

medincell.

Commercial Long-Acting Injectables, State and Perspectives

Adolfo López-Noriega, Head of R&D

Introduction

Clinical LAs: Market and Trends

Examples of Commercial LAI Technologies

MedinCell BEPO® Technology

Challenges

INTRODUCTION

Why Long-Acting?

More than 50% of patients do not follow their treatment correctly

(oversight, lack of awareness, side effects, auto-diagnosis, social pressure, etc.)

Long-Acting formulations can be a solution

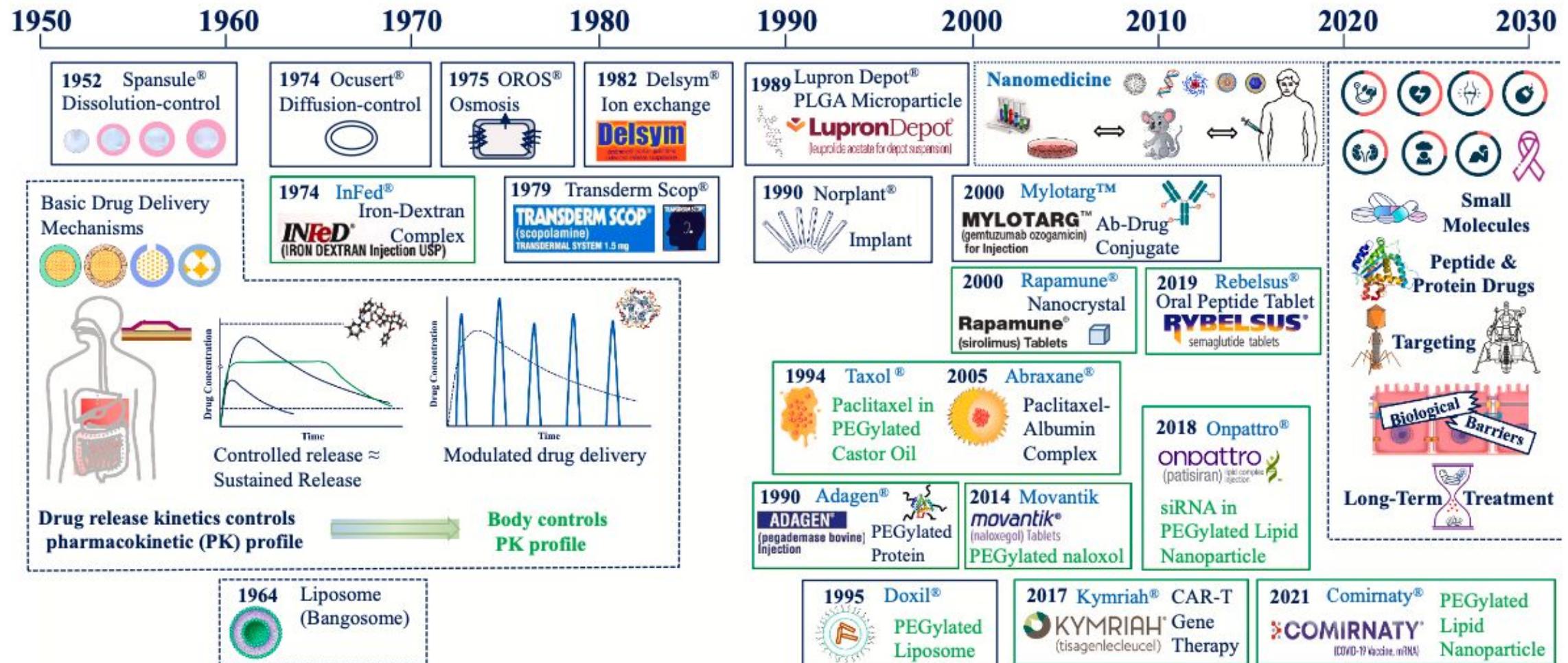
- **by ensuring compliance and adherence to treatment**
- **and potentially improving efficacy while reducing side effects**

INTRODUCTION

Why Long-Acting?

INTRODUCTION

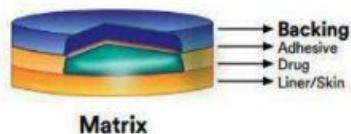
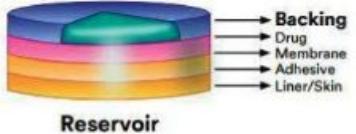
Long history of long-acting medication



INTRODUCTION

Long-acting pharmaceutical forms

Patches



Comfort

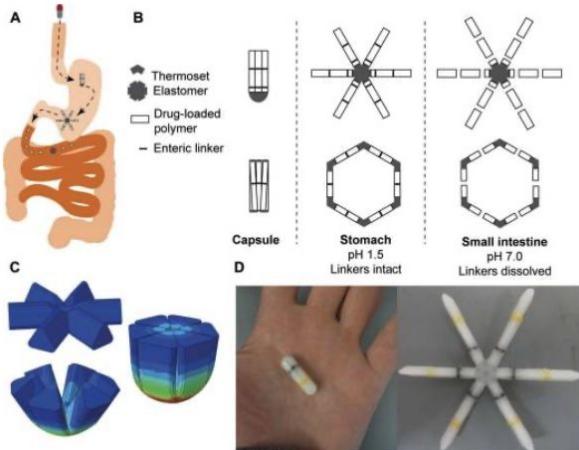
Complex manufacturing

Short duration

Variable absorption

Removable by patient

Capsules

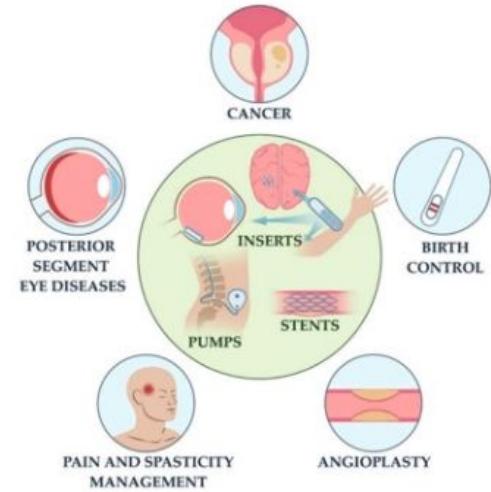


Comfort

Short duration (<1 month)

