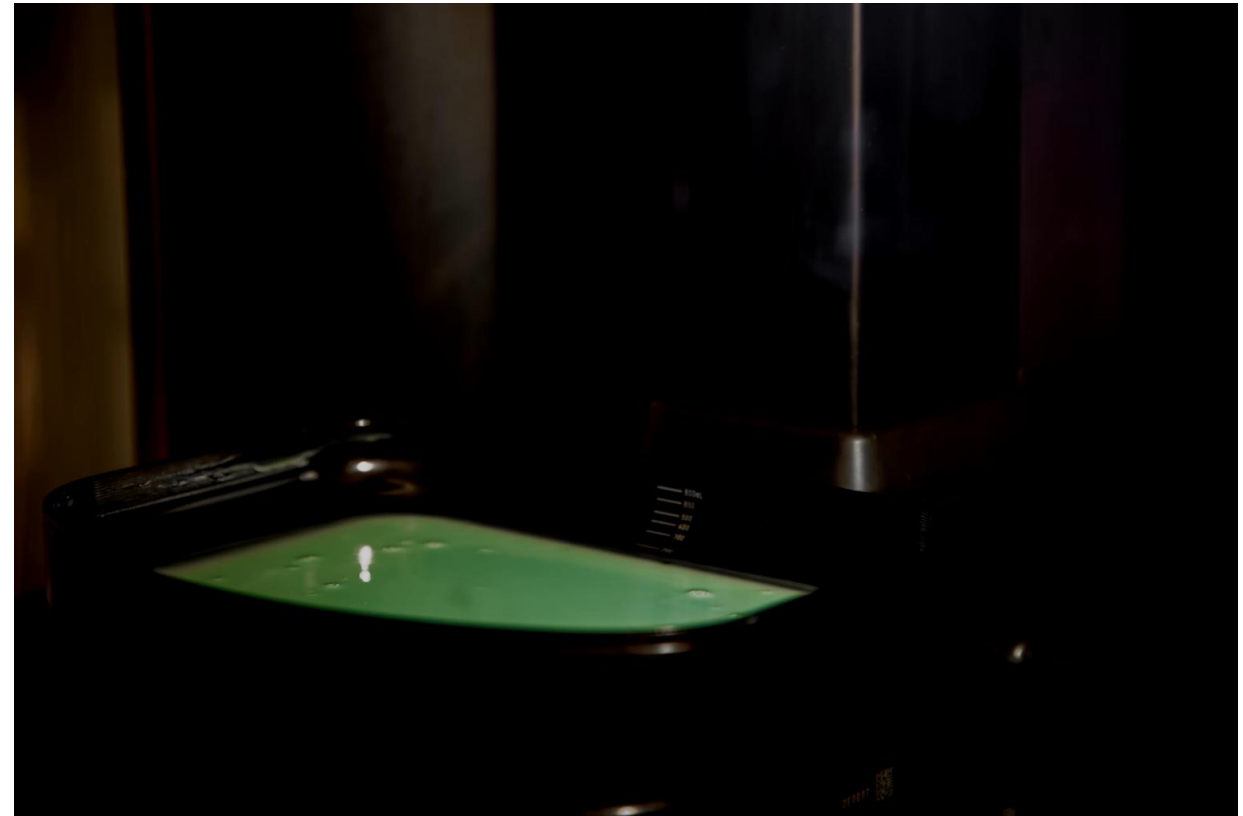
ANELLEO 

Where 3D printing meets women's health

3D Printing of Intravaginal Rings (IVRs) with CLIP

- Freedom of design allows us to completely **re-engineer the IVR**
- Ability to use design to control release parameters
- Ability to incorporate previously **incompatible APIs/multiple APIs**
- Complete drug release
- Rapid device development **tailored to new indications & specific TPP**

