ULTRA-LONG-ACTING BIODEGRADABLE POLYMERIC SOLID IMPLANTS FOR HIV TREATMENT MAINTENANCE

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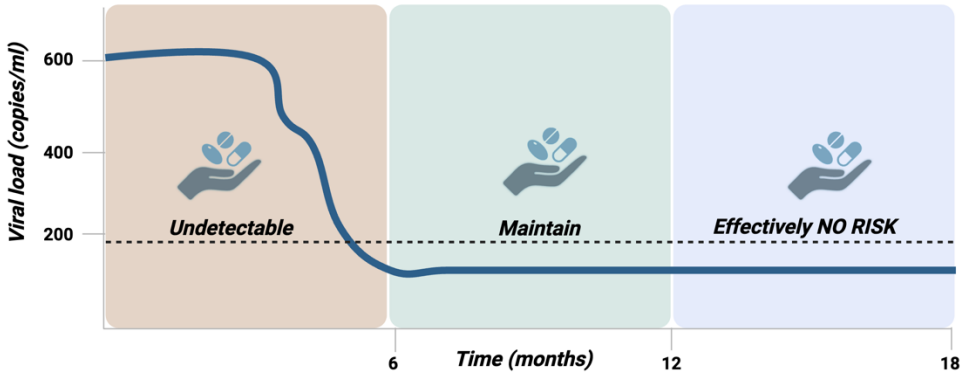
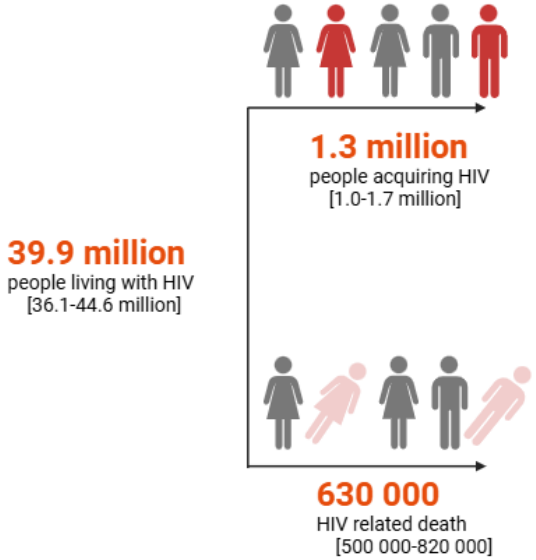
NEXT-GENERATION DELIVERY INNOVATIONS

Hurdles In HIV Treatment Progress

Problem

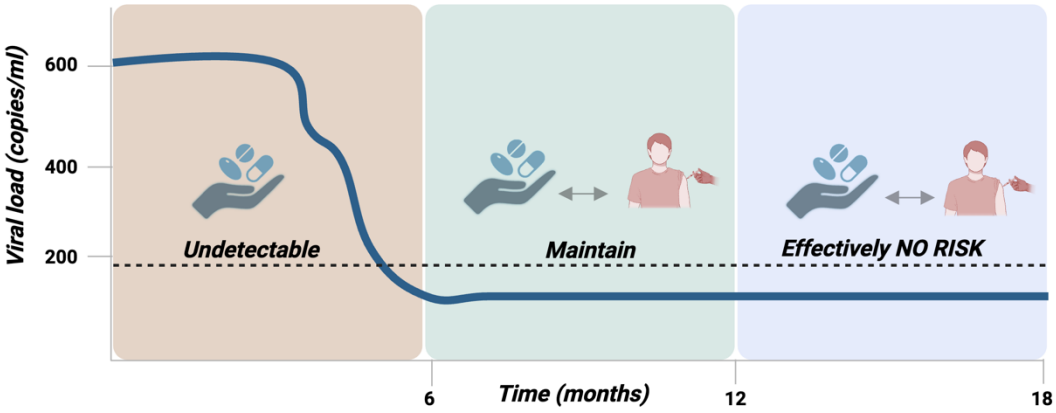
- 39 million people are living with HIV.
- 53% of all people living with HIV are women and girls.
- Heavy pill burden leading to poor patient adherence.





*Figures created using Bio render, adapted from source **WHO**,2024 & NIAID*

Bridging Gaps in HIV Treatment Maintenance



Cabenuva (Cabotegravir 600 mg/3mL & Rilpivirine 900 mg/3 mL) is not removable, up to 6 injections a year, painful IM injections, missed doses can lead to drug resistance.

