LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

Developed by

medicines patent pool

UNIVERSITY OF LIVERPOOL

CELT

Supported by

Unitaid
Innovation in Global Health

leap

BEPO®

Based on public information

Developer(s)

MEDINCELL

Originator

www.medincell.com

France

MedinCell® is a pharmaceutical company at premarketing stage that develops innovative long-acting injectable medicines in many therapeutic areas. Products of our portfolio are based on our BEPO® technology and aim to ensure patient compliance, improve the effectiveness and accessibility of treatments, and reduce their environmental footprint.

Sponsor(s)

No sponsor indicated

Partnerships

TEVA Pharmaceuticals
www.tevapharm.com

Arthritis Innovation Corporation (AIC)
www.aic.com/about-us

UNITAID
www.unitaid.org

The Bill and Melinda Gates Foundation
www.gatesfoundation.org

CORBION
www.corbion.com

Abbvie
https://www.abbvie.com/

Technology information

Type of technology

In-situ forming gel/implant

Administration route

Subcutaneous, Intra-articular

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Risperidone

Development Stage

Marketed

Regulatory Approval

FDA approved (UZEDY)

Description

BEPO® is a simple yet flexible technology based on MedinCell®'s custom proprietary copolymers, which forms a fully bioresorbable depot once injected. BEPO® technology has the potential to control regular delivery of an API at an optimal therapeutic dose for several days, weeks or months. BEPO® can be administered subcutaneously for systemic exposure of APIs or locally for targeted treatments.

Technology highlight

From systemic to local delivery, BEPO® is a clinically advanced proprietary long acting injectable technology that enables the controlled delivery of various active ingredients, to address a broad range of therapeutic needs. BEPO® technology makes possible to control and guarantee the regular delivery of a drug at the optimal therapeutic dose for several days, weeks or months. At the time of the injection, the BEPO technology forms a deposit of polymers of a few millimeters under the skin for a systemic action, or locally for a targeted action. The deposit diffuses the active ingredient by resorbing for the desired duration, like a mini pump that would be injectable and bioresorbable.

Technology main components

Three core components: a- A combination of diblock (DB) and triblock (TB) copolymers containing hydrophilic and water-soluble blocks (polyethylene glycol – PEG) linked with hydrophobic and amorphous blocks (Poly(D,L-lactic acid) – PLA) which precipitate in forming a depot when exposed to an aqueous environment. They are functional excipients, ensuring the controlled drug release. b- A pharmaceutically acceptable organic solvent, e.g. DMSO, to dissolve the copolymers and make the entire system injectable. c- An API to ensure pharmacological activity. The API can be a small molecule, a peptide or a therapeutic protein. The API is entrapped within the polymer matrix and is released thereafter by diffusion and following polymer degradation.

Information on the raw materials sourcing, availability and anticipated price

The core functional copolymer excipients are exclusively manufactured and supplied through a joint Venture made between Medincell and Corbion, called CMB. Corbion manufactures the copolymers with the appropriate quality standards and scale to ensure sufficient availability.

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Small molecules

Small molecules are best suited for formulating. Compatibility needs to be determined on a case-by-case basis.

Proteins

Case by case basis. Complex biomacromolecules like therapeutic proteins have inherent challenges that need to be tackled specifically during formulation development

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

0.1-60%

API co-administration

1 single API :

LogP

Min: -2.5 Max: 6.1

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Not provided

Specific analytical instrument required for characterization of formulation

Not provided

Clinical trials

Celecoxib LA: Safety and Activity of F14 for Management of Pain Following Total Knee Replacement

Identifier

NCT03541655

Link

https://clinicaltrials.gov/study/NCT03541655

Phase

Phase II

Status

Completed

Sponsor

Arthritis Innovation Corporation

More details

The safety and activity of a single, 3.5 mL dose of F14 (celecoxib) concurrent with standard of care analgesia administered following total knee replacement will be compared to standard of care analgesia alone.

