The TIP Program is developing a novel, biodegradable and reversible implantable device with long-acting (LA) antiretroviral (ARV) release for HIV pre-exposure prophylaxis (PrEP).

To date, the program has:
- Achieved tunable drug release from 0.1 to 1 mg/day with a single rod in vitro and in vivo
- Down-selected optimal device parameters: polymer type, excipient, wall thickness
- Demonstrated that the platform is drug agnostic by achieving constant release (6-12 months) with ARVs from multiple drug classes including the prodrug tenofovir alafenamide (TAF)
- Optimized fabrication for scale and subcutaneous delivery of device with existing applicator systems
- Evaluated the safety, efficacy, pharmacokinetics (PK), pharmacodynamics (PD), and insertion/retrievability of devices in exploratory preclinical studies

The TIP implantable device is a membrane-controlled reservoir system comprised of a formulated drug core encapsulated in an extruded polycaprolactone (PCL) tube.

- Drug passively diffuses through the membrane at a constant rate, offering sustained zero-order release of drug for LA prevention.
- PCL is biocompatible and biodegradable. The device is removable through therapeutic duration.

Efforts at RTI place an emphasis on early-stage feedback from potential end-users and health care providers to inform product development. Key findings to date include:
- Preference for longer duration (≥ 6 months) over size of device or number of rods
- Interest in a biodegradable system (no removal of device needed)
- Importance of a neat rod geometry & relative flexibility of device
- Providers preference for use of commercially available trocars for insertion

Device form factor and materials have been selected to ensure alignment with scale-up manufacturing needs & clinical translation. Devices have been engineered to incorporate:
- Manufacturing scale-up considerations
- Compatibility with approved trocars
- Formulations with greater aqueous stability

Discrete Choice Experiment randomly combines levels of attributes to generate hypothetical product profiles and choice sets from which participants choose their preference. We will assess key preferences and implant characteristics and estimate tradeoffs among attributes among young women in sub-Saharan Africa.
**TAF Implantable Devices In-Vitro Summary**

- Demonstrated tunable release rates from devices based on adjusting wall thickness and core formulation with both TAF salt (hemifumarate) and TAF base
- Dosing range compatible with estimates for HIV prevention
- Device (2.5mm x 40mm) loaded with TAF releasing at mid dose level (~0.35mg/day) is expected to last 1 year
- Showed high stability in storage under accelerated conditions (40°C/75% RH in closed foil pouches)
- Showed 6-month stability during administration under physiological conditions (37°C, pH7.4 in an aqueous buffer)

**TIP Program In-Vivo Summary**

Release of TAF scales inversely with wall thickness; demonstrated tunable release from ~0.1 → 1 mg/day

\[ y = 0.1 + 46.4x^{1} \]
\[ R^2 = 0.99 \]

- **Dose Groups**
  - Low dose (LD) 8 378.5 (87-1196)
  - Mid dose (MD) 11 868.5 (206-1669)
  - High dose (HD) 20 1619 (395-3710)

TAF devices demonstrate favorable systemic PK in macaques:
- High and sustained TFV-DP in PBMCs that exceeded daily oral TAF at a fraction of the oral dose
- Dose proportionality in PBMCs provides flexible scalability.
- Estimated in vivo release rate is in high agreement with measured in vitro release rate.
- Device designs were compatible with an approved contraceptive trocar for insertion.
- Devices remained intact at retrieval after up to 180 days.

**Selected Publications and Presentations**


**Next steps:**
- Evaluation of other drug classes in animal models
- Assess dual drug release from platform
- Prepare for first in human trials

**Selected Presentations**