LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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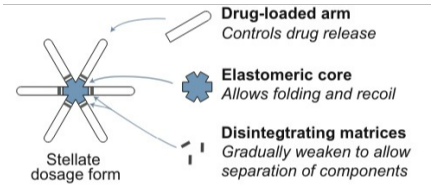


LYNX

Based on public information

Developer(s)

Lyndra Therapeutics

https://lyndra.com/

United States of America

In 2015, Lyndra Therapeutics was founded by Robert Langer to create a pipeline of long-acting drugs. Since its creation, Lyndra has made significant progress, developing 25 medicines in the lab, finishing 12 clinical studies, and establishing a proof of concept for weekly oral dosing in 5 therapeutic areas, all of which validate the viability of its platform with various APIs.

Sponsor(s)

No sponsor indicated

Partnerships

National Institute of Health

https://www.nih.gov

Bill & Melinda Gates Foundation

https://www.gatesfoundation.org

Gilead Sciences, Inc.

https://www.gilead.com

Abbvie Pharmaceuticals

https://www.abbvie.co.uk

Technology information

Type of technology

Oral solid form

Administration route

Oral

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Risperidone

Development Stage

Phase III

Regulatory Approval

IND application was approved for LYN-005 by US FDA on 2020

Description

Lynx is an oral drug delivery system that releases the API slowly over time. It has the potential to decrease the number of times a drug needs to be taken from once a day to once a week. This system consists of a standard size capsule (00EL) with a core elastomer and six drug arms folded inside like a stellate. When the capsule dissolves, this stellate structure extends and lodges in the stomach for a week. It is gastric-resistant system which contains a carrier polymer component linked with one or more coupling polymers. This polymer is responsible for the extended release of the API.

Technology highlight

• LYNX consists of a central core attached with six polymer arms . • Each arm contains a concentrated amount of the API. • The capsule is coated with a proprietary material. • This coating makes it easy to swallow and ensures the capsule remains intact in the oesophagus, preventing premature drug release. • The elastomer material used in the arms of LYNX is porous. • This porosity allows for a slow and steady release of the drug into the system. • As a result, the therapeutic concentration of the API is maintained in the plasma for an extended period. • Thus, LYNX helps reduce the peaks and troughs in drug plasma levels. • The arms are connected to the core using biodegradable linkers. • Once the drug release is complete, these linkers soften and disintegrates.

Technology main components

(i) Carrier polymer (eg: polycaprolactone, polyanhydrides, polyphosphazenes, and polycyanoacrylates); (ii) API; (iii) Release enhancer; (iv) Dispersant (eg: carboxymethylcellulose, hypromellose, magnesium aluminum silicate, CABOSIL M-5P); (v) Solubilizer; (vi) Stabilizer (vii) Capsule coating (eg: Eudragit RS, Dichloromethane)

Information on the raw materials sourcing, availability and anticipated price

Not provided

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Not provided

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

50wt%

API co-administration

Not provided

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

In terms of scale up prospective, Lyndra has begun ramping up new manufacturing operations in Lexington, Massachusetts. The plant began producing materials in April in preparation for the company's Phase II clinical trials, which are slated to begin later this year. In order to meet the demands of both upcoming and ongoing clinical studies as well as potential commercialization, Lyndra keeps growing its manufacturing capacity.

Tentative equipment list for manufacturing

Haake MiniCTW, Twin-screw extruders, triangular cross-section rods, coating pan and dip coater.

Manufacturing

• Initially, three 1-kg batches of a matrix formulation were produced and characterized for performance and stability. • Blends of drug, polymer, and excipients blended by continuous twin screw compounding at 500 g/h. • Blends are formed into triangular cross-section rods and cut to length to form drug arms. • Analysis showed good uniformity in both intra-batch and inter-batch. • The prepared formulation is dip-coated, assembled into stellate dosage forms, and analysed for storage stability.

Specific analytical instrument required for characterization of formulation

HPLC with precolumn derivatization, NMR, X-ray diffraction and UV spectroscopy.

Clinical trials

LYN-014-C-101

Identifier

NCT05251376

Link

https://clinicaltrials.gov/study/NCT05251376

Phase

Phase I

Status

Withdrawn

Sponsor

Lyndra Inc.