Purpose

Safety and Activity of F14 for Management of Pain Following Total Knee Replacement

Interventions

Intervention 1

Bupivacaine HCl

Potential application(s)

Bupivacaine HCl (Dosage: 0.25%)

Intervention 2

F14 (celecoxib in BEPO)

Potential application(s)

Celecoxib (Dosage: F14 (mdc-CWM))

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-05-04

Anticipated Date of Last Follow-up

2020-07-08

Estimated Primary Completion Date

2018-05-30

Estimated Completion Date

2018-05-30

Actual Primary Completion Date

2019-06-20

Actual Completion Date

2020-03-30

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Male and/or female indicated for primary, unilateral TKR * Between 45-80 years of age inclusive at the time of signing the informed consent * Capable of giving signed informed consent and complying with requirements and restrictions listed in the informed consent form (ICF) and in this protocol * Body Mass Index (BMI) ≤ 40 kg/m² * Medically stable as determined by the Investigator based on pre-study medical history, physical examination, clinical laboratory tests, and 12-lead electrocardiogram (ECG) findings * Absence of fixed flexion deformity exceeding 15° * Absence of varus or valgus deformity exceeding 15° * Minimum pre-operative flexion arc of 100° * Absence of steroid, hyaluronic acid, platelet rich plasma, or any other type of therapeutic injection(s) in the i

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

20

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Single blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intra-articular

Use case

Treatment

Key results

Not provided

Risperidone LA: Study to Evaluate TV-46000 as Maintenance Treatment in Adult and Adolescent Participants With Schizophrenia (RISE)

Identifier

NCT03503318

Link

https://clinicaltrials.gov/study/NCT03503318

Phase

Phase III

Status

Completed

Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

More details

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of Risperidone Extended-Release Injectable Suspension (TV-46000) for Subcutaneous Use as Maintenance Treatment in Adult and Adolescent Patients With Schizophrenia: The purpose of the study is to evaluate the efficacy, safety, and tolerability of different dose regimens of TV-46000 administered subcutaneously (SC) as compared to placebo during maintenance treatment in adult and adolescent participants with schizophrenia. The study will include male and female participants, 13 to 65 years of age, who have a confirmed diagnosis of schizophrenia, are clinically stable, and are eligible for risperidone treatment

Purpose

Study to Evaluate TV-46000 as Maintenance Treatment in Adult and Adolescent Participants With Schizophrenia

Interventions

Intervention 1

TV-46000

Potential application(s)

Risperidone (Dosage: TV-46000)

Intervention 2

Placebo

Countries

Bulgaria
United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-04-27

Anticipated Date of Last Follow-up

2023-02-08

Estimated Primary Completion Date

2018-04-19

Estimated Completion Date

2018-04-19

Actual Primary Completion Date

2020-09-30

Actual Completion Date

2020-12-03

Studied populations

Age Cohort

- Adolescents
- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * The participant has a diagnosis of schizophrenia for \>1 year and has had ≥1 episode of relapse in the last 24 months. * The participant has been responsive to an antipsychotic treatment (other than clozapine) in the past year based on discussions with family members or healthcare professionals. * The participant has a stable place of residence for the previous 3 months before screening, and changes in residence are not anticipated over the course of study participation. * The participant has no significant life events that could affect study outcomes expected throughout the period of study participation. * Women of childbearing potential and sexually-

active female adolescents must agree not to try to become pregnant, and, unless they have exclusively same-sex partne

Health status

Not provided
Other health status: persons with schizophrenia

Study type

Interventional (clinical trial)

Enrollment

544

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Study protocol: https://cdn.clinicaltrials.gov/large-docs/18/NCT03503318/Prot_002.pdf

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

Risperidone LA: SHINE: A Study to Test if TV-46000 is Safe for Maintenance Treatment of Schizophrenia

Identifier

NCT03893825

Link

https://clinicaltrials.gov/study/NCT03893825

Phase

Phase III

Status

Completed

Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

More details

The primary objective of the study is to evaluate the long-term safety and tolerability of TV-46000. The primary safety and tolerability endpoint is the frequency of all adverse events, including serious adverse events. For new participants, the total duration of participant participation in the study is planned to be up to 80 weeks (including a screening period of up to 4 weeks, a 12-week oral conversion/stabilization stage \[Stage 1\], a 56-week double-blind maintenance stage \[Stage 2\], and a follow-up period \[8 weeks\]). For roll-over participants, the total duration of participant participation in the study is planned to be up to 64 weeks (including up to 56 weeks in the maintenance stage \[Stage 2\] and a follow-up period \[8 weeks\]). Participants who started Stage 2 who relapse o

Purpose

A Study to Test if TV-46000 is Safe for Maintenance Treatment of Schizophrenia

Interventions

Intervention 1

TV-46000

Potential application(s)

Risperidone (Dosage: TV-46000)