First hepatic pass

Implants



Extra-long duration

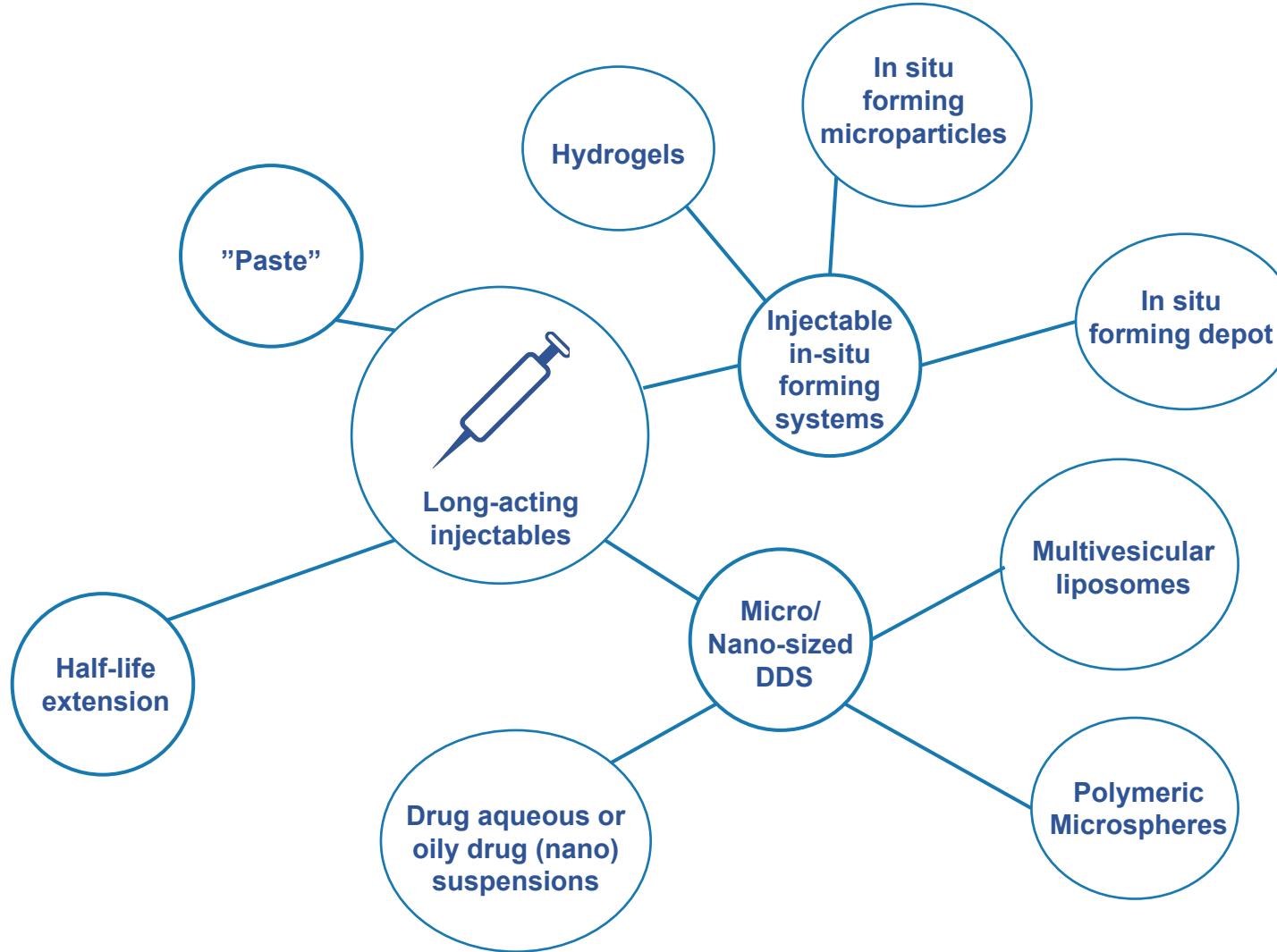
Local delivery

Administration procedure

Some are non bioresorbable

INTRODUCTION

Long acting injectables



- ✓ **Bioresorbable**
- ✓ **Wide range of durations**
- ✓ **Local and systemic delivery**
- ✓ **Many different technologies**
- ✓ **Peptides**

Introduction

Clinical LAs: Market and Trends

Examples of Commercial LAI Technologies

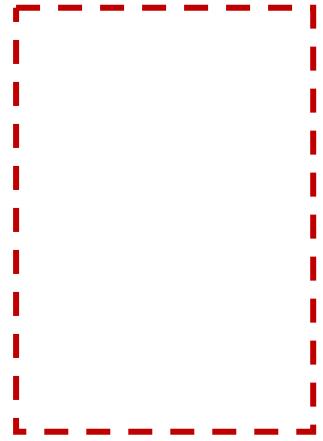
MedinCell BEPO® Technology

Challenges

CLINICAL LAIs - MARKET A

Type of molecule

Global LAI
market
32B\$ from
reported sales
(41 products)