Example of Fabrication

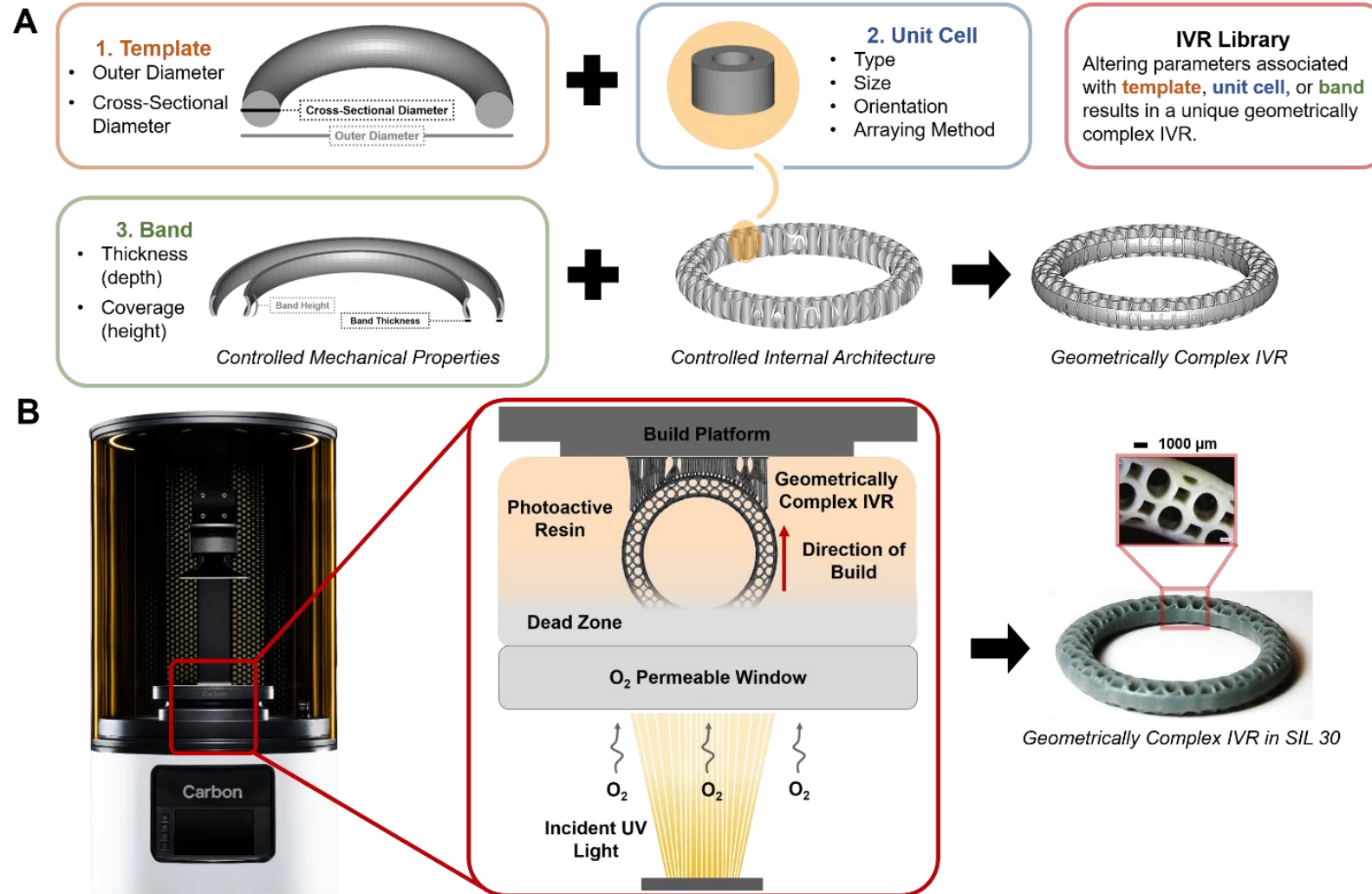


Janusiewicz R., Benhabbour S. R. *et al.*; *Advanced Materials Technologies*, **2020**.

Janusiewicz R., Benhabbour S. R. *et al.*; *Materials Today Chemistry*, **2022**.

US PTO 11,219,595 B2 / European Patent 3432889 / Canadian Patent No. 3,018,148 / US PCT/US21/50949 / U.S. Provisional Patent No. 63/762,296

Design and Fabrication Approach



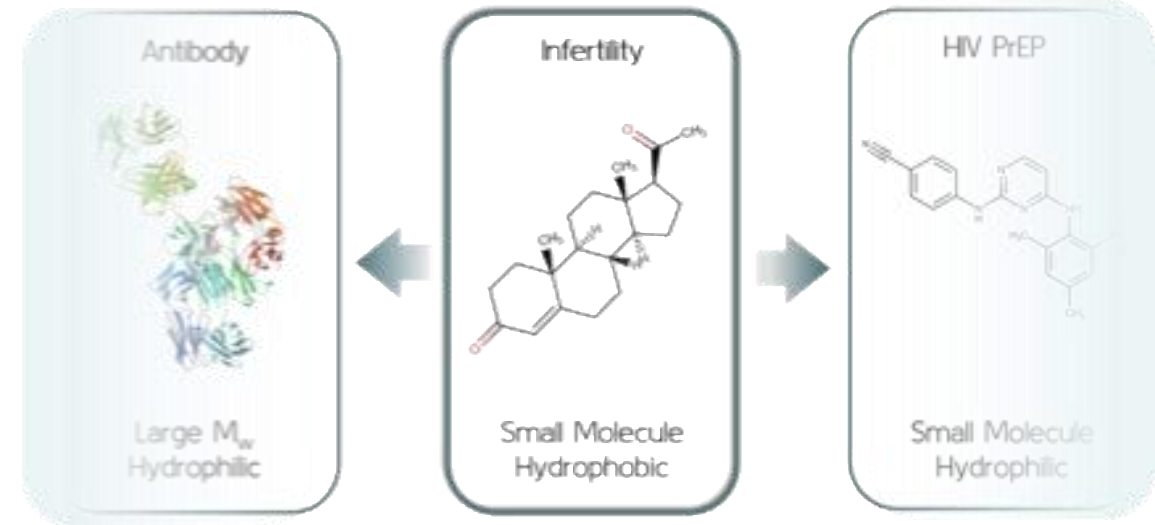
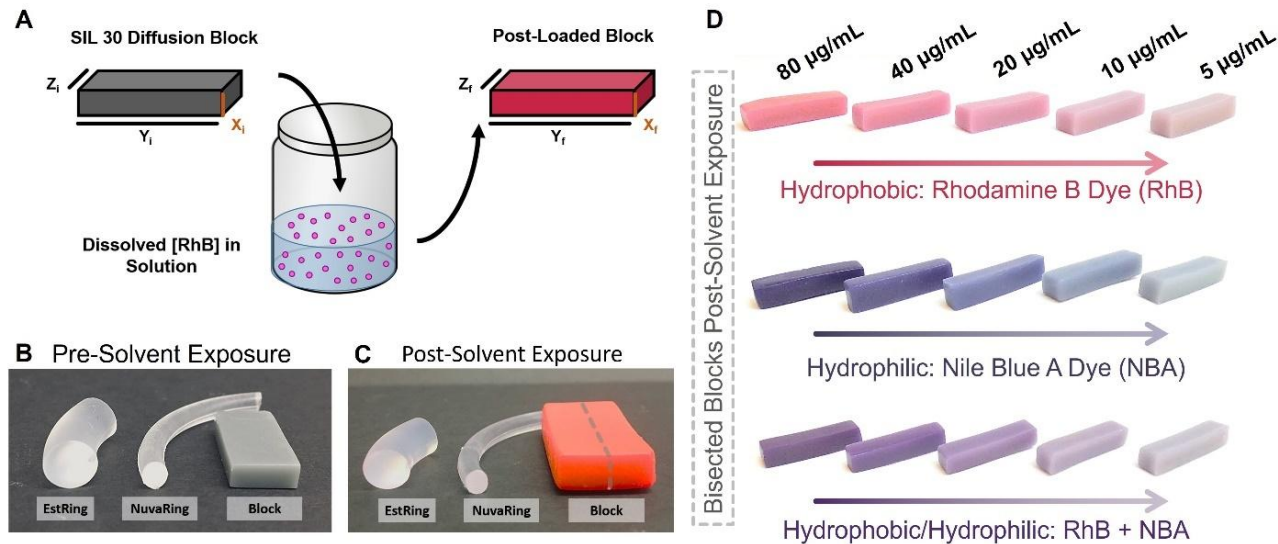
Januszewicz R., Benhabbour S. R. *et al.*; *Advanced Materials Technologies*, 2020