Intervention 2

Placebo

Countries

United States of America

Canada

Israel

France

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-04-17

Anticipated Date of Last Follow-up

2022-12-05

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2021-12-02

Actual Completion Date

2021-12-02

Studied populations

Age Cohort

- Children
- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: Participants Rolling Over from the Pivotal Efficacy Study TV46000-CNS-30072: * The participant must have participated in the pivotal efficacy study (Study TV46000-CNS-30072) without experiencing relapse events and without important protocol deviations. * If the participant was taking antidepressants or mood stabilizers in Study TV46000-CNS-30072, no dose changes or initiation of treatment with these medications will be permitted. * The participant, in the investigator's judgment, requires chronic treatment with an antipsychotic medication. * The

participant is able to understand the nature of the study and follow protocol requirements, including the prescribed dosage regimens (oral and SC administration) and non-use of prohibited concomitant medications; can read and

Health status

Not provided
Other health status: persons with schizophrenia

Study type

Interventional (clinical trial)

Enrollment

336

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

Celecoxib LA: Safety of F14 Following Total Knee Replacement (100-CIP03-P)

Identifier

NCT04860635

Link

https://clinicaltrials.gov/study/NCT04860635

Phase

Phase II/III

Status

Suspended

Sponsor

Arthritis Innovation Corporation

More details

Study superseded by alternative Phase 3 trial Open-label single-arm study in which all subjects receive F14 as part of a scheduled TKR and multimodal analgesia

Purpose

Safety of F14 Following Total Knee Replacement

Interventions

Intervention 1

F14 (sustained release celecoxib)

Potential application(s)

Celecoxib (Dosage: F14 (mdc-CWM))

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-09-01

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-01-29

Estimated Primary Completion Date

2025-09-01

Estimated Completion Date

2025-09-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: 1. Male and/or females indicated for primary, unilateral TKR 2. Between 45-80 years of age 3. Capable of giving signed informed consent 4. Body Mass Index (BMI) ≤ 40 kg/m2 5. Medically stable as determined by the Investigator, based on physical examination, clinical laboratory tests, and 12-lead ECG findings, as well as medical history from subject and pre-study source documents from other care providers 6. Absence of fixed flexion deformity exceeding 15deg 7. Absence of varus or valgus deformity exceeding 15deg 8. Minimum pre-operative flexion arc of 100deg 9. American Society of Anesthesiologists Physical Status Classification System (ASA-PSC) score ≤ 3 10. Females of childbearing potential with a negative serum pregnancy test at screening or males with a partner tha

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

100

Allocation

Non-randomized

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intra-articular

Use case

Treatment

Key results

Not provided

A Celecoxib LA: Phase 3 Study of F14 for Management of Pain Following Total Knee Replacement (100-CIP02-P)

Identifier

NCT05603832

Link

https://clinicaltrials.gov/study/NCT05603832

Phase

Phase III

Status

Active, not recruiting

Sponsor

Arthritis Innovation Corporation

More details

This is a Phase 3, randomized, double blind, multicenter study to evaluate the analgesic efficacy and safety of a single intra-articular dose of F14 (625 mg sustained release celecoxib) administered concurrent with multimodal analgesia in patients undergoing total knee replacement surgery, compared to multimodal analgesia alone.

Purpose

A Phase 3 Study of F14 for Management of Pain Following Total Knee Replacement

Interventions

Intervention 1

F14 (celecoxib in BEPO(r))

Potential application(s)

Celecoxib (Dosage: 625 mg F14 (mdc-CWM))

Intervention 2

0.25 % Bupivacaine HCl

Potential application(s)

Bupivacaine HCl (Dosage: 0.25%)

Intervention 3

Acetaminophen

Potential application(s)

Acetaminophen

Intervention 4

Methocarbamol

Potential application(s)

Methocarbamol

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-11-17

Anticipated Date of Last Follow-up

2024-01-29

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2024-08-01

Actual Primary Completion Date

2023-11-22

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Male and/or females indicated for primary, unilateral total knee replacement (TKR) * Between 45-80 years of age inclusive at the time of signing the informed consent * Capable of giving signed informed consent and complying with requirements and restrictions listed in the informed consent form (ICF) and in this protocol * Body Mass Index (BMI) ≤ 40 kg/m2 * Medically stable as determined by the

Investigator, based on physical examination, clinical laboratory tests, and 12-lead electrocardiogram (ECG) findings, as well as medical history from patient and pre-study source documents from other care providers * Absence of moderate to severe fixed flexion deformity * Absence of moderate to severe varus or valgus deformity * Minimum pre-operative flexion arc of 100 degrees