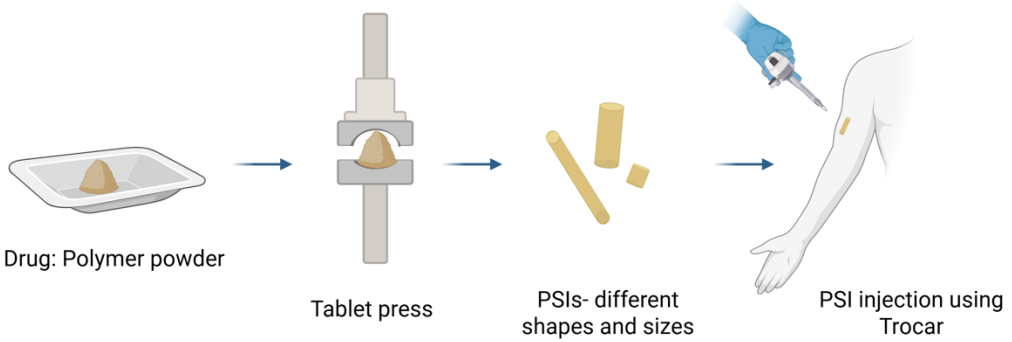
Figures created using Bio render, Source: https://www.cabenuva.com/

Bridging Gaps in HIV Treatment Maintenance

Solution

Polymeric Solid Implants (PSI)

- Technology derived from ***Injectable in-situ forming implants (ISFI).***



Advantages:

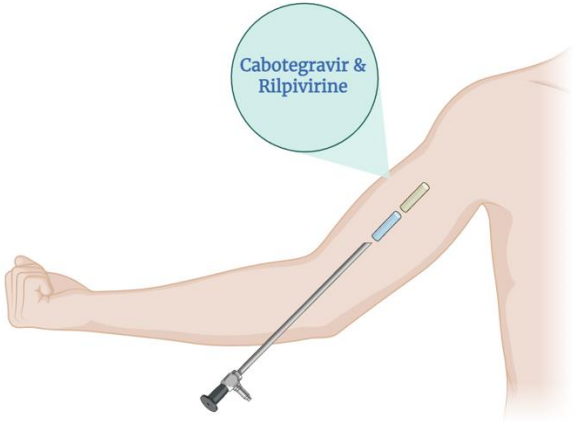
1. Ultra-Long-Acting ($\geq 1 year$).
2. Solvent-free (low toxicity), biodegradable and removal if treatment termination is required.
3. High drug loading(~90 wt%), accommodate multiple drugs, variability in size and shape.

Figures created using Bio render, Source: Maturavongsadit, Panita, et al. "Biodegradable polymeric solid implants for ultra-long-acting delivery of single or multiple antiretroviral drugs." International journal of pharmaceutics 605 (2021): 120844. Benhabbour, S. Rahima, et al. "Ultra-long-acting tunable biodegradable and removable controlled release implants for drug delivery." Nature communications 10.1 (2019): 4324.

Antiretroviral loaded PSIs for HIV Treatment Maintenance

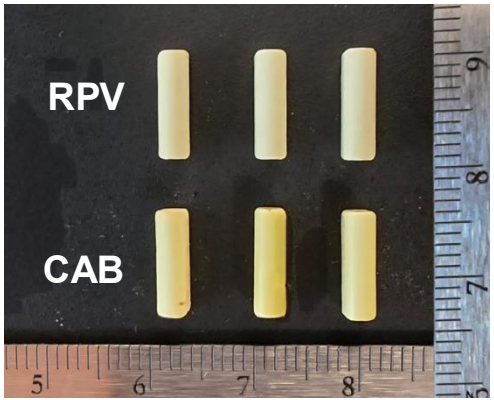
Overcome current limitations of Long-Acting therapies

- Cabotegravir and Rilpivirine loaded PSIs.
- PSIs API loading comparable to Cabenuva.
- Achieve *in vitro* release for longer duration (> 6 months) to minimize clinic visits and enhance adherence.
- PSIs capable of delivering CAB and RPV *in vivo* above their targeted plasm drug concentration ($> 4 \times$ PA-IC_{90}).