US PTO 11,219,595 B2 / US PCT/US21/50949 European Patent 3432889 / Canadian Patent No. 3,018,148 / US PCT/US21/50949 / U.S. Provisional Patent No. 63/762,296

Drug loading independent of IVR manufacturing

3D printed IVRs compatible with a wide range of APIs

Drug Incorporation



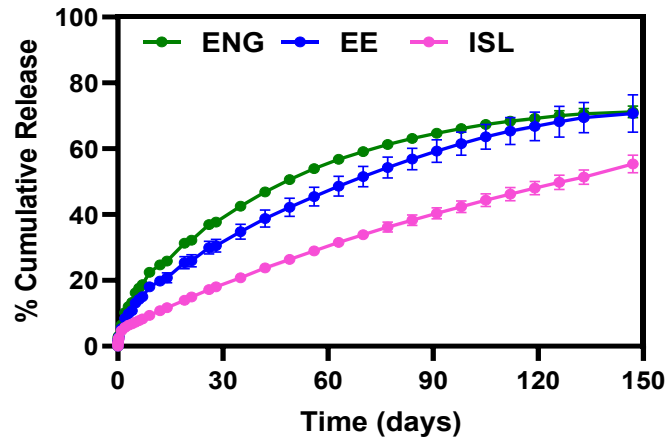
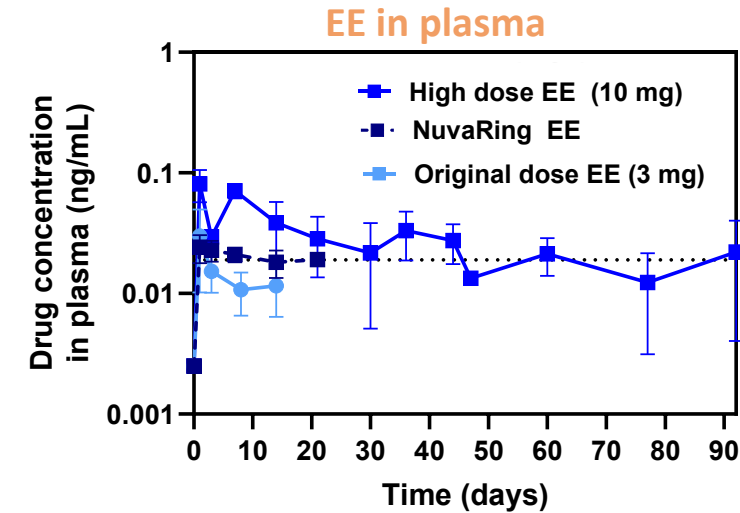
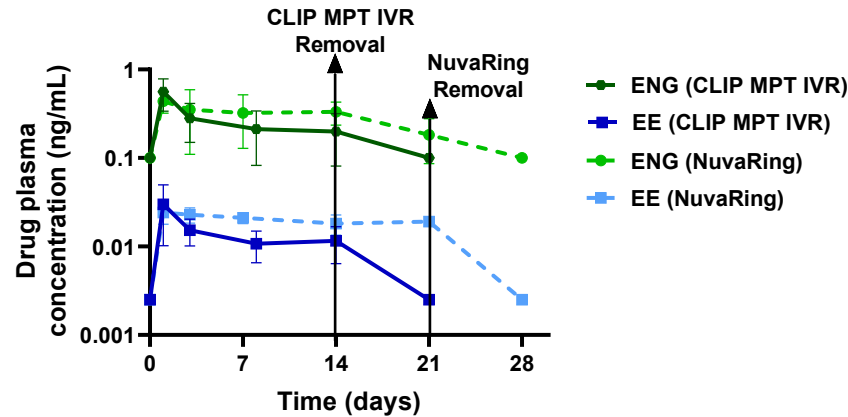
PCT/US21/50949, Benhabbour & Januszewicz

Januszewicz R. et al. *Materials Today Chemistry*, **2022**.