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

151

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key results

Not provided

Olanzapine Prolonged-Release Suspension for Subcutaneous Administration A 21-Week, Multicenter, Open-Label, Multiple-Dose Trial to Assess the Comparative BioavailabilityTV44749-BA-10196

Identifier

NCT06315283

Link

https://clinicaltrials.gov/study/NCT06315283

Phase

Phase I

Status

Recruiting

Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

More details

The primary objective of the study is to evaluate the comparative bioavailability of TV-44749 administered subcutaneous (sc) to oral olanzapine (ZYPREXA®) at steady state in participants with schizophrenia. A secondary objective of this trial is to evaluate the safety and tolerability of multiple doses of TV-44749 administered sc in participants with schizophrenia. Another secondary objective of this trial is to compare additional pharmacokinetic parameters of TV-44749 administered sc with oral olanzapine (ZYPREXA®) at steady state in participants with schizophrenia. The total duration of participation in the trial for each participant is planned to be approximately 21 weeks.

Purpose

An Open-Label Trial to Assess the Comparative Bioavailability of TV-44749 to Oral Olanzapine in Participants With Schizophrenia

Interventions

Intervention 1

TV-44749

Potential application(s)

Olanzapine (Dosage: TV-44749)

Intervention 2

Oral olanzapine

Potential application(s)

Olanzapine (Dosage: 10mg)

Countries

Croatia

France

Germany

Spain

United Kingdom

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-03-20

Anticipated Date of Last Follow-up

2024-07-24

Estimated Primary Completion Date

2025-04-18

Estimated Completion Date

2025-04-18

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Agree to maintain current smoking or nonsmoking status at the time informed consent is obtained and throughout the trial until completion of the EOT or ET visit (ie, nonsmoking participants must agree not to start smoking and participants who smoke will be excluded if they plan to discontinue smoking during the

trial period). * Have a current confirmed diagnosis of schizophrenia according to an evaluation by the Investigator, as defined by the DSM-5 (American Psychiatric Association 2013a). * Are clinically stable on oral olanzapine 20 mg daily (ie, dose has not changed in the last 4 weeks) and not currently on other antipsychotic treatments at the time of screening. Participants on alternative olanzapine regimens (eg, 10 mg twice daily) may be considered for inclusi

Health status

Not provided
Other health status: Persons with schizophrenia

Study type

Interventional (clinical trial)

Enrollment

116

Allocation

Non-randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

Olanzapine extended-release suspension for subcutaneous injection (TV-44749) and Zyprexa in Chinese patients with schizophrenia: Safety, tolerability and pharmacokinetic studies in patients with schizophrenia

Identifier

CTR20233083

Link

http://www.chinadrugtrials.org.cn/

Phase

Phase I

Status

Recruiting

Sponsor

Teva/Pliva

More details

Not provided

Purpose

To evaluate the safety, tolerability and pharmacokinetics of single-dose olanzapine extended-release suspension for subcutaneous injection (TV-44749) and Zyprexa in Chinese patients with schizophreni

Interventions

Intervention 1

Olanzapine for Extended-Release Injectable Suspension (TV-44749)

Potential application(s)

Olanzapine (Dosage: 0.9-1.2-1.5 mL)

Intervention 2

oral olanzapine

Potential application(s)

Olanzapine (Dosage: 15-20 mg)

Countries

China

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-03-28

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2025-03-28

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- Male
- Female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Not provided

Health status

Not provided
Other health status: patients with schizophrenia

Study type

Interventional (clinical trial)

Enrollment

36

Allocation

Non-randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

Olanzapine:SOLARIS: A Randomized, Double-Blind, Placebo-Controlled Study With an Open-Label, Long-Term Safety Phase to Evaluate the Efficacy and Safety of TV-44749 in Adults With Schizophrenia

Identifier

NCT05693935

Link

https://clinicaltrials.gov/study/NCT05693935

Phase

Phase III

Status

Completed

Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

More details

The primary objective of this study is to evaluate the efficacy of TV-44749 in adult participants with schizophrenia. A key secondary objective is to further evaluate the efficacy of TV-44749 based on additional parameters in adult participants with schizophrenia. A secondary objective is to evaluate the safety and tolerability of TV-44749 in adult participants with schizophrenia Another secondary objective of this study is to evaluate the efficacy of TV-44749 from baseline to endpoint in Period 1 in adult participants with schizophrenia. Total study duration is up to 61 weeks, and treatment duration is up to 56 weeks, with weekly visits during the first 8 weeks and then monthly in-clinic visits with weekly calls during the remainder of the treatment

period.

