LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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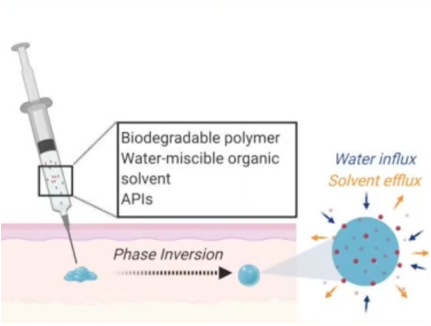

Ultra-Long-Acting Multi-Purpose In-situ Forming Implant (ISFI)

Verified by the innovator, on Apr 2022

Developer(s)

University of North Carolina at Chapel Hill
https://benhabbour.web.unc.edu/

US

Harnessing engineering, chemistry, and pharmacology tools to design and engineer innovative drug delivery platform technologies for disease treatment and prevention.

Sponsor(s)

NIH-NIAID

https://www.niaid.nih.gov/

Partnerships

No partner indicated

Technology information

Type of technology

In-situ forming gel/implant

Administration route

Subcutaneous

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Cabotegravir (CAB), Medroxyprogesterone acetate (MPA)

Development Stage

Pre-clinical

Regulatory Approval

Not provided

Description

The in-situ forming implant (ISFI) consists of a liquid co-formulation utilizing excipients that form a biodegradable depot after subcutaneous injection for a controlled sustained release of active ingredients. It is based on a biodegradable polymer such as PLGA, a water miscible organic solvent such as NMP and the API or combination APIs of interest.

Technology highlight

First-in-line, ultra-long-acting injectable MPT that offers durable and sustained protection from HIV transmission, high efficacy of contraception, increased user compliance, and the ability to be removed if required. The ISFI offers at least 3 months sustained release after a single subcutaneous administration. It is biodegradable yet removable in case of adverse events or need for treatment reversibility.

Technology main components

poly(DL-lactide-co-glycolide) (PLGA), N-methyl-2-pyrrolidone (NMP), dimethyl sulfoxide (DMSO)

Information on the raw materials sourcing, availability and anticipated price

Polymers readily available on the market

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Water-soluble molecules

Water-insoluble molecules

Small molecules

Dolutegravir (DTG), Cabotegravir (CAB), Rilpivirine (RPV)

Nucleic acids

Confidential

Proteins

Confidential

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

To be provided

API co-administration

2 different APIs : at least 2 different APIs

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

To be determined

Tentative equipment list for manufacturing

To be determined

Manufacturing

To be determined

Specific analytical instrument required for characterization of formulation

To be determined

Clinical trials

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Biodegradable
- Drug-eluting
- Monolithic
- Removable
- Single-use
- Room temperature storage
- At least 1 year shelf life
- Needs insertion kit

Release properties

Zero order release

Injectability

26-16 gauge needles

Safety

Absence of adverse local or systemic inflammation when administered to mice or non-human primates

Stability

To be determined

Storage conditions and cold-chain related features

To be determined

Potential application(s)

Therapeutic area(s)

Contraception

Multipurpose technology : "HIV PrEP and contraception"

Diabetes

HBV

TB

COVID 19

HIV

Pain management

Oncology

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Treatment

Use of technology

Ease of administration

- Administered by a nurse
- Administered by a specialty health worker
- To be determined

Frequency of administration

To be determined

User acceptance

To be determined

Targeted user groups

Age Cohort

- Adults

Genders

- All
- Male
- Female
- Cisgender female
- Cisgender male
- Transgender female
- Transgender male
- Intersex
- Gender non-binary

Pregnant individuals

Yes

Lactating individuals

Yes

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

Cabotegravir (CAB), Medroxyprogesterone acetate (MPA)

Class(es)

Not provided

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Cabotegravir (CAB), Etonogestrel (ENG)

Class(es)

Not provided

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

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Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Technology patent families

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Injectable, biodegradable and removable polymer based drug suspension for ultra-long-acting drug delivery Expiry date: 2042-06-30 Injectable, biodegradable and removable polymer based drug suspension for ultra-long-acting drug delivery are disclosed. Ultra-long-acting in-situ forming implant (ISFI) drug suspension delivery systems as multipurpose prevention technologies for a multitude of applications are also provided. Methods of use, including treatment of subjects, using the disclosed compositions and ISFIs are also provided.	WO2023278695		The University Of North Carolina At Chapel Hill	No	Company