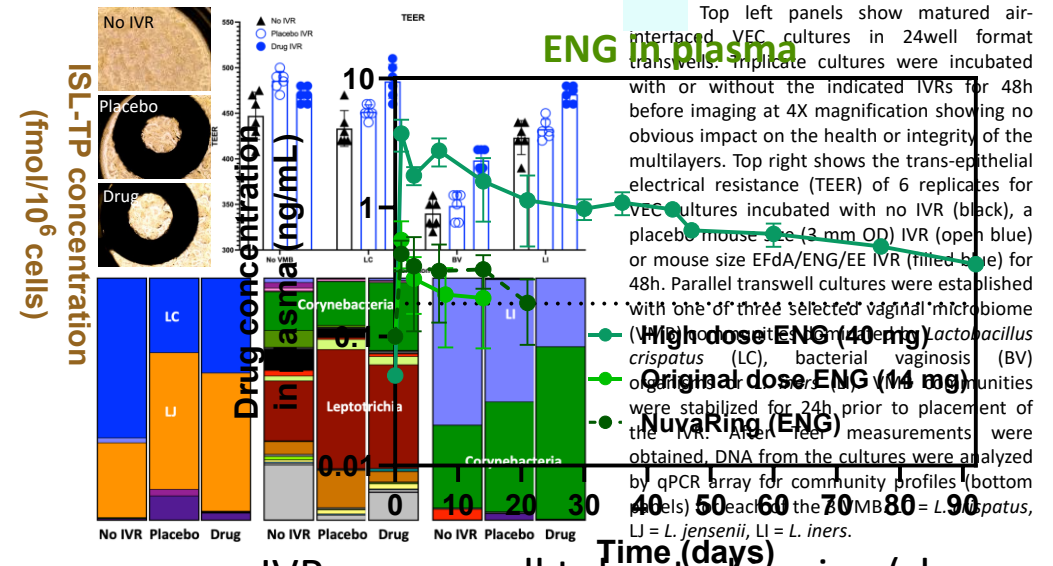
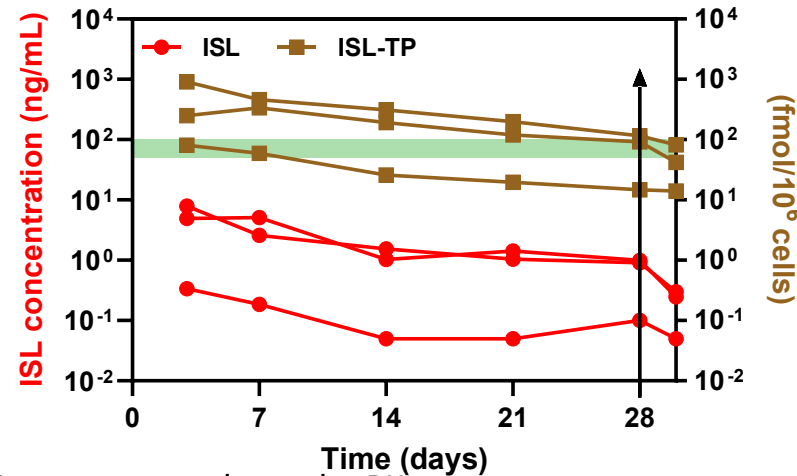
ISL/EE/ENG CLIP MPT IVR

MPT IVRs

- ❖ Islatravir (ISL or EFdA) – Antiretroviral (HIV)
- ❖ Ethynyl estradiol (EE) – Contraceptive
- ❖ Etonogestrel (ENG) – Contraceptive