Purpose

A Randomized, Double-Blind, Placebo-Controlled Study With an Open-Label, Long-Term Safety Phase to Evaluate the Efficacy and Safety of TV-44749 in Adults With Schizophrenia

Interventions

Intervention 1 Potential application(s)

Olanzapine

Not provided

Countries

Bulgaria
Romania
United States of America
China
Türkiye

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-01-24

Anticipated Date of Last Follow-up

2024-04-18

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2025-01-13

Actual Primary Completion Date

2024-03-19

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * The participant has a current confirmed diagnosis of schizophrenia according to the DSM-5, for \>1 year * The participant has exacerbation of schizophrenia that started ≤8 weeks prior to screening and would benefit from psychiatric hospitalization or continued hospitalization for symptoms of schizophrenia. * Participants who have received an antipsychotic treatment (other than clozapine) in the past year must have been responsive based on the investigator's judgment (and

based on discussions with family members, caregivers, or healthcare professionals, as applicable). * Body mass index between 18.0 and 40.0 kg/m2, inclusive, at the time of screening * Women may be included only if they have a negative beta-human chorionic gonadotropin (β-HCG) test at screening and ba

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

675

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key results

Not provided

Olanzapine: TV44749-PK-10188 : Safety, Tolerability, and Pharmacokinetic Study of TV-44749 in Chinese Patients With Schizophrenia

Identifier

NCT06253546

Link

https://clinicaltrials.gov/study/NCT06253546

Phase

Phase I

Status

Recruiting

Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

More details

Primary Objective: To evaluate the safety and tolerability of single doses of TV-44749 for subcutaneous (sc) use in Chinese participants with schizophrenia. Secondary Objectives: * To evaluate the pharmacokinetics (PK) of single doses of TV-44749 administered sc. * To evaluate the pharmacokinetics of oral olanzapine tablets following multiple dose administration. * To monitor the safety and tolerability of multiple doses of oral olanzapine tablets given in the study.

Purpose

Safety, Tolerability, and Pharmacokinetic Study of TV-44749 in Chinese Patients With Schizophrenia

Interventions

Intervention 1

TV-44749

Potential application(s)

Olanzapine

Intervention 2

Oral Olanzapine

Countries

China

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-03-28

Anticipated Date of Last Follow-up

2024-05-08

Estimated Primary Completion Date

2025-01-31

Estimated Completion Date

2025-01-31

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Body weight \>50 kg and body mass index (BMI) between 18.5 to 38.0 kg/m2, inclusive, at the time of screening. * A current confirmed diagnosis of schizophrenia according to an evaluation by the investigator, using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) * Are clinically stable, on oral olanzapine (i.e., dose has not changed in the last 4 weeks), and not currently on other antipsychotic treatment at the time of screening. * No hospitalization for worsening of schizophrenic symptoms and no significant exacerbation of schizophrenic symptoms, as judged by the investigator, within the 3 months prior to screening. * Female participants must have a negative serum pregnancy test at screening, are sterile or postmenopausal, and not pla

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

36

Allocation

Not provided

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key results

Not provided

Olanzapine: TV44749-NPC-10205

Identifier

NCT06319170

Link

https://clinicaltrials.gov/study/NCT06319170

Phase

Phase I

Status

Recruiting

Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

More details

The primary objective of the study is to characterize the pharmacokinetics of 3 formulations of olanzapine. A secondary objective is to evaluate the safety and tolerability of 3 formulations of olanzapine. Another secondary objective is to characterize the pharmacokinetics of ZYPREXA. The planned duration of the study for each participant is 19 weeks.