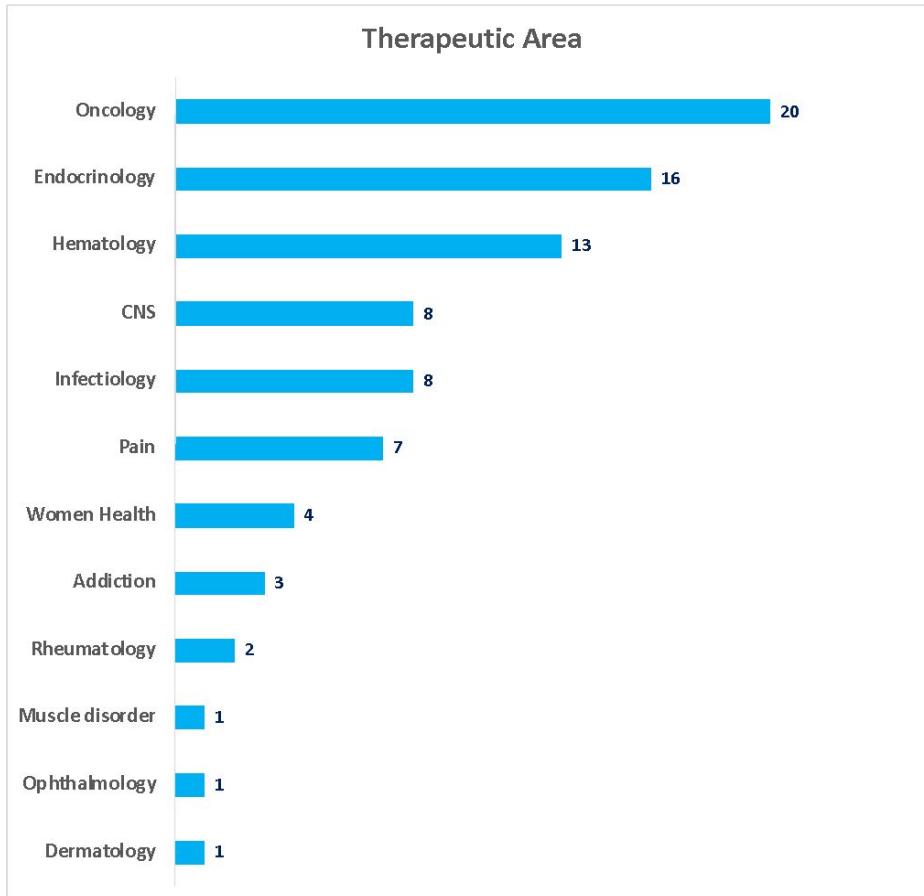
50% peptides
and biologics

Source: MedinCell proprietary database 2023

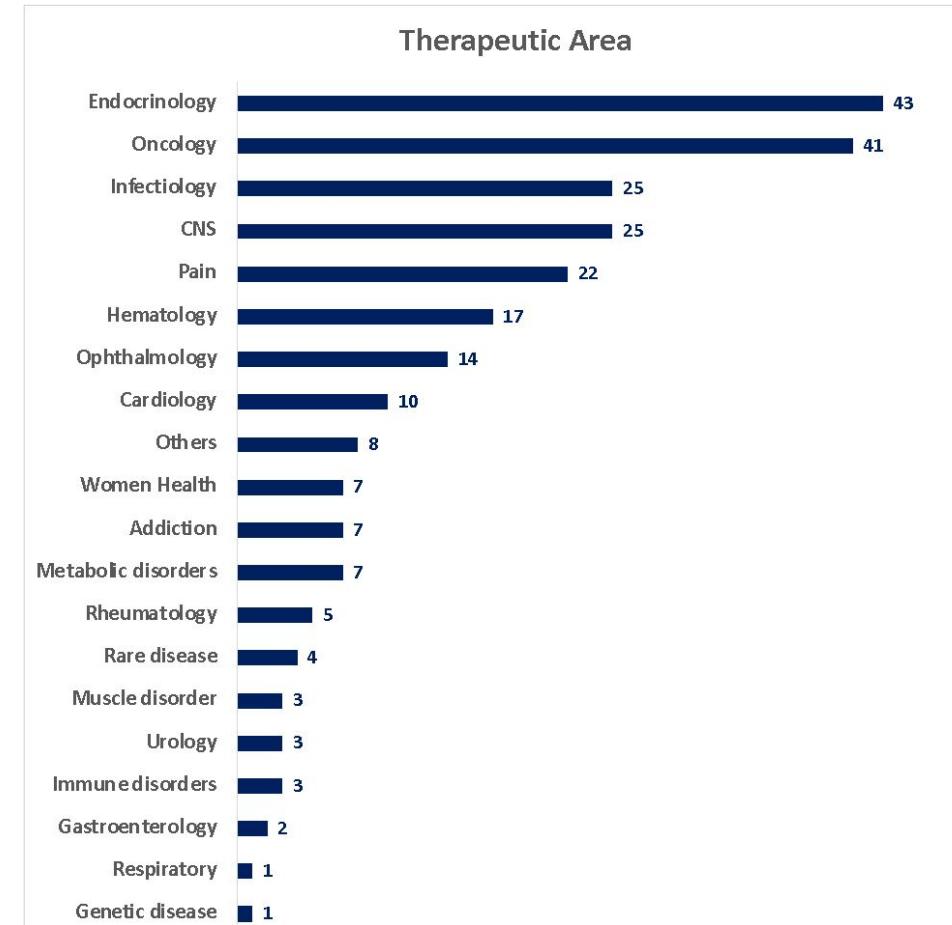
CLINICAL LAIs – MARKET AND TRENDS

Therapeutic areas

Approved



Clinical & preclinical

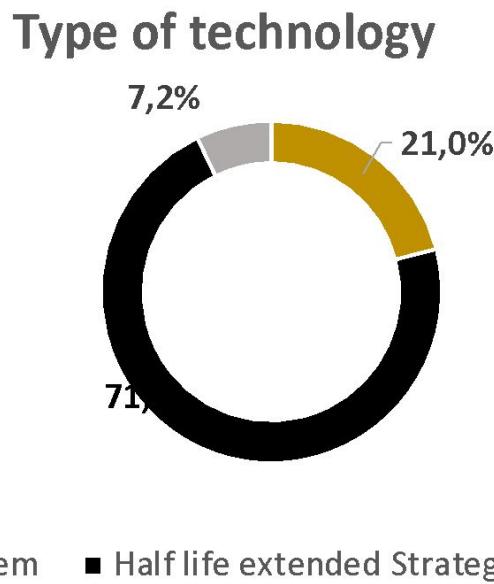


Source: MedinCell proprietary database 2023

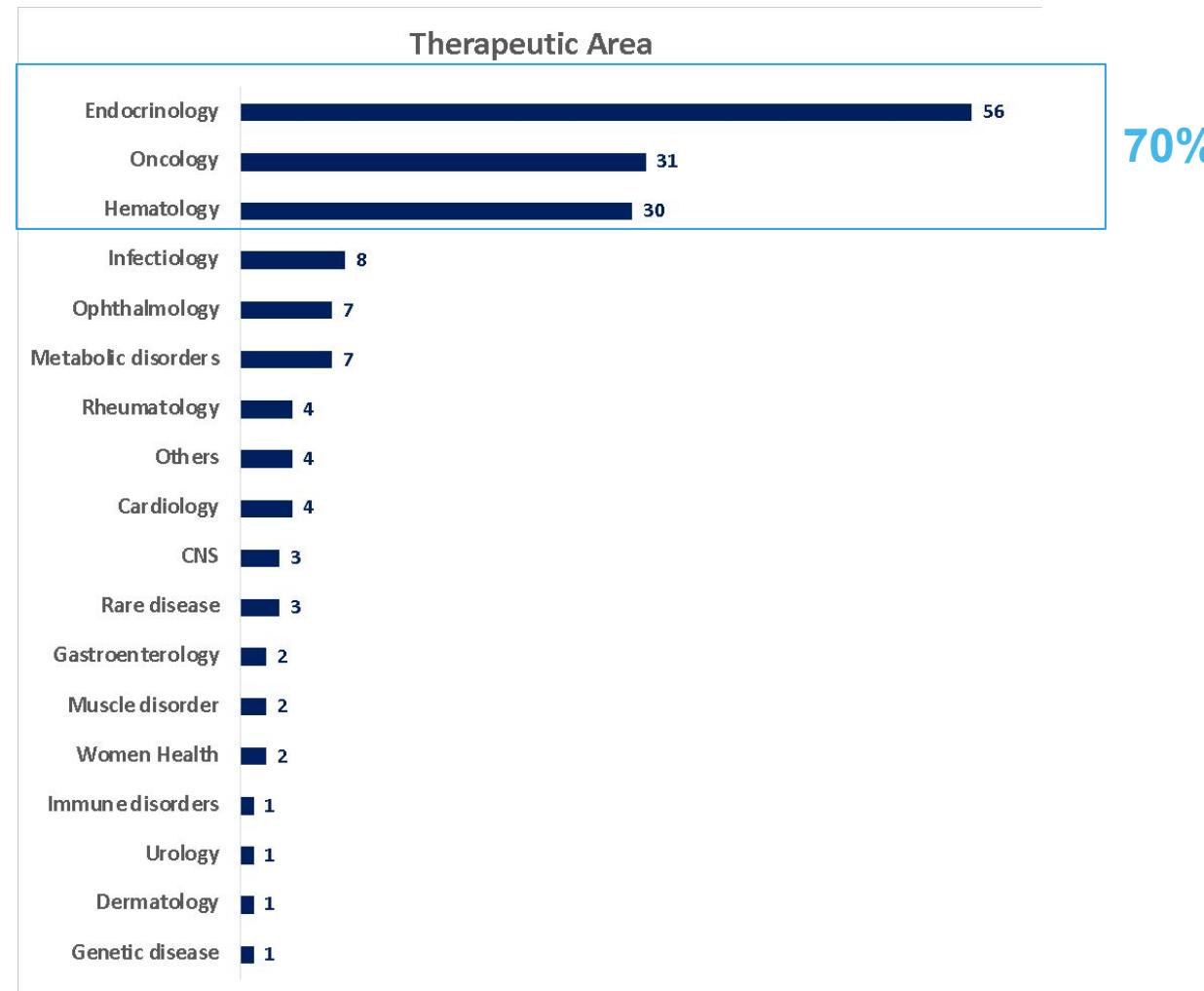
CLINICAL LAIs – MARKET AND TRENDS

Focus on peptides and biologics

Marketed, Clinical & preclinical
N=167

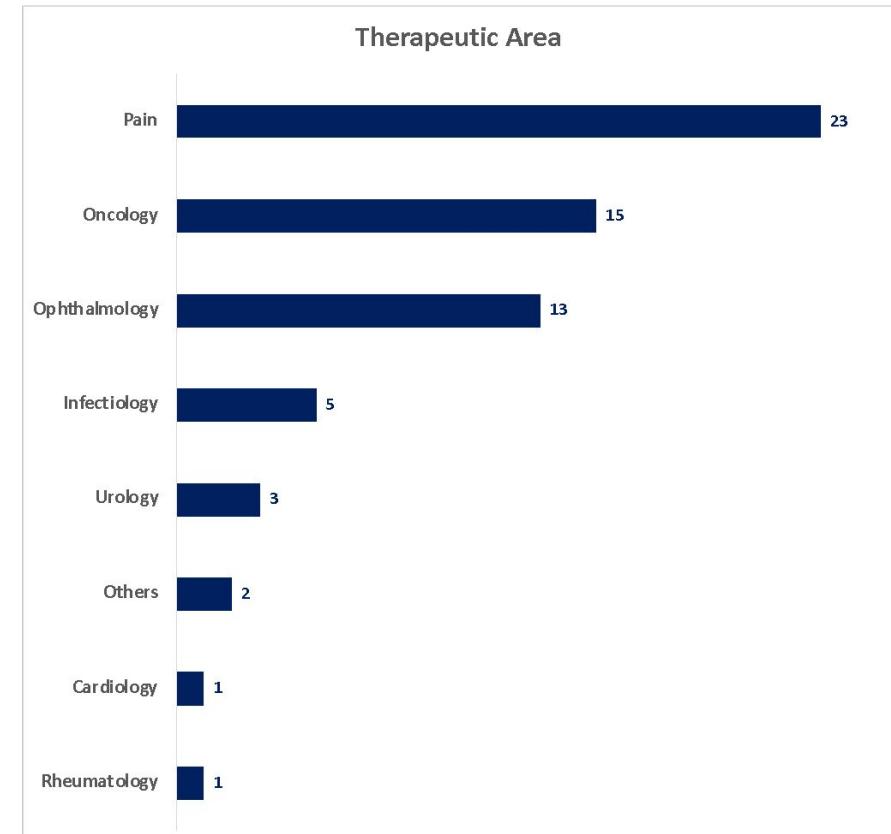
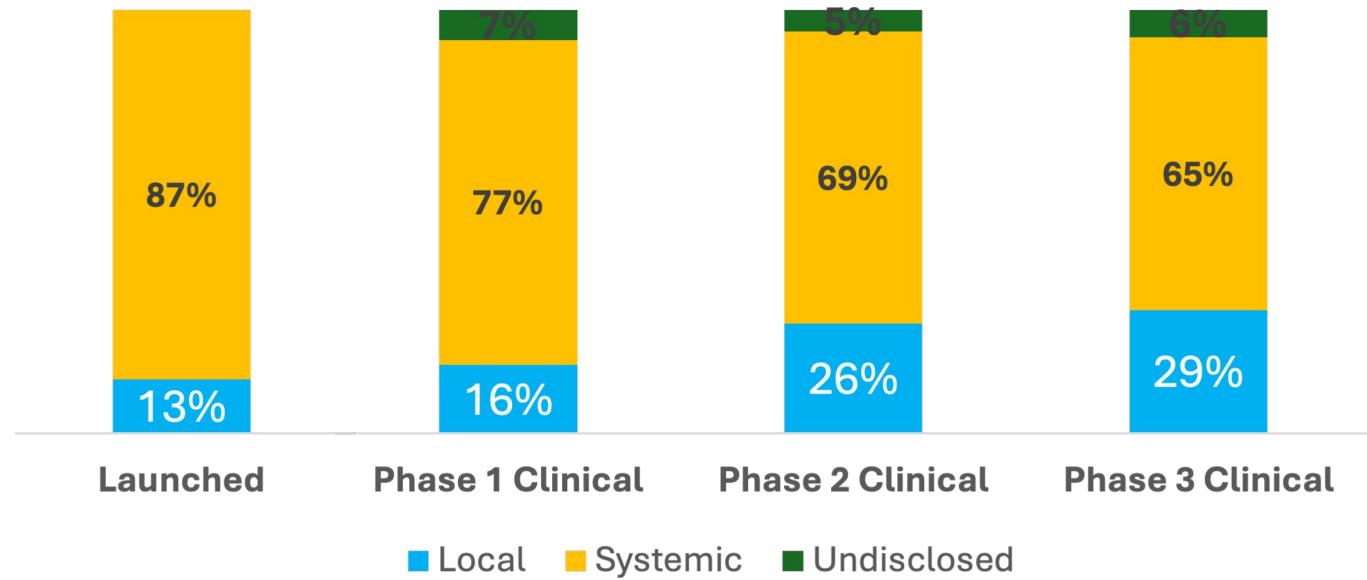


Source: MedinCell proprietary database 2023



CLINICAL LAIs – MARKET AND TRENDS

Systemic vs local



Likelihood of increase of approved local LAI

Source: MedinCell proprietary database 2023

CLINICAL LAIs – MARKET AND TRENDS

What type of technology?

332
LAIs



Source: MedinCell proprietary database 2023

Introduction

Clinical LAs: Market and Trends