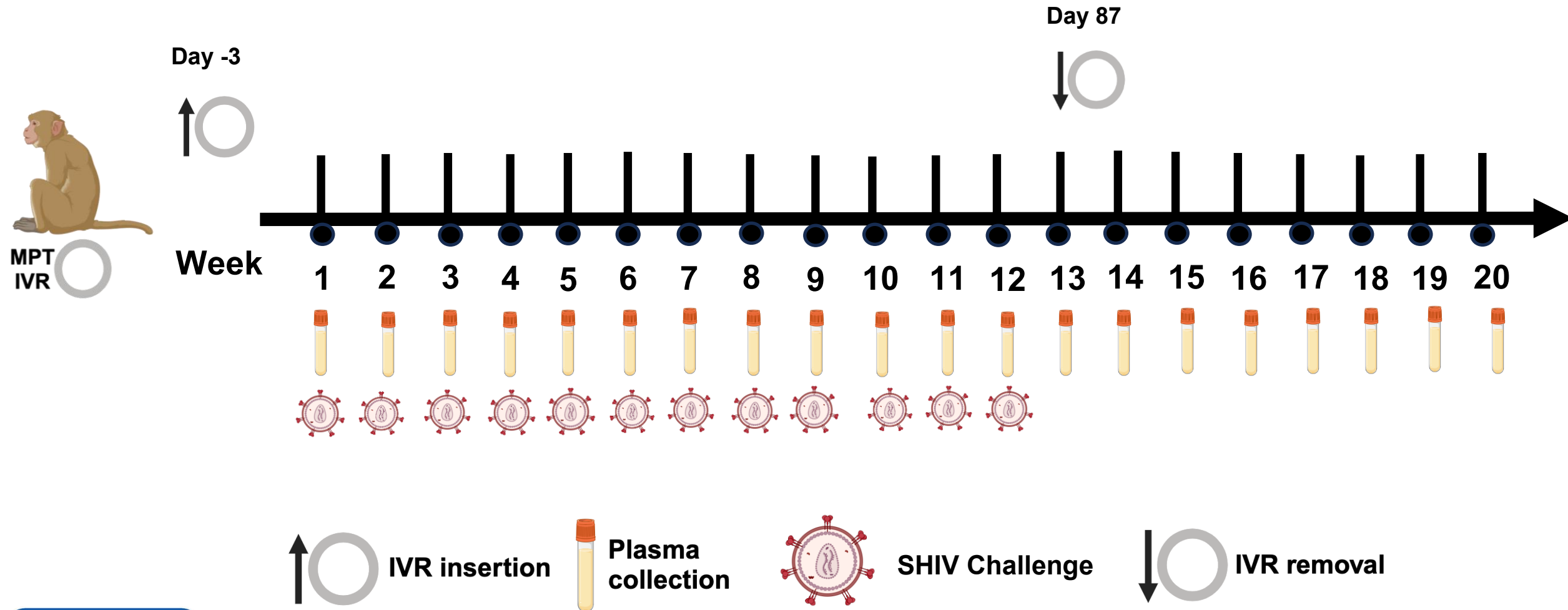


ISL-TP concentrations from PBMCs are near or above the PK benchmark after 28 days

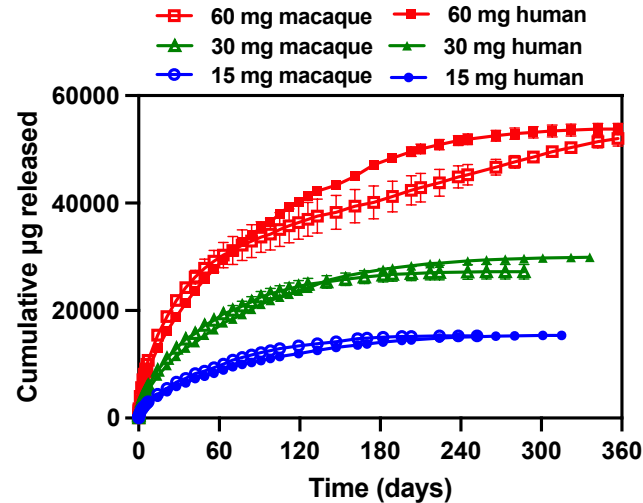
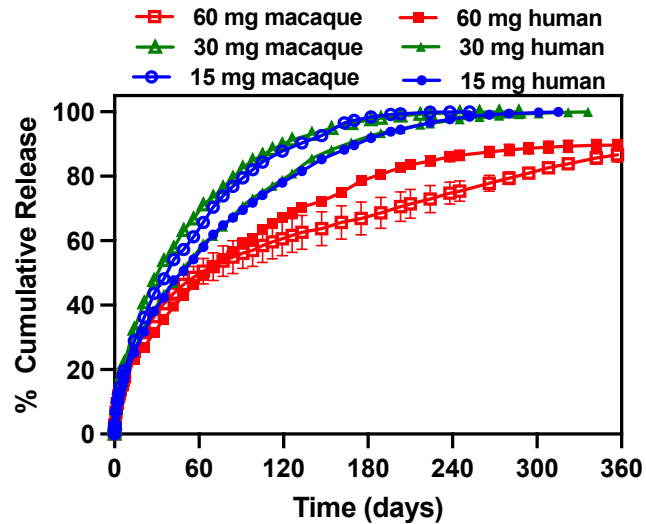


IVRs were well tolerated in vivo (sheep and macaque) and ex vivo (VMB and VEC)