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		
Filed	Albania, North Macedonia, Serbia, Türkiye	Canada, Austria, Belgium, Switzerland, Cyprus, Czechia, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Liechtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, Netherlands, Norway, Poland, Portugal, Sweden, Slovenia, Slovakia, San Marino, Japan, United States of America, Bulgaria, Romania

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO)	World Intellectual Property Organization (WIPO)

MPP Licence(s)

Supporting material

Publications

** Effects of Injection Volume and Route of Administration on Dolutegravir In Situ Forming Implant Pharmacokinetics.
 Joiner, J. B., King, J. L., Shrivastava, R., Howard, S. A., Cottrell, M. L., Kashuba, A., Dayton, P. A., & Benhabbour, S. R. (2022).
 ?Pharmaceutics, 14(3), 615. https://doi.org/10.3390/pharmaceutics14030615 **

Due to the versatility of the in situ forming implant (ISFI) drug delivery system, it is crucial to understand the effects of formulation parameters for clinical translation. We utilized ultrasound imaging and pharmacokinetics (PK) in mice to understand the impact of administration route, injection volume, and drug loading on ISFI formation, degradation, and drug release in mice. Placebo ISFIs injected subcutaneously (SQ) with smaller volumes (40 µL) exhibited complete degradation within 30–45 days, compared to larger volumes (80 µL), which completely degraded within 45–60 days. However, all dolutegravir (DTG)-loaded ISFIs along the range of injection volumes tested (20–80 µL) were present at 90 days post-injection, suggesting that DTG can prolong ISFI degradation. Ultrasound imaging showed that intramuscular (IM) ISFIs flattened rapidly post administration compared to SQ, which coincides with the earlier Tmax for drug-loaded IM ISFIs. All mice exhibited DTG plasma concentrations above four times the protein-adjusted 90% inhibitory concentration (PA-IC90) throughout the entire 90 days of the study. ISFI release kinetics best fit to zero order or diffusion-controlled models. When total administered dose was held constant, there was no statistical difference in drug exposure regardless of the route of administration or number of injections.

Keywords: long-acting, in situ, injectable, biodegradable, implants, PLGA, controlled release, drug delivery, ultrasound, pharmacokinetics

** Multipurpose Prevention Technologies: Oral, Parenteral, and Vaginal Dosage Forms for Prevention of HIV/STIs and Unplanned Pregnancy. Young IC, Benhabbour SR. ?Polymers. 2021; 13(15):2450. https://doi.org/10.3390/polym13152450 **

There is a high global prevalence of HIV, sexually transmitted infections (STIs), and unplanned pregnancies. Current preventative daily oral dosing regimens can be ineffective due to low patient adherence. Sustained release delivery systems in conjunction with multipurpose prevention technologies (MPTs) can reduce high rates of HIV/STIs and unplanned pregnancies in an all-in-one efficacious, acceptable, and easily accessible technology to allow for prolonged release of antivirals and contraceptives. The concept and development of MPTs have greatly progressed over the past decade and demonstrate efficacious technologies that are user-accepted with potentially high adherence. This review gives a comprehensive overview of the latest oral, parenteral, and vaginally delivered MPTs in development as well as drug delivery formulations with the potential to advance as an MPT, and implementation studies regarding MPT user acceptability and adherence. Furthermore, there is a focus on MPT intravaginal rings emphasizing injection molding and hot-melt extrusion manufacturing limitations and emerging fabrication advancements. Lastly, formulation development considerations and limitations are discussed, such as nonhormonal contraceptive considerations, challenges with achieving a stable coformulation of multiple drugs, achieving sustained and controlled drug release, limiting drug–drug interactions, and advancing past preclinical development stages. Despite the challenges in the MPT landscape, these technologies demonstrate the potential to bridge gaps in preventative sexual and reproductive health care.