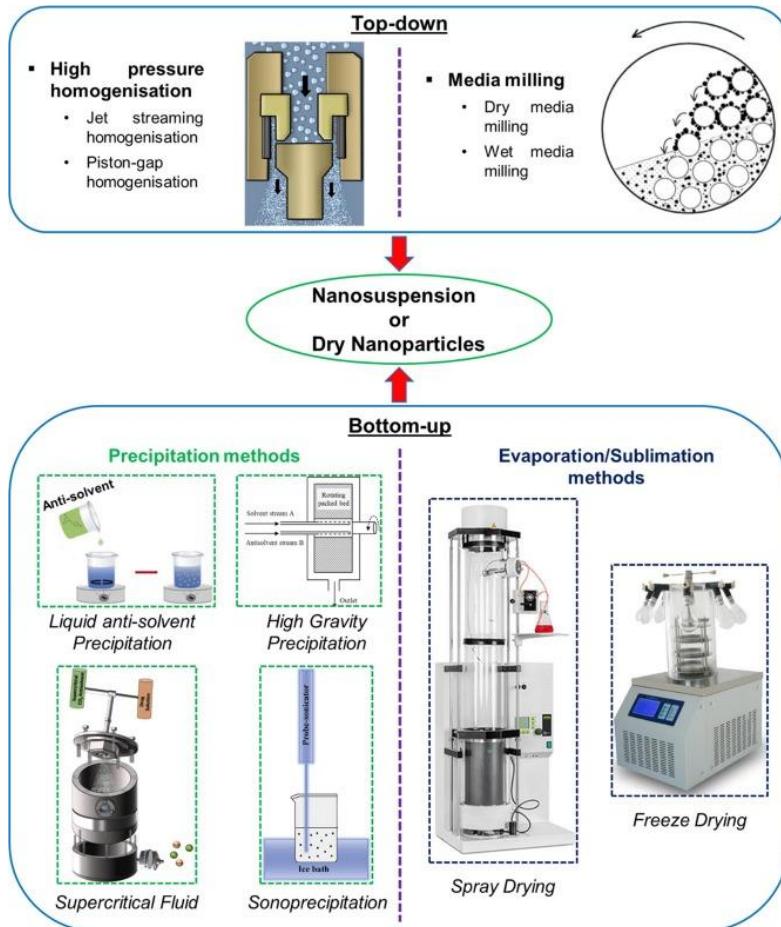
Examples of Commercial LAI Technologies

MedinCell BEPO® Technology

Challenges

EXAMPLES OF COMMERCIAL LAI TECHNOLOGIES

Drug nanosuspensions



TOP DOWN	BOTTOM UP	
Start with Larger crystal and break them down mechanically	Approach	Start with drug molecule in solution which form nanocrystal in changed condition
<ul style="list-style-type: none"> Industrial capable Easier to control the size Avoid the use of organic crystal 	Advantages	<ul style="list-style-type: none"> Low energy input Use for thermolabile drugs Possible to prepare small particle
<ul style="list-style-type: none"> More expensive and high energy input Long processing time Contamination from the Equipment 	Disadvantages	<ul style="list-style-type: none"> Crystal growth need to control Require good solvent Remove toxic organic solvent
Wet ball milling and high pressure homogenization	Example	Supercritical fluid technology, Precipitation