Dose-Ranging PK & Efficacy of a 90-Day MPT IVR



In vitro Optimization of ISL IVRs



Human size IVR



Avg mass: 7488 mg
Outer diameter: 54.07 mm
Cross-section: 7.45 mmx

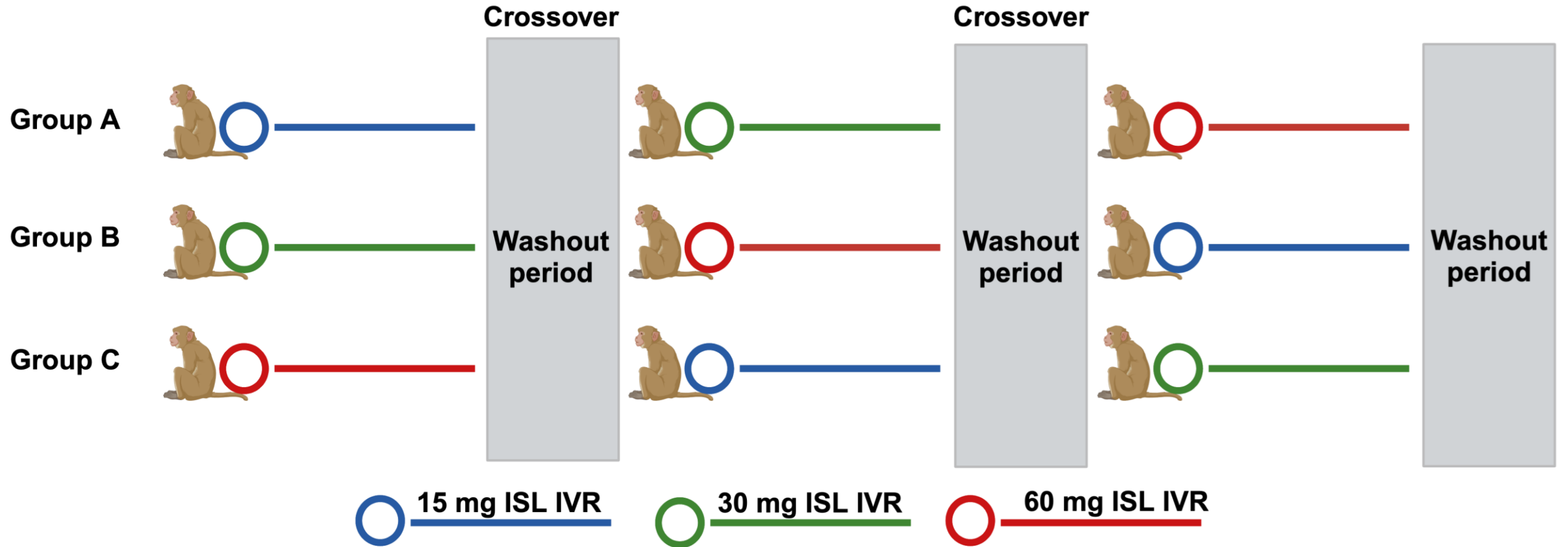
Macaque size IVR



Avg mass: 1967 mg
Outer diameter: 24.98 mm
Cross-section: 5.98 mm

Amount ISL loaded in IVR (mg)	Burst at 24h (%)	Burst at 24h (µg)	% Cumulative Release	Zero-order release rate (µg/day)	
Macaque: 60 Human: 60	Macaque: 6.50±0.28 Human: 6.04±0.11	Macaque: 4032.3±174.8 Human: 3381.9±59.8	% release at day 342 Macaque: 85.68±1.94 Human: 89.60±1.81	Day 2-49 Macaque: 508 Human: 433	Day 49-342 Macaque: 75 Human: 91
Macaque: 30 Human: 30	Macaque: 7.13±0.22 Human: 5.93±0.17	Macaque: 2182.1±68.5 Human: 1896.3±54.1	% release at day 336 Macaque: 100% Human: 100%	Day 2-49 Macaque: 292 Human: 264	Day 49-336 Macaque: 38 Human: 50
Macaque: 15 Human: 15	Macaque: 6.34±0.38 Human: 5.72±0.29	Macaque: 1077.3±65.4 Human: 915.4±46.31	% release at day 315 Macaque: 100% Human: 100%	Day 2-49 Macaque: 151 Human: 136	Day 49-315 Macaque: 31 Human: 39

30-Day In vivo Dose-Ranging PK Study



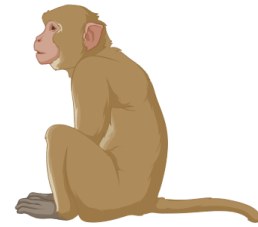
Lampe Joint Department
of Biomedical Engineering



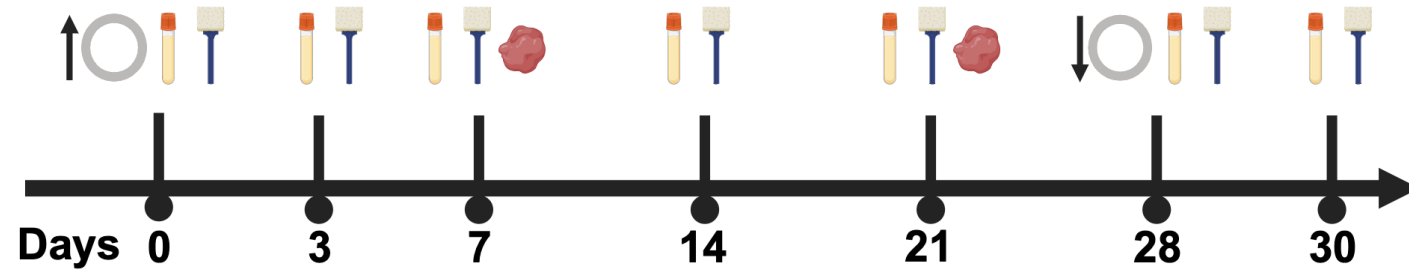
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30-Day In vivo Crossover PK Study



MPT
IVR



IVR insertion



Plasma
collection



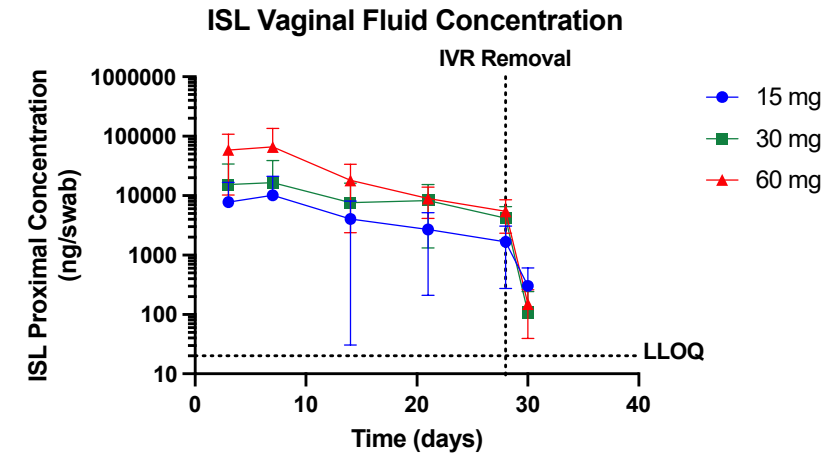
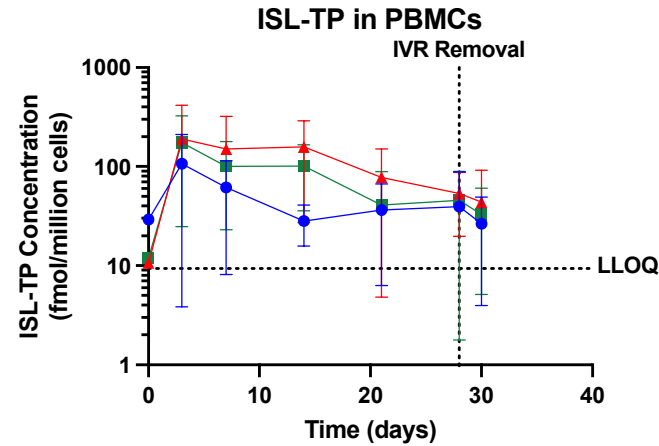
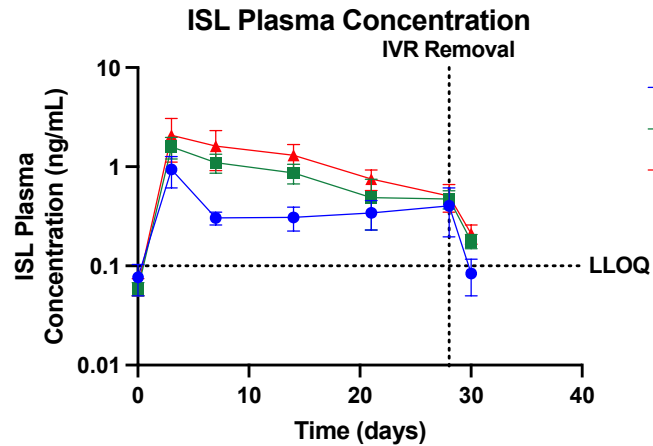
Vaginal fluid
collection