Additional documents

No documents were uploaded

Useful links

- LAI for prevention of HIV and unplanned pregnancy, I. Young, CROI2022

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

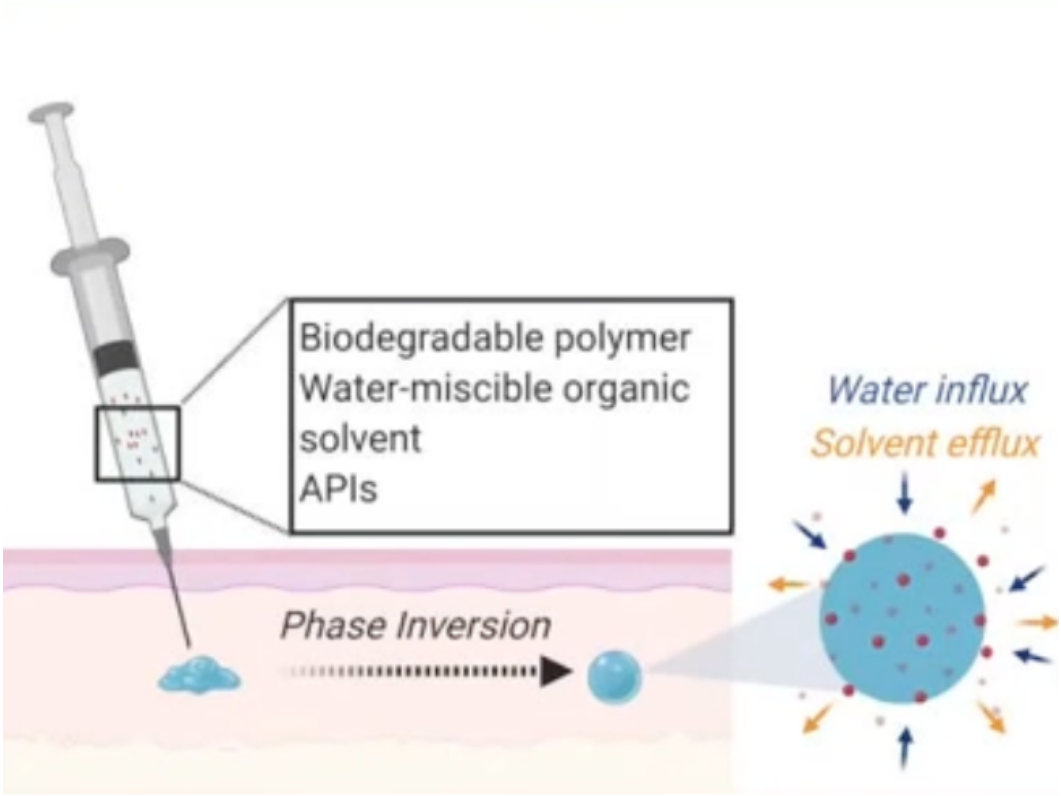
Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

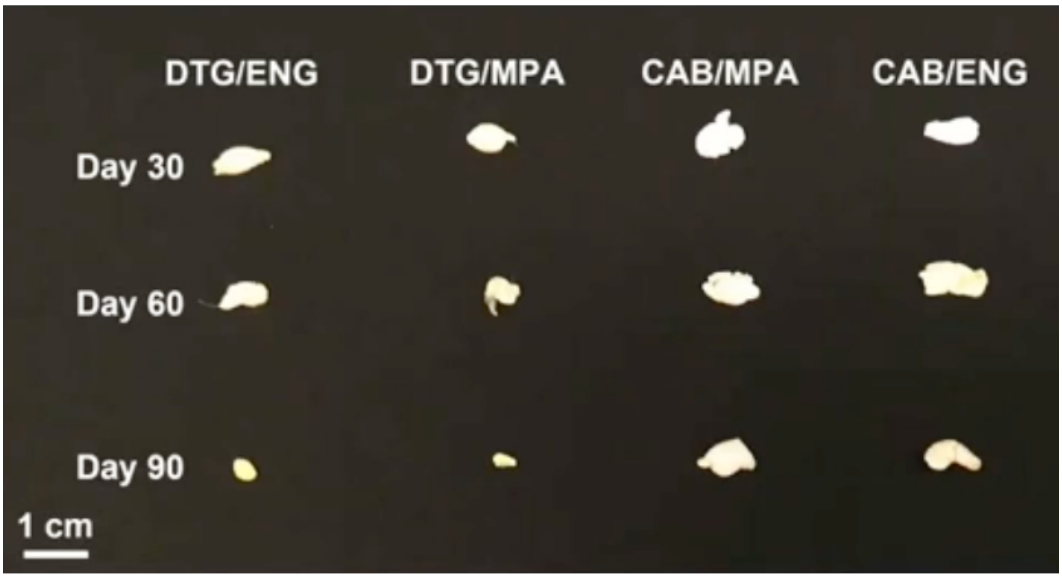
Comment & Information

Illustrations



ISFI mechanism and drug release. A liquid solution incorporating a biodegradable polymer, water-miscible organic solvent, and APIs is subcutaneously administered and undergoes a phase inversion

Young I, Benhabbour SR et al. CROI, 2022



Depots retrieved 90 days post subcutaneous administration in mice model to quantify residual drug and polymer degradation

Young I, Benhabbour SR et al. CROI 2022