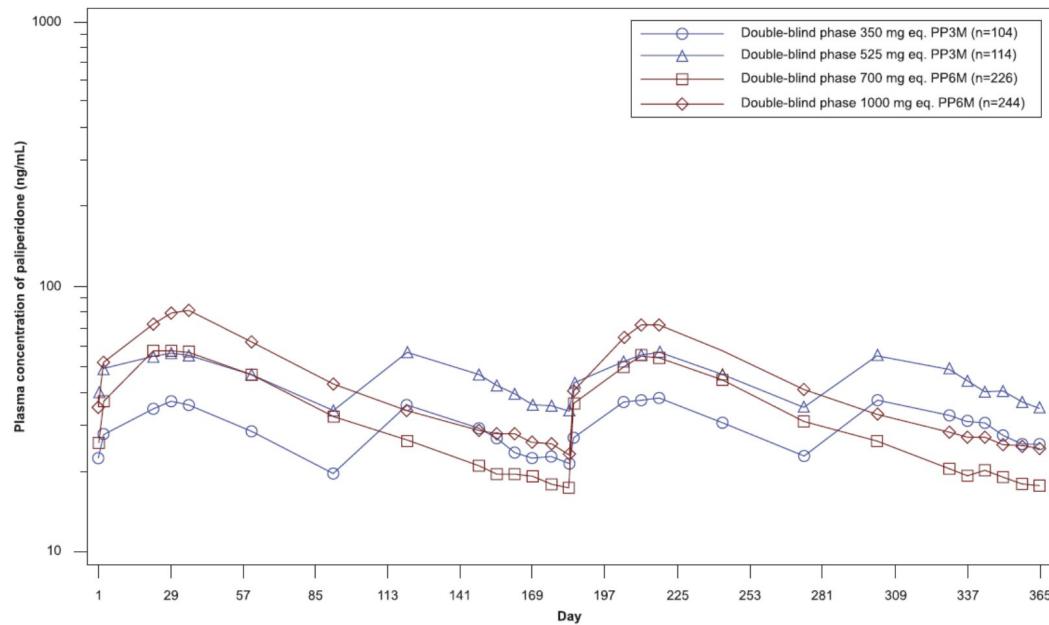
High doses can be administered

Allows flexibility in release duration, from weeks to months

No need for release modifier excipients

EXAMPLES OF COMMERCIAL LAI TECHNOLOGIES

Drug nanosuspensions



Only suited for drugs with specific physicochemical properties: low solubility

Intramuscular administration

- Not removable
- Larger needles
- More painful

Release kinetics only driven by dissolution rate of the engineered particles

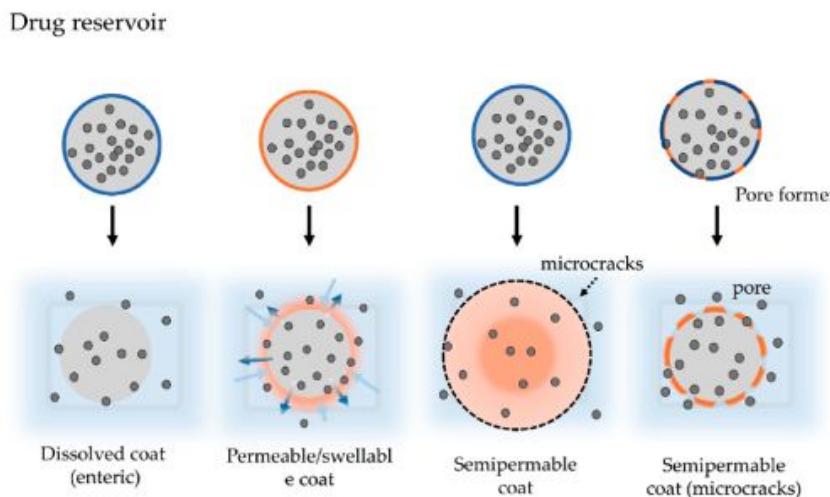
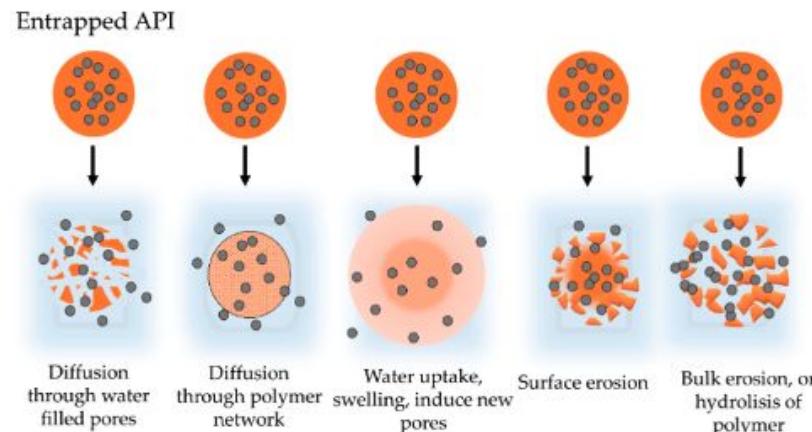
Sterilization might be difficult



<https://www.janssenscience.com/products/invega-hafyera/medical-content/pharmacokinetics-of-invega-hafyera>

EXAMPLES OF COMMERCIAL LAI TECHNOLOGIES

Microspheres



Wide range of release durations possible, from few weeks to several months

Typically, long shelf life

Compatible with peptides

Aqueous based

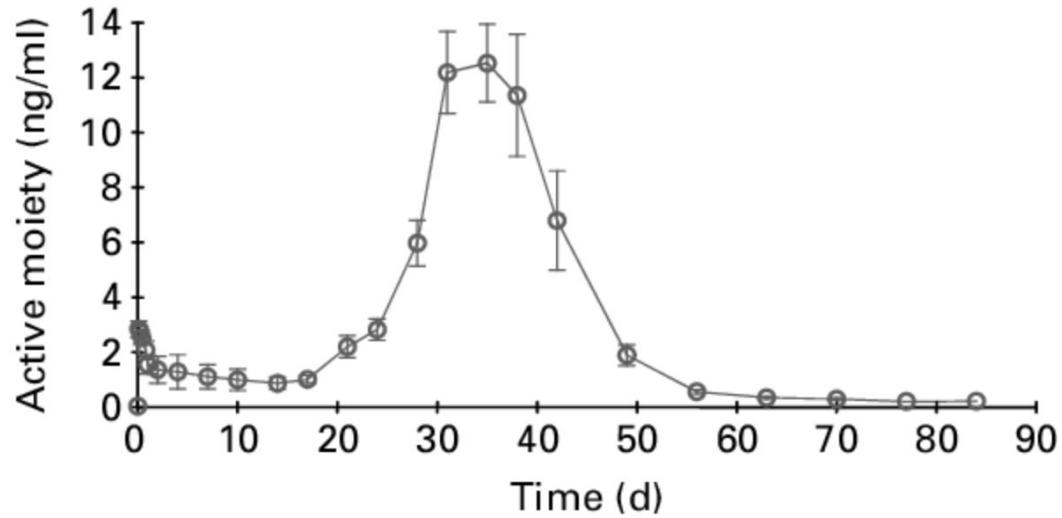
Can be used for local delivery

Many fabrication techniques:

- Emulsion-based
- Spray-drying
- Coaxial electrospray
- Microfluidic
- Hydrogel template
- 3D printing
- ...