Vaginal
biopsy

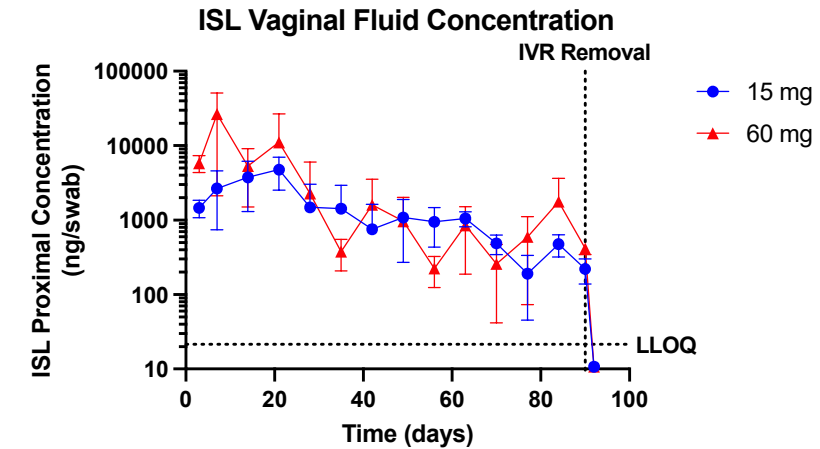
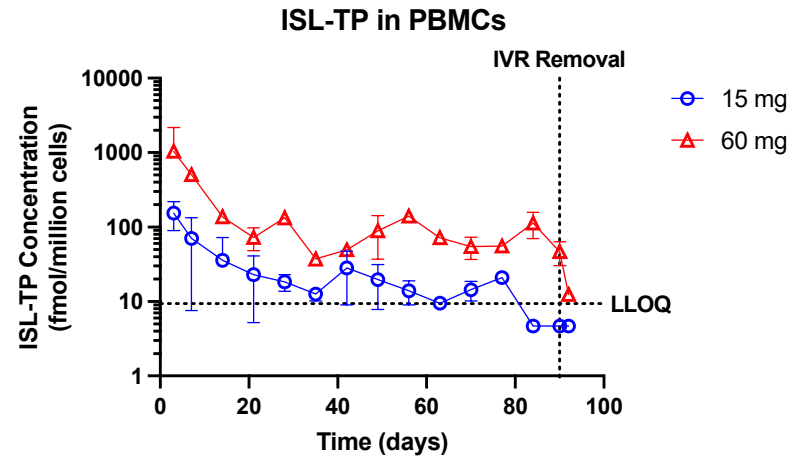
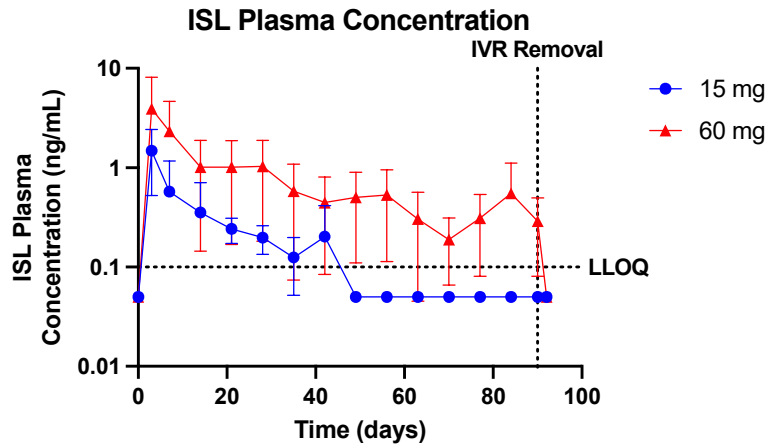
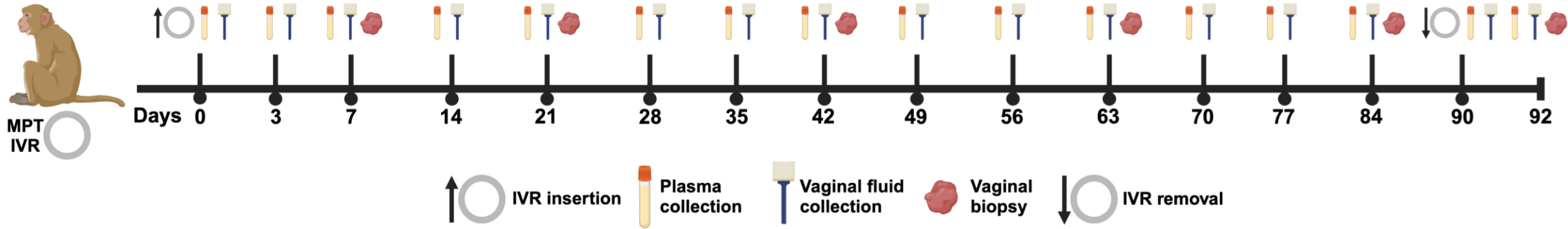