More details

A Phase 1, Single Dose, Open-label, Safety, Tolerability, and Pharmacokinetic Study of LYN-014 in Individuals with Opioid Use Disorder Who are Stable on Methadone Therapy

Purpose

Study of LYN-014 in Individuals With Opioid Use Disorder Who Are Stable on Methadone Therapy

Interventions

Intervention 1

Levomethadone HCl

Intervention 2

Methadone

Intervention 3

Morphine Sulfate

Intervention 4

x-ray

Intervention 5

blood tests

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-02-28

Anticipated Date of Last Follow-up

2023-01-17

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2022-12-19

Actual Completion Date

2022-12-19

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: To be eligible to participate in the study, individuals must meet all the following inclusion criteria at Screening (and at other timepoints, where specified): Male or female aged ≥18 and ≤59 years. Body mass index of ≥18 kg/m2 and ≤33 kg/m2. Moderate or severe OUD according to the DSM-5 criteria. Clinically stable (for at least 6 months) on oral daily methadone therapy at a dose of 80 to 100 mg and have been taking the same dose for at least 3 months, and are stably engaged in a methadone program, confirmed by a methadone provider and defined as (1) demonstrates evidence of regular attendance, (2) has not had problems with missed visits, and (3) consistently demonstrates drug-negative urine samples (except for cannabis). Agree to provide the study site with contact

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

Not provided

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Tablet

Studied route(s) of administration

Oral

Use case

Treatment

Key results

Not provided

LYN-163-C-101

Identifier

ACTRN12621001218886

Link

https://anzctr.org.au/Trial/Registration/TrialReview.aspx?id=381955&isReview=true

Phase

Phase I

Status

Not provided

Sponsor

Lyndra Therapeutics, Inc

More details

This single ascending dose study will evaluate the safety, tolerability, pharmacokinetics (PK) of LYN-163in healthy individuals. The PK of ivermectin will be assessed. Data from this study will be a key indicator of feasibility of the product concept and will inform formulation optimization and dose selection for further development. This study will enroll individuals who are in good health. Healthy volunteers are most suitable for providing the initial characterization of the LYN-163safety and PK profile after a single dose.

Purpose

Prevention

Interventions

Intervention 1

Ivermectin 28mg

Intervention 2

Ivermectin 56mg

Countries

Australia

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2021-10-15

Actual Start Date

2022-05-26

Anticipated Date of Last Follow-up

2023-11-16

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2023-04-15

Actual Primary Completion Date

2023-02-14

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Adolescents

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Not provided

Health status

Not provided

Other health status: Malaria

Study type

Interventional (clinical trial)

Enrollment

15

Allocation

Not provided

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Tablet

Studied route(s) of administration

Not provided

Use case

Treatment

Key results

Not provided

LYN 005-C-301

Identifier

NCT05779241

Link

https://clinicaltrials.gov/study/NCT05779241

Phase

Phase III

Status

Completed

Sponsor

Lyndra Inc.

More details

Lyndra Therapeutics, Inc. is developing LYN-005, a long-acting oral (LAO) capsule (LYNX™ dosage form) of risperidone. This pivotal study (LYN-005-C-301) will evaluate the PK as well as safety and tolerability of multiple administrations of the LYN-005 formulation at two dose levels.

Purpose

Study to Evaluate the Pharmacokinetics (PK) and Safety/Tolerability of Long-Acting Oral LYN-005

Interventions

Intervention 1

LYN-005

Intervention 2

Risperidone immediate release (IR)

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-04-13

Anticipated Date of Last Follow-up

2024-03-11

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2023-11-03

Actual Completion Date

2023-12-01

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: 1. Male or female aged ≥18 and ≤64 years. 2. Current diagnosis of schizophrenia or schizoaffective disorder according to Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria as confirmed by the Mini International Neuropsychiatric Interview for Psychotic Disorder Studies (MINI) version 7.0.2. 3. The following psychiatric criteria are to be used to determine participant eligibility: 1. Duration of diagnosis of schizophrenia or schizoaffective disorder of ≥2 years. 2. Outpatient; not hospitalized for worsening of schizophrenia within the last 6 months (partial hospitalization for social management within this time period is acceptable). 3. Medically stable over the last month and psychiatrically stable without significant symptom exacerbation o

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

83

Allocation

Non-randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Tablet

Studied route(s) of administration

Not provided

Use case

Treatment

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

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Biodegradable
- Drug-eluting
- Room temperature storage
- At least 1 year shelf life

Release properties

• The LYNX gastric residence system can release the API for a cumulative four to ten days, achieving near-zero-order drug release over a week. • The release characteristics are mainly based on the eudragit & dichloromethane-coated polymer matrix, which tends to release the API linearly over the first 24h once the surface drug is dissolved. • The dispersant added to the formulation also controls the initial burst release and maintains the percentage of drug release over a week. In addition to that, burst release and release rate can be modified by using varied concentrations of dispersants.

Injectability

Not applicable

Safety

Interim analysis of ongoing clinical trials of LYN-005 (Oral Weekly Risperidone) shows positive results based on the PANSS score in schizophrenia. LYNN-005 is generally safe and well-tolerated.

Stability

LYNX gastric resistance system has an extended shelf life of three years

Storage conditions and cold-chain related features

LYN-005 is meant to be stored at 15–25 °C. The capsules are to be handled carefully to avoid squeezing or crushing.