EXAMPLES OF COMMERCIAL LAI TECHNOLOGIES

Microspheres



Release usually showing an initial lag: oral supplementation needed

Complex manufacturing process

Limited drug encapsulation

Need of reconstitution before administration

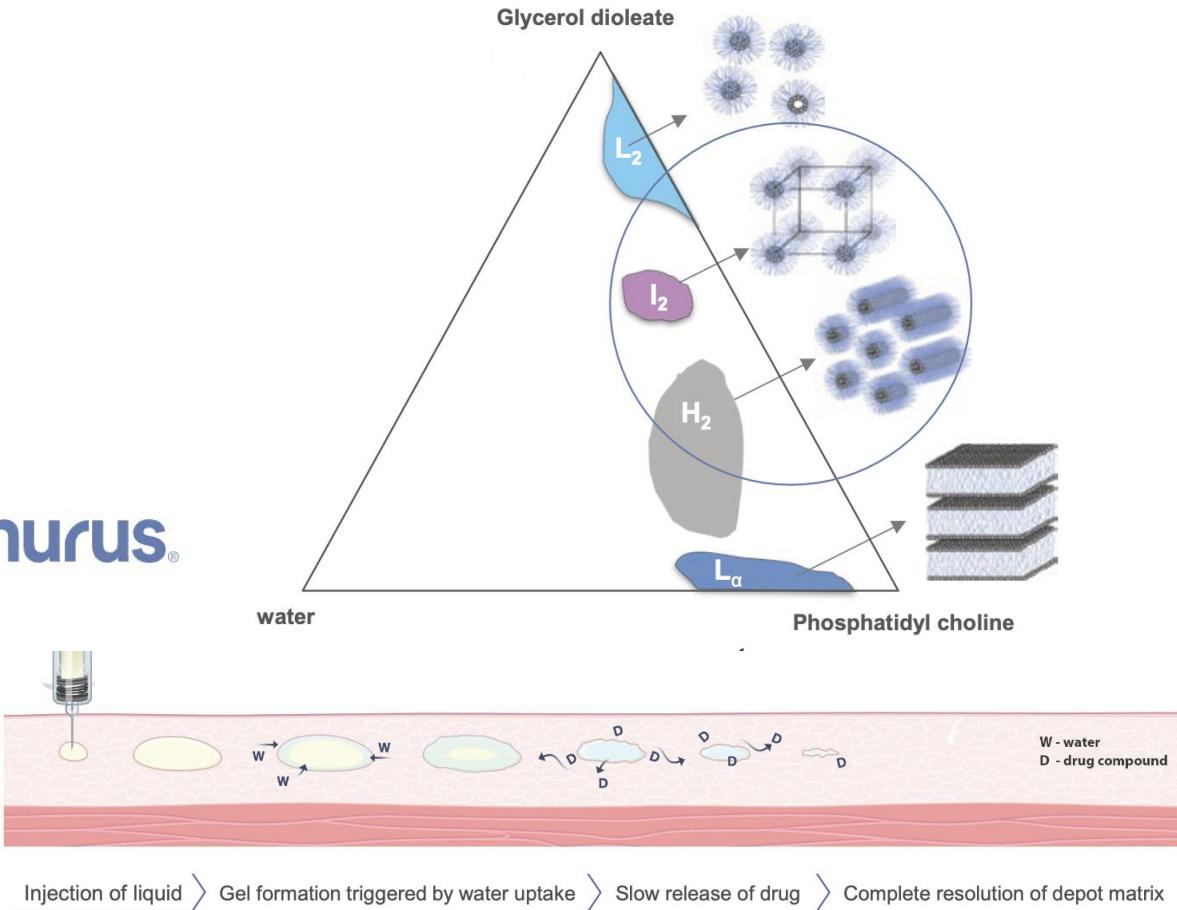
Typically intramuscular administration

Low pH microenvironment

EXAMPLES OF COMMERCIAL LAI TECHNOLOGIES

Liquid crystal technology

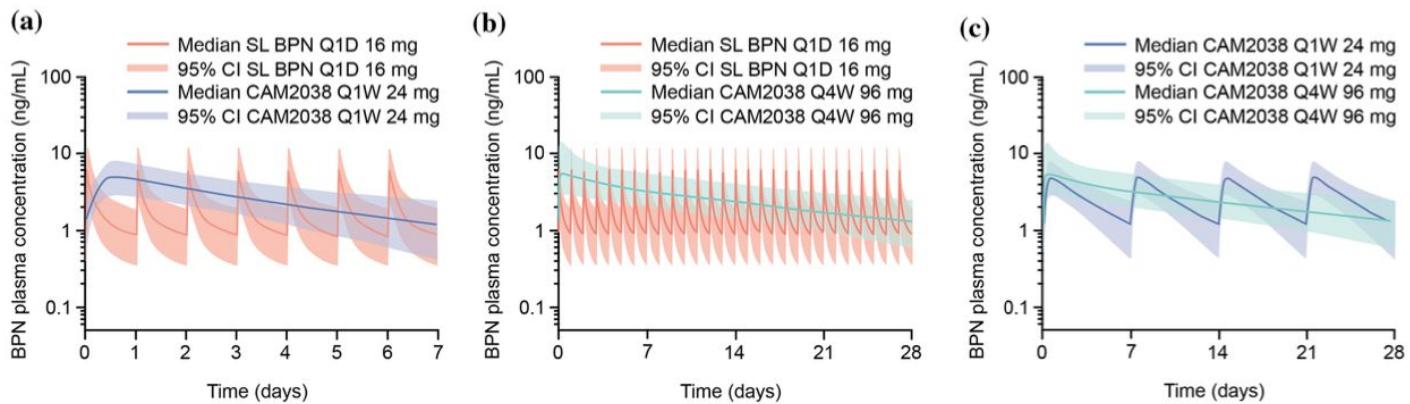
camurus®



- ✓ Ready to use formulations
- ✓ Small needle
- ✓ Compatible with peptides
- ✓ Subcutaneous, less pain