Purpose

Open-label Trial Characterizing the PK of 3 SC Olanzapine Extended-release Formulations in Participants With Schizophrenia/Schizoaffective Disorder

Interventions

Intervention 1

Olanzapine Extended Release

Potential application(s)

Olanzapine

Intervention 2

Olanzapine

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-03-28

Anticipated Date of Last Follow-up

2024-06-11

Estimated Primary Completion Date

2024-12-11

Estimated Completion Date

2024-12-11

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Body weight \>50 kg and body mass index (BMI) within the range 18.5 to 38.0 kg/m2, inclusive, at the time of screening * Agree to maintain current smoking or nonsmoking status at the time informed consent is obtained and throughout the trial until completion of the end of treatment or early termination (ET) visit (ie, nonsmoking participants must agree not to start smoking and participants who smoke will be excluded if they plan to discontinue smoking during the trial * Agree to the inpatient periods required during the trial period * Have a current confirmed diagnosis of schizophrenia or schizoaffective disorder according to an evaluation by the Investigator, using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (American Psychiatric

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

95

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key results

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

Confidential information

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Biodegradable
- Room temperature storage
- At least 1 year shelf life
- Drug-eluting
- Non-removable
- Single-use

Release properties

BEPO® technology has the potential to control regular delivery of an API at an optimal therapeutic dose for several days, weeks or months. The technology can provide a sustained release profile of an API with low initial burst. The hygroscopy and consequently the API release kinetics from the depots can be fine-tuned by adjusting the hydrophilicity of the DB and TB and their relative ratio.

Injectability

BEPO® drug products are liquid and can be injected using standard injection device with standard 21 gauge needle or even thinner depending on the formulation characteristics.

Safety

We currently have 3 clinically advanced drug products based on BEPO® technology, including one at NDA stage with TEVA pharmaceuticals. The RISE clinical phase III study completed in November 2020 did not raise any safety signals that were inconsistent with the known safety profile of other risperidone formulations.

Stability

Our technology may allow long-term storage at room temperature with shelf life well above 1 year.

Storage conditions and cold-chain related features

Room Temperature storage possible. Cold chain is not mandatory, except in instances where the drug substance requires refrigeration for long term storage.

Potential application(s)

Therapeutic area(s)

Malaria

Contraception

Disease agnostic

COVID 19

Pain management

Mental health

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Treatment

Use of technology

Ease of administration

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

Frequency of administration

Depending on product, once weekly up to once annually, Weekly, Monthly, Bi-yearly, Yearly, Once every 8 weeks

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

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

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

Risperidone

Class(es)

antipsychotic

Development stage

Marketed

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Schizophrenia

Foreseen user group

UZEDY (risperidone) extended-release injectable suspension is a prescription medicine used to treat schizophrenia in adults.

Foreseen duration between application(s)

1 or 2 months

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

FDA approved (UZEDY)

Celecoxib

Class(es)

anti inflammatory

Development stage

Phase III

Clinical trial number(s)

NCT05603832

Foreseen/approved indication(s)

post-operative pain and inflammation

Foreseen user group

Not provided

Foreseen duration between application(s)

Once every 12 weeks

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Ivermectin

Class(es)

Not provided

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Malaria Transmission prevention

Foreseen user group

persons at risk of malaria and their communities

Foreseen duration between application(s)

Single intervention per year (3 months action duration)

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Progestin

Class(es)

Not provided

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

contraception

Foreseen user group

persons desiring contraception use

Foreseen duration between application(s)

6 months

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Olanzapine

Class(es)

Not provided

Development stage

Phase III

Clinical trial number(s)

NCT05693935

Foreseen/approved indication(s)

schizophrenia management

Foreseen user group

Adults with schizophrenia

Foreseen duration between application(s)

1 month

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not yet approved

Patent info

Technology patent families

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Method for morselizing and/or targeting pharmaceutically active principles to synovial tissue Expiry date: 2036-11-16 A method of targeting to the synovial tissue biodegradable drug delivery compositions or morselizing biodegradable drug delivery compositions are described. The biodegradable drug composition comprises a triblock copolymer containing a polyester and a polyethylene glycol and a diblock copolymer containing a polyester and an end-capped polyethylene glycol, as well as at least one pharmaceutically active principle is disclosed.	WO2017085561	Process	Medincell	Yes	MPP search

Patent status

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

Patent status/countries	Low, Low- middle and upper-middle	High income
Filed	Albania, Serbia, Türkiye, North Macedonia	Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, San Marino, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, United States of America
Not in force	World Intellectual Property Organization (WIPO), Morocco, Bosnia and Herzegovina, Montenegro, Moldova, Republic of	World Intellectual Property Organization (WIPO), United States of America

MPP Licence(s)

MPP/MedinCell licence on a long-acting formulation of ivermectin developed using BEPO® technology

https://medicinespatentpool.org/licence-post/long-acting-technology-for-malaria-vector-control