IVR removal



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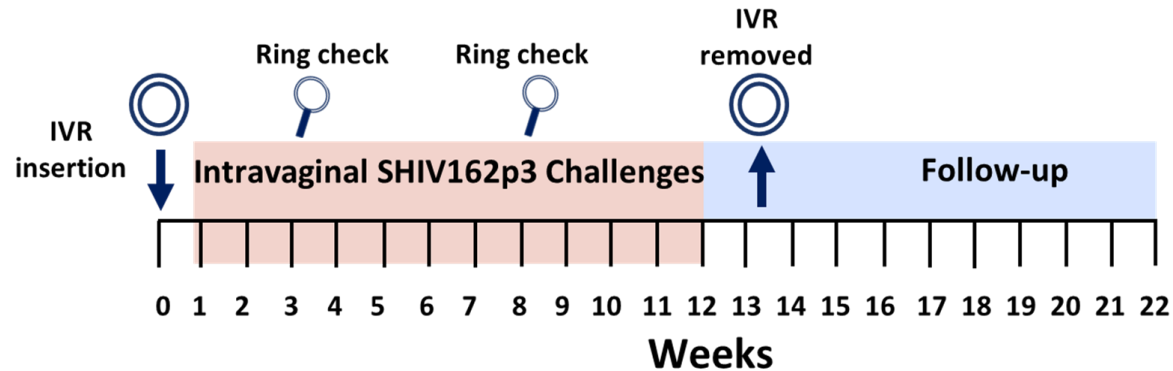
90-day In vivo Dose-Ranging PK Study



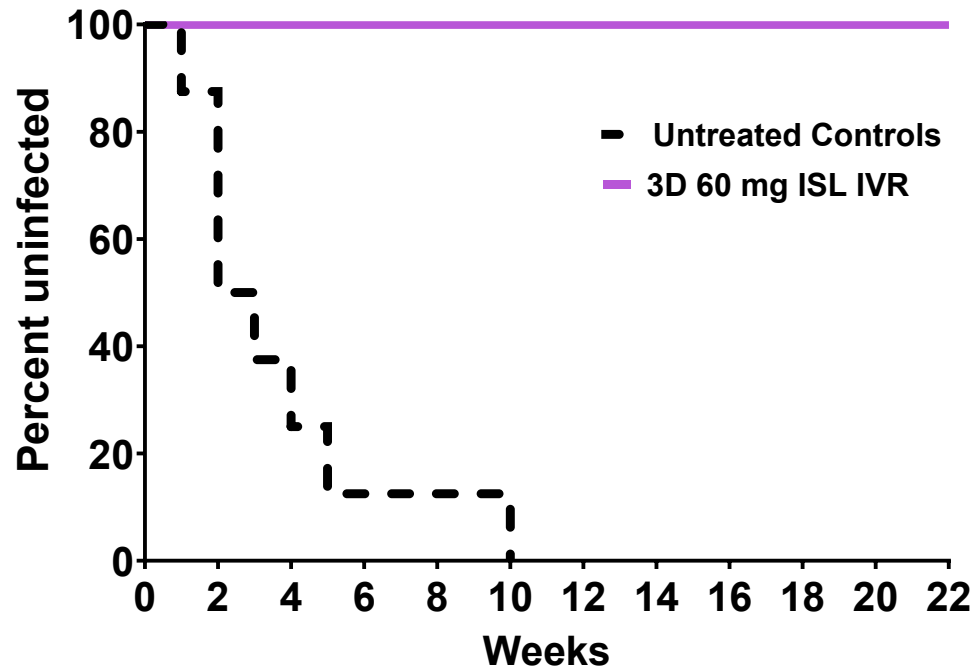
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In vivo Macaque Efficacy Study

EFFICACY AGAINST REPEAT LOW DOSE CHALLENGE



Animal ID	043	173	334	156	138	407
% of ISL Released	67.9	59.2	53.1	61.8	69.6	68.4



In vivo efficacy of ISL-treated macaques following SHIV162p3 challenges. Percent uninfected macaques post IVR insertion. (n=2 real time, n=6 historical controls, n= 6 3D 60 mg ISL IVR).

First ever PrEP of a 90-day ISL IVR demonstrating complete protection from 12 weekly exposures of SHIV162p3 in pigtailed macaques.

Summary

- Demonstrated ISL IVRs elicited sustained drug release for > 90 days following a single administration
- ISL IVRs were well tolerated at all three doses of ISL
- We completed the first ever pre-exposure prophylaxis (PrEP) efficacy evaluation of a 90-day IVR in preventing vaginal SHIV162p3 acquisition in a repeat low-dose weekly challenge macaque model
- We demonstrated complete protection from 12 weekly exposures (22 weeks including follow up)
- Findings support further development of a 90-day MPT IVR co-formulated with ISL/EE/ENG for long-acting HIV PrEP and hormonal contraception in women

Acknowledgments

My Lab

Collaborators

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