EXAMPLES OF COMMERCIAL LAI TECHNOLOGIES

Liquid crystal technology



Limited loading

Action duration above 1 month may be challenging to achieve

Unknown if suited for local delivery

Possibility to remove the depot not demonstrated

Introduction

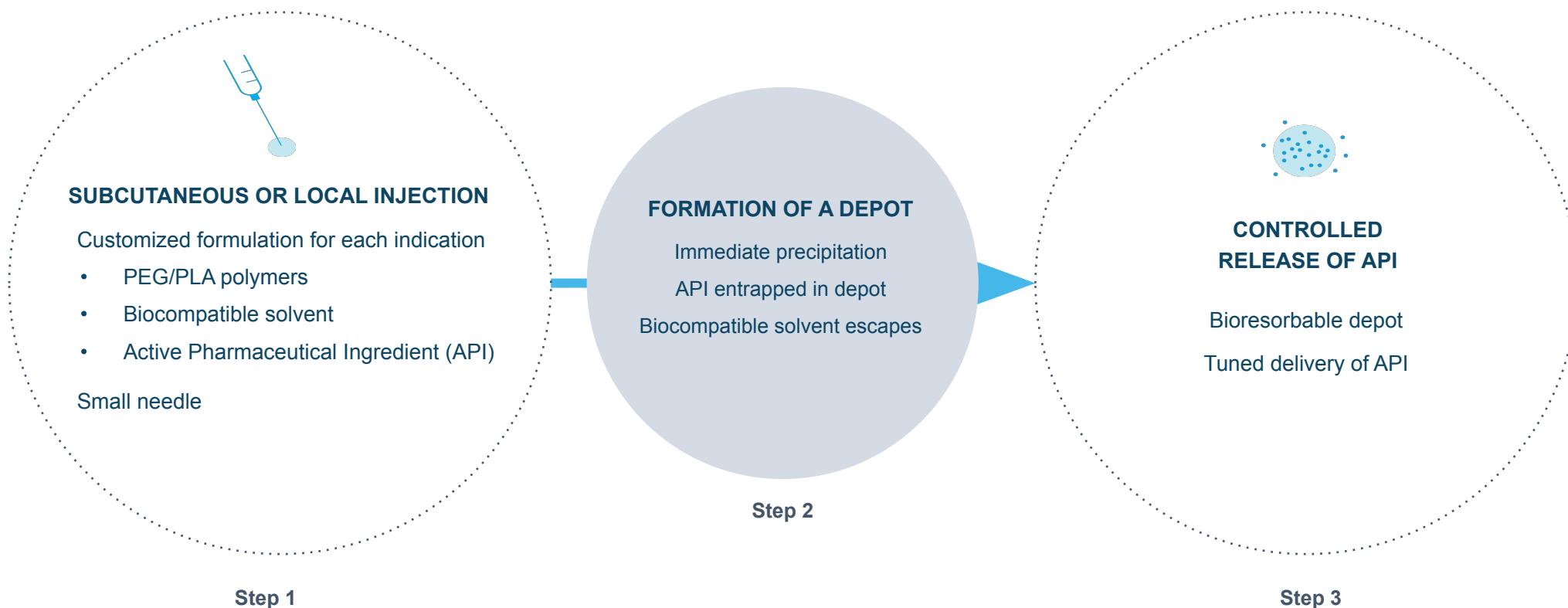
Clinical LAs: Market and Trends

Examples of Commercial LAI Technologies

MedinCell BEPO[®] Technology

Challenges

In situ forming depot – solvent exchange



Core components**ACTIVE PHARMACEUTICAL INGREDIENTS**

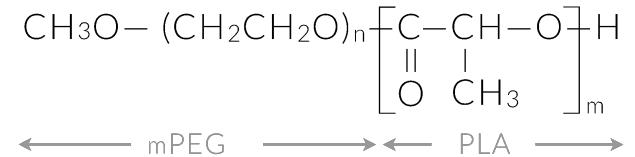
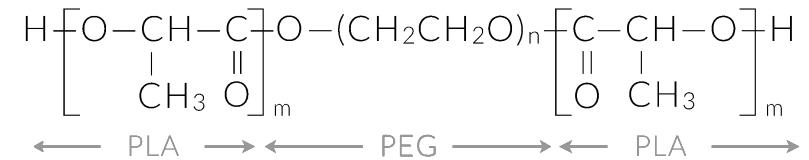
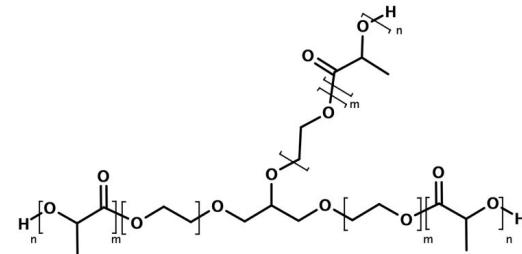
Pharmacological activity
Small molecules
Macromolecules possible

**SOLVENT**

Pharmaceutically acceptable
Makes the system injectable

COPOLYMERS

Bioresorbable
Controlled release

Diblock copolymer**Triblock copolymer****BEPO® STAR****Star-shaped copolymer**

Formulation variables

SOLVENT

Type of solvent
(Water miscibility and API solubility/stability)

Solvent content

Addition of Co-solvent

Melting Point

Influence on:

- Action Duration
- Injection Volume
- Solution vs Suspension
- Release Profile
- Viscosity/Injectability
- Stability of the Drug Product
- Depot Bioresorption timeframe

API

API loading

API polymorphic form

API free form vs salt form

API particle size distribution when relevant

Suspension vs solution

COPOLYMER

Linear PEG-PLA

Polymer content

TB / DB ratio

PLA / PEG molar ratio

PLA Mw in TB and DB

PEG Mw in TB and DB

Star PEG-PLA

of arms in star PEG-PLA

Polymer content

PLA / star PEG molar ratio

PLA Mw in star PEG-PLA

Star PEG Mw

Performance *in vivo*

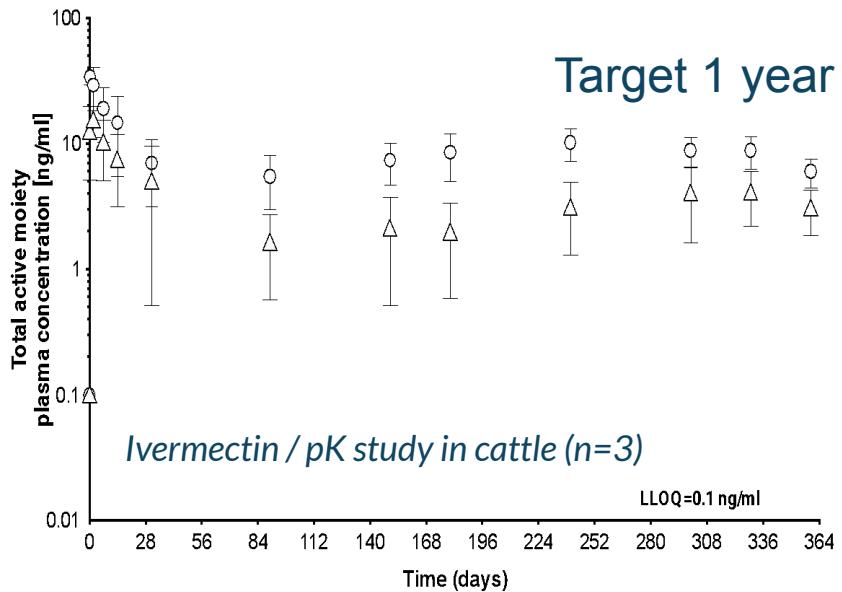
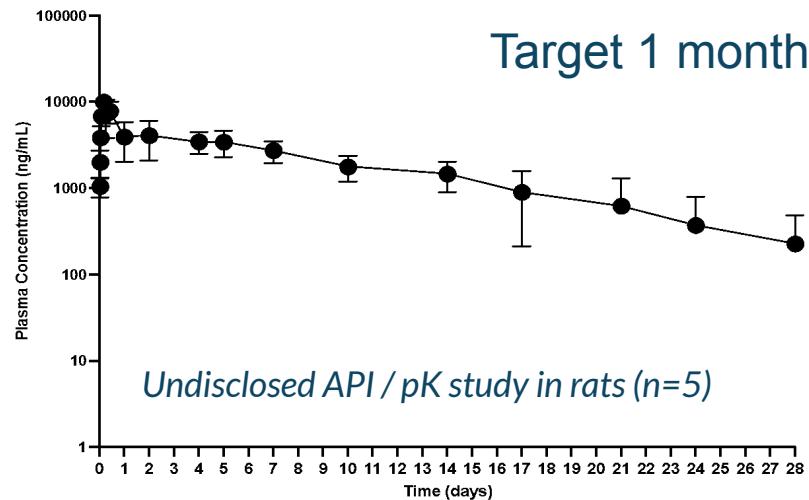
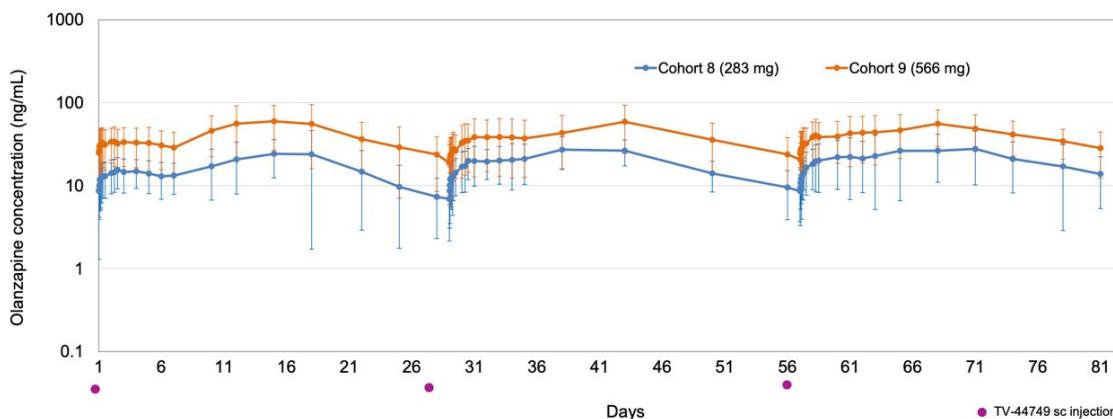
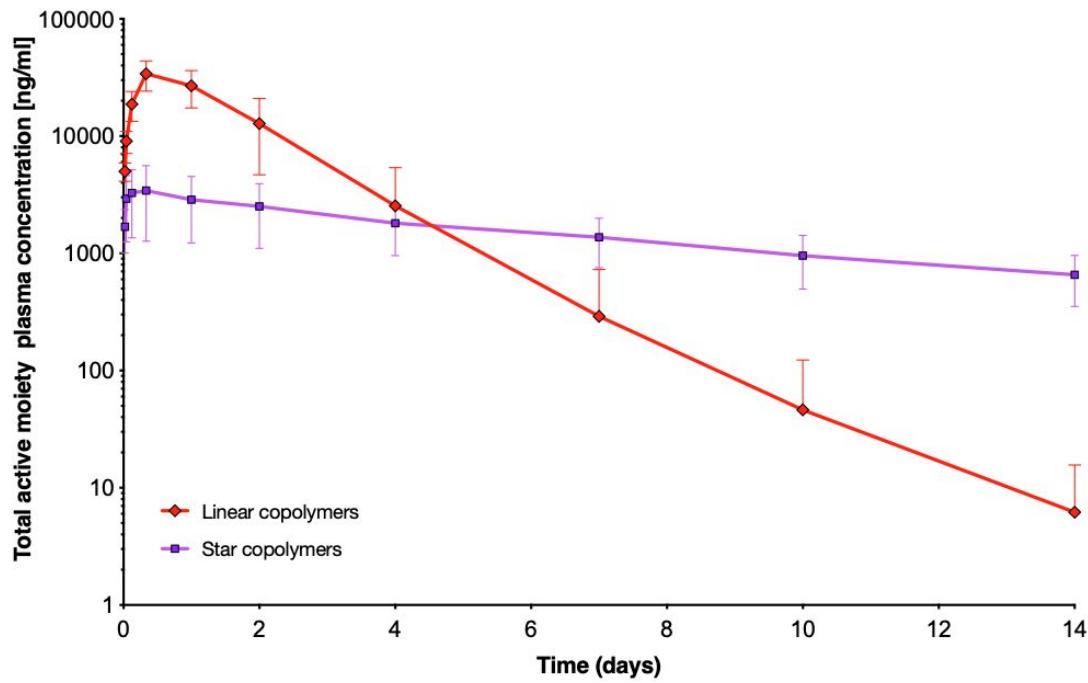