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Biodegradable drug delivery composition comprising triblock polymer and diblock polymer Expiry date: 2033-06-27 A biodegradable drug delivery compositions comprising a triblock copolymer containing a polyester and a polyethylene glycol and a diblock copolymer containing a polyester and an end-capped polyethylene glycol, as well as at least one pharmaceutically active principle or hydrophobic active principle such as medroxyprogesterone acetate, levonorgestrel, cyclosporine, progesterone or bupivacaine is disclosed.	WO2014001904	Composition	Medincell	Yes	MPP source

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Brazil, China, Kazakhstan, Montenegro, India, Mexico, Tunisia, Ukraine, South Africa, Indonesia, Malaysia, Viet Nam	Australia, Canada, Chile, Russian Federation, Liechtenstein, Italy, United Kingdom, Hungary, Switzerland, Spain, Cyprus, France, Germany, Hong Kong, Israel, Japan, Korea, Republic of, Singapore, Brunei Darussalam
Filed	Algeria, Nigeria	United Arab Emirates, Qatar

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Colombia, Costa Rica, Cuba, Tajikistan, Belarus, Azerbaijan, Turkmenistan, Armenia, Kyrgyzstan, Albania, Serbia, Bosnia and Herzegovina, Türkiye, North Macedonia, Morocco, Egypt, Thailand	World Intellectual Property Organization (WIPO), Norway, Malta, Denmark, Belgium, Greece, Netherlands, Croatia, San Marino, Slovenia, Austria, Romania, Iceland, Finland, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, United States of America, New Zealand

MPP Licence(s)

MPP/MedinCell licence on a long-acting formulation of ivermectin developed using BEPO® technology

https://medicinespatentpool.org/licence-post/long-acting-technology-for-malaria-vector-control

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Biodegradable drug delivery composition covering BEPO® technology Expiry date: 2031-12-29 A biodegradable drug delivery compositions comprising a triblock copolymer containing a polyester and a polyethylene glycol and a diblock copolymer containing a polyester and an end-capped polyethylene glycol, as well as a pharmaceutically active principle is disclosed.	WO2012090070		Medincell	Yes	Company

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Brazil, China, Kazakhstan, Türkiye, Mexico, Malaysia, Ukraine, South Africa, India, Indonesia, Viet Nam	Australia, Canada, Chile, Russian Federation, Liechtenstein, Italy, Norway, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Sweden, Israel, Japan, Korea, Republic of, New Zealand, Singapore, United States of America, Hong Kong
Filed	Thailand	United States of America

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Colombia, Cuba, Tajikistan, Belarus, Azerbaijan, Moldova, Republic of, Turkmenistan, Armenia, Kyrgyzstan, Albania, Serbia, Bosnia and Herzegovina, Montenegro, Türkiye, North Macedonia, Morocco, Tunisia, Algeria, Costa Rica, Egypt, Nigeria	World Intellectual Property Organization (WIPO), Liechtenstein, Norway, Malta, Denmark, Belgium, Greece, Hungary, Croatia, Switzerland, San Marino, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, Bulgaria, Slovakia, Latvia, Ireland, Estonia, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, United States of America, United Arab Emirates, Qatar, Brunei Darussalam

MPP Licence(s)

MPP/MedinCell licence on a long-acting formulation of ivermectin developed using BEPO® technology

https://medicinespatentpool.org/licence-post/long-acting-technology-for-malaria-vector-control

Supporting material

Publications

** BEPO®: Bioresorbable diblock mPEG-PDLLA and triblock PDLLA-PEG-PDLLA based in situ forming depots with flexible drug delivery kinetics modulation, Journal of Controlled Release, Volume 319, 2020, Pages 416-427 Christophe Roberge, Jean-Manuel Cros, Juliette Serindoux, Marie-Emérentienne Cagnon, Rémi Samuel, Tjasa Vrlinic, Pierre Berto, Anthony Rech, Joël Richard, Adolfo Lopez-Noriega
 **

This article presents BEPO®, an in situ forming depot (ISFD) technology mediated by a solvent-exchange mechanism. The matrix of the in situformed drug delivery depot is composed of the combination of a diblock (DB) and a triblock (TB) polyethylene glycol-polyester copolymer. This combination offers a broad capability to tune the release of a wide variety of drugs to the desired pharmacokinetics. The work described in the present article demonstrates that the delivery rate and profile can be adjusted by changing the composition of either TB or DB or the relative ratio between them, among other parameters. It has been shown that the polymeric composition of the formulation has a substantial impact on the solvent exchange rate between the organic solvent and the surrounding aqueous medium which subsequently determines the internal structure of the resulting depot and the delivery of the therapeutic cargo. This has been demonstrated studying the in vitro release of two model molecules: bupivacaine and ivermectin.