Cabotegravir and Rilpivirine PSIs for HIV Treatment Maintenance

Targeted Drug loading

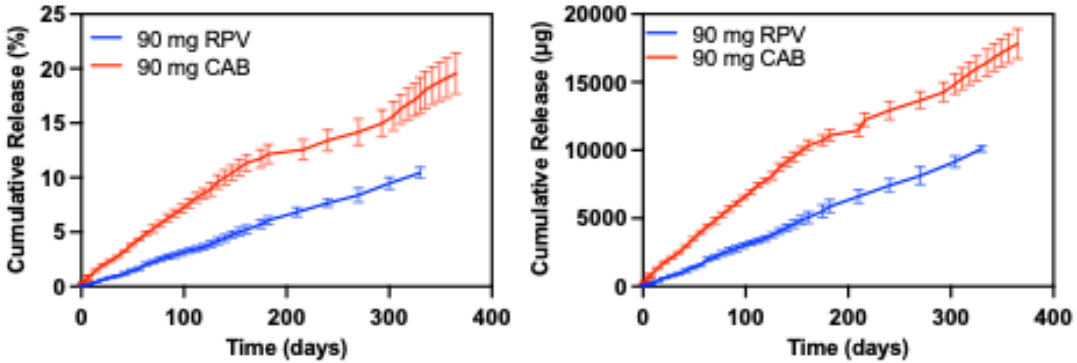


Physical Dimensions and Weights of CAB and RPV PSIs

PSI	Analytical Drug loading (mg/g)	Weight (mg)	Length (mm)	Height (mm)	Width (mm)	Surface Area (mm^2)	Specific Surface Area (mm^{-1})
CAB PSIs	886.76± 0.79	102.70	10	3.01	2.80	132.80	1.58
		106.81	10	3.25	2.74	137.61	1.54
		99.60	10	2.99	2.86	134.10	1.56
RPV PSIs	900.01± 17.22	107.91	10	3.70	2.81	151.01	1.45
		96.20	10	3.68	2.80	150.20	1.46
		102.90	10	3.69	2.81	150.74	1.45

Cabotegravir and Rilpivirine PSIs for HIV Treatment Maintenance

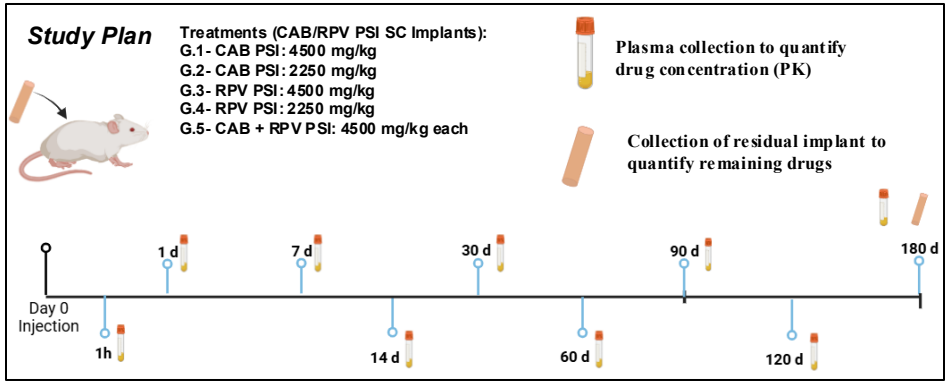
Targeted Drug loading and in vitro release study

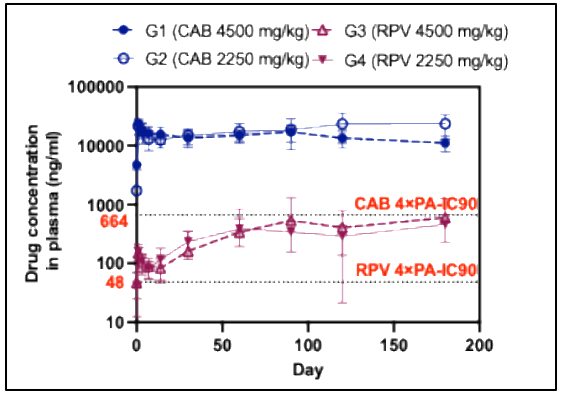


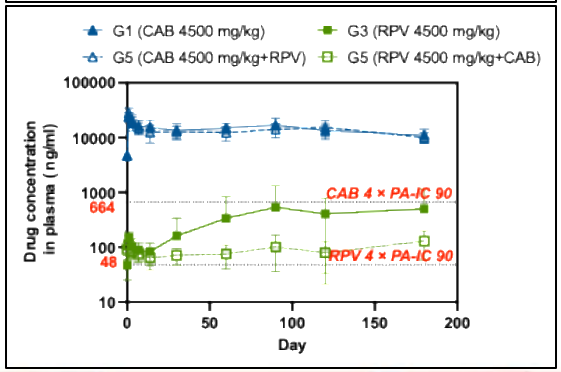
Drug	Drug loading/PSI (wt%)	Total drug per PSI (mg)	Burst release at 24 h (%)	Burst release at 24 h (µg)	Cumulative µg/day release (1-7 d)	Cumulative µg/day release (7-60 d)	Cumulative µg/day release (60-365 d)	Estimated time to 100% release (days)
CAB	90	91.36 ± 3.2	0.17 ± 0.06	157.38 ± 63.42	87.31	64.88	61.22	~ 1918 days
RPV	90	92.09± 5.28	0.03 ± 0.01	27.48 ± 6.36	20.75	25.67	35.71	~ 3134 days