Figure 4. Mean (\pm SD) olanzapine plasma concentrations following three once monthly TV-44749 sc injections in patients with schizophrenia

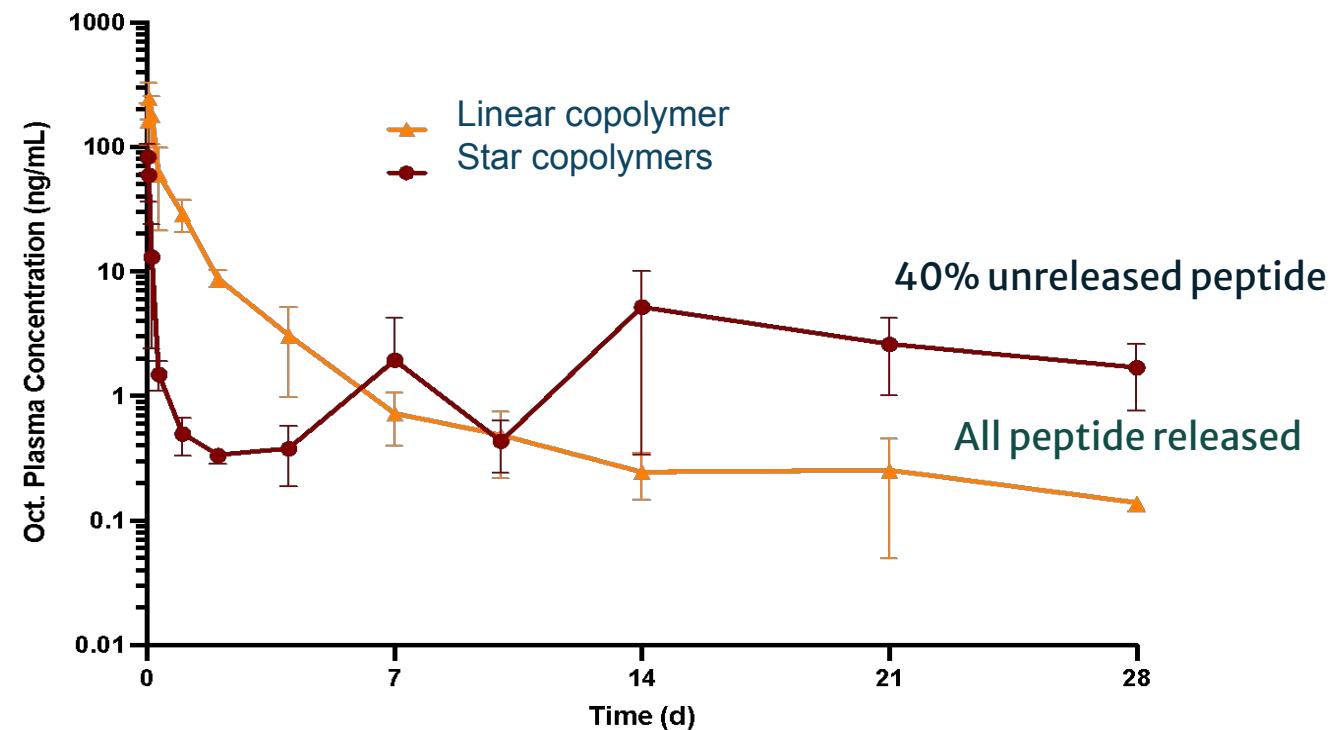


Data presented at the 2023 SIRS Annual Congress, Toronto, CANADA

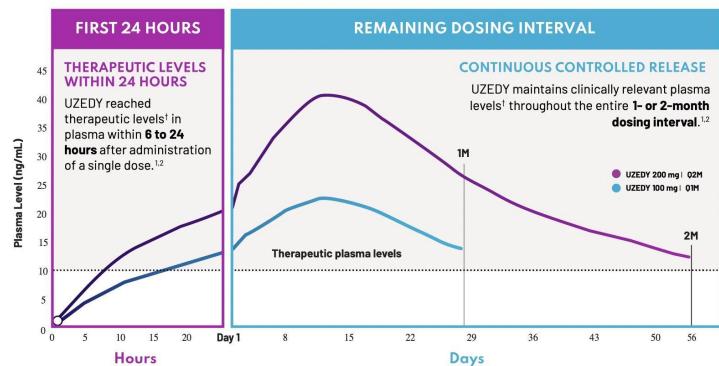
Meloxicam / pK study in rats (n=5)



Peptide / pK study in rats (n=5)



Superior long acting injectables



<https://www.uzedyhcp.com/dosing>

- ✓ Ready to use
- ✓ High loadings affordable
- ✓ Possible to formulate suspensions
- ✓ Long shelf-life, depending on the drug
- ✓ Subcutaneous
- ✓ Possible to excise
- ✓ Immediate onset of action
- ✓ Usable for local delivery
- ✓ Possible to formulate biologics*

* Molecular Cancer Therapeutics (2018) 17 (9): 1927–1940

* Journal of Controlled Release (2022), 341, 578-590

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Pipeline

MARKET



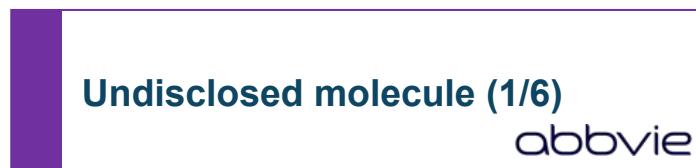
CLINICAL PHASE 3



PRECLINICAL



FORMULATION



+9 in-house or partnered active programs

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Challenges

CHALLENGES

What is missing?

TECHNICAL

Very long term delivery of peptides and biologics

Long term delivery of small hydrophilic drugs

Local long term delivery to specific organs

Challenging therapeutic areas

MARKET

Adapted to physician: need of long shelf-life, easy to use products

Adapted to patient: autoinjectors

Global access

THANK YOU

Want to know more?

adolfo.lopeznoriega@medincell.com
www.medincell.com