Formulations releasing these drugs have been administered to animal models to show the possibility of delivering therapeutics from weeks to months by using BEPO® technology.

** In Vitro and In Vivo Hydrolytic Degradation Behaviors of a Drug-Delivery System Based on the Blend of PEG and PLA Copolymers , Feifei Ng, Victor Nicoulin, Charlotte Peloso, Silvio**

**Curia, Joël Richard, and Adolfo Lopez-Noriega , ACS Applied Materials & Interfaces 2023 15 (48), 55495-55509 , DOI: 10.1021/acsami.2c13141 **

This paper presents the in vitro and in vivo degradation of BEPO, a marketed in situ forming depot technology used for the formulation of long-acting injectables. BEPO is composed of a solution of a blend of poly(ethylene glycol)-block-poly(lactic acid) (PEG–PLA) triblock and diblock in an organic solvent, where a therapeutic agent may be dissolved or suspended. Upon contact with an aqueous environment, the solvent diffuses and the polymers precipitate, entrapping the drug and forming a reservoir. Two representative BEPO compositions were subjected to a 3-month degradation study in vitro by immersion in phosphate-buffered saline at 37 °C and in vivo after subcutaneous injection in minipig. The material erosion rate, as a surrogate of the bioresorption, determined via the depot weight loss, changed substantially, depending on the composition and content of polymers within the test item. The swelling properties and internal morphology of depots were shown to be highly dependent on the solvent exchange rate during the precipitation step. Thermal analyses displayed an increase of the depot glass transition temperature over the degradation process, with no crystallinity observed at any stage. The chemical composition of degraded depots was determined by 1H NMR and gel permeation chromatography and demonstrated an enrichment in homopolymers, i.e., free PLA and (m)PEG, to the detriment of (m)PEG–PLA copolymers in both formulations. It was observed that the relative ratio of the degradants within the depot is driven by the initial polymer composition. Interestingly, in vitro and in vivo results showed very good qualitative consistency. Taken together, the outcomes from this study demonstrate that the different hydrolytic degradation behaviors of the BEPO compositions can be tuned by adjusting the polymer composition of the formulation.

** Evaluating the in vivo stability of water-soluble PEG-PLA copolymers using FRET imaging,Reactive and Functional Polymers, Sophie Bou, Feifei Ng, Elise Guegain, Charlotte Peloso, Adolfo Lopez-Noriega, Mayeul Collot,Volume 187,2023,105579,ISSN**

1381-5148, https://doi.org/10.1016/j.reactfunctpolym.2023.105579.</p>

Biodegradable and biocompatible polymer materials with tunable physical properties present a great interest for controlled drug delivery applications. A good example is BEPO®, a clinical-stage in situ-forming depot technology based on the utilization of a blend of poly(ethylene glycol)-b-poly(D,L-lactic acid) (PEG-PLA) diblock and triblock amphiphilic copolymers dissolved in an organic solvent. Once injected, this technology will form a bioresorbable solid polymer depot that will allow the release of a drug from weeks to months. The safety of the final degradation products from this technology, i.e., PEG and lactic acid, is well-documented. However, little information exists about the fate of intermediate degradants, specifically of water-soluble PEG-PLA chains where the molecular weights of the PLA block are short. Herein, we designed a Förster Resonance Energy Transfer (FRET) system for short copolymers, suitable for longitudinal in vivo imaging in the subcutaneous space, allowing to follow the stability of these products. Our results confirm that these species, that might be leaked from BEPO® depots during degradation, are rapidly hydrolyzed in the subcutaneous space of mice, forming approved products by Health Authorities, i.e., PEG and PLA homopolymers and/or lactic acid.

Additional documents

No documents were uploaded

Useful links

- Video presenting BEPO technology
- Teva and Medincell report positive data for TEV-‘749 in schizophrenia trial
- Teva and Medincell Announce Positive Phase 3 Efficacy Results from SOLARIS Trial Evaluating TEV-‘749
- Teva & MedinCell Announce FDA Acceptance of New Drug Application for TV-46000/mdc-IRM as treatment

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

More information available at : https://www.medincell.com/en/

Illustrations

To be determined

To be determined