Cabotegravir and Rilpivirine PSIs for HIV Treatment Maintenance

In vivo PK Study

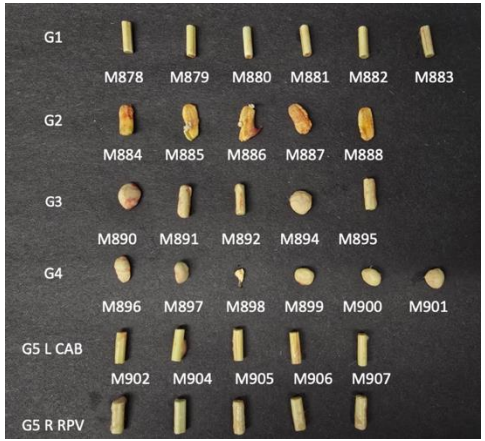




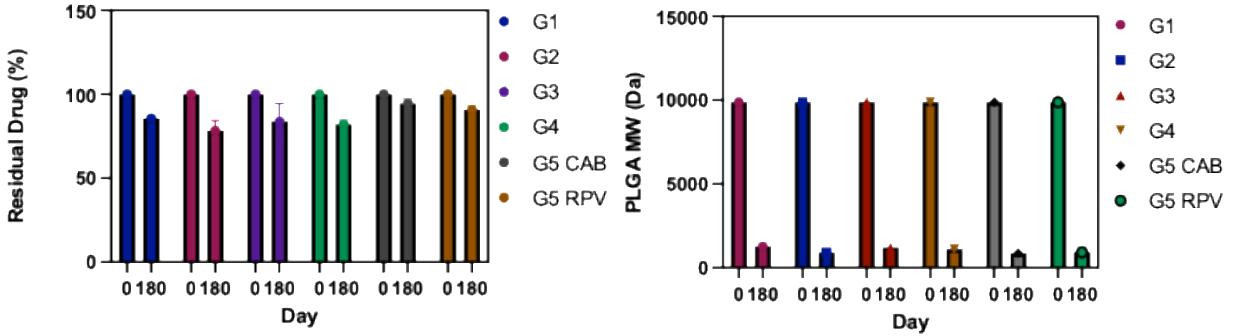


Cabotegravir and Rilpivirine PSIs for HIV Treatment Maintenance

In vivo PK Study 180 d



PSIs retrieved at d180 post administration

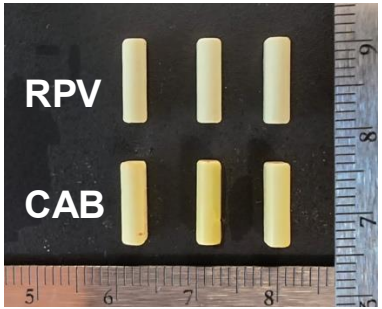


Group	API	Dose (mg/kg)	Administered PSI average weight (mg)	~ % residual drug	~ % PLGA Degradation
G1	CAB	4500	100.21 ±2.57	85.66 ± 0.19	87.25
G2	CAB	2250	100.70 ±1.50	78.32 ± 5.65	90.81
G3	RPV	4500	99.78 ±1.21	83.43 ± 10.79	88.94
G4	RPV	2250	103.30 ±1.27	82.09 ± 2.49	88.75
G5	CAB	4500	104.11±2.43	94.41 ± 3.83	91.37
G5	RPV	4500	103.70 ±1.52	90.86 ± 2.26	90.69

**N=2-3 for each group*

Conclusion

- Developed Polymeric Solid Implants that can accommodate antiretrovirals (CAB ~900 mg/g, and RPV ~900 mg/g).
- Sustained zero order release kinetics *in vitro* for ~365 days.
- CAB/RPV PSIs elicited sustained CAB and RPV release with plasma drug concentrations >4 × PA-IC90 (664 ng/ml – CAB; 48 ng/ml – RPV) for 180 days.



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