Potential application(s)

Therapeutic area(s)

Malaria

Contraception

Other(s) : "Hyperlipidaemia and Pain Management"

HIV

Substance use disorders

Mental health

Use case(s)

Treatment

Use of technology

Ease of administration

- Self-administered

Frequency of administration

Weekly, Monthly

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

- All

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Yes

Comment

Not provided

Potential associated API(s)

Risperidone

Class(es)

Antipsychotic

Development stage

Phase III

Clinical trial number(s)

NCT04567524

Foreseen/approved indication(s)

Antipsychotic

Foreseen user group

Not provided

Foreseen duration between application(s)

Once weekly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

IND application was approved for LYN-005 by US FDA on 2020

rosuvastatin

Class(es)

HMG-CoA reductase inhibitor

Development stage

Phase I

Clinical trial number(s)

ACTRN12621000101886

Foreseen/approved indication(s)

Hyperlipidemia

Foreseen user group

Not provided

Foreseen duration between application(s)

Once weekly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

levomethadone

Class(es)

Drug Abuse

Development stage

Phase I

Clinical trial number(s)

NCT05251376

Foreseen/approved indication(s)

Opioid Use Disorder

Foreseen user group

Not provided

Foreseen duration between application(s)

Once weekly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Received IND on May 2021 and Fast Track designation from FDA

Ivermectin

Class(es)

Antimalarial

Development stage

Phase I

Clinical trial number(s)

ACTRN12621001218886

Foreseen/approved indication(s)

Malaria infection

Foreseen user group

Not provided

Foreseen duration between application(s)

Once every two weeks

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

memantine

Class(es)

NMDAR antagonist

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Alzheimer's disease

Foreseen user group

Not provided

Foreseen duration between application(s)

Once weekly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Dolutegravir (DTG)

Class(es)

HIV integrase inhibitor

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV

Foreseen user group

Not provided

Foreseen duration between application(s)

Once a week

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Rilpivirine (RPV)

Class(es)

Non-nucleoside reverse transcriptase inhibitors

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV

Foreseen user group

Not provided

Foreseen duration between application(s)

Once a week

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Cabotegravir (CAB)

Class(es)

HIV integrase inhibitors

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV

Foreseen user group

Not provided

Foreseen duration between application(s)

Once a week

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Opioids

Class(es)

Narcotic analgesic

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Pain Management

Foreseen user group

Not provided

Foreseen duration between application(s)

Once a week

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

naloxone

Class(es)

Drug Abuse

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Opioid dependence

Foreseen user group

Not provided

Foreseen duration between application(s)

Once a week

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Gastric Residence Systems with Release rate-modulating Films

Brief description

The gastric resistance system relates to systems which remain in the stomach for extended period for sustained release of pharmaceutics and methods of use thereof.

Representative patent

WO2018227147

Category

formulation

Patent holder

Lyndra Therapeutics

Exclusivity

Not provided

Expiration date

June 8, 2038

Status

Not provided

Description

Gastric Residence Systems for Sustained Release of Therapeutics Agents and Methods of use thereof

Brief description

Gastric residence systems comprise therapeutic agent formulations for sustained gastric release of therapeutic agents as well as methods for using such systems. The systems are by using a dispersant in the formulations, which improves the burst release characteristics and long-term release rate characteristics of the systems. Milling of the therapeutic agent can be performed to prepare agent particles of the desired size.

Representative patent

US11576859

Category

formulation

Patent holder

Lyndra Therapeutics

Exclusivity

Not provided

Expiration date

October 21, 2036

Status

Not provided

Supporting material

Publications

** Kanasty, R., Low, S., Bhise, N., Yang, J., Peeke, E., Schwarz, M., ... & Bellinger, A. M. (2019). A pharmaceutical answer to nonadherence: Once weekly oral memantine for Alzheimer's disease. Journal of controlled release, 303, 34-41. https://doi.org/10.1016/j.jconrel.2019.03.022 **

The formulation of memantine hydrochloride is the first oral dosage form to achieve sustained drug release for a week with near zero-order kinetics and efficient delivery. In the dog model, relative memantine bioavailability approaches 100%, with sustained plasma levels over seven days. A single gastric resistant dosage form achieves an AUC equivalent to seven daily treatments with the marketed daily capsule, with a Cmax no higher than the daily product. This formulation methodology is applicable to many water-soluble drugs and may enable the development of long-acting oral therapies for various conditions.

** Kirtane AR, Abouzid O, Minahan D, Bensel T, Hill AL, Selinger C, Bershteyn A, Craig M, Mo SS, Mazdiyasni H, Cleveland C, Rogner J, Lee YL, Booth L, Javid F, Wu SJ, Grant T, Bellinger AM, Nikolic B, Hayward A, Wood L, Eckhoff PA, Nowak MA, Langer R, Traverso G. Development of an oral once-weekly drug delivery system for HIV antiretroviral therapy. Nat Commun. 2018 Jan 9;9(1):2. doi: 10.1038/s41467-017-02294-6. **

The efficacy of antiretroviral therapy is significantly compromised by medication non-

adherence. Long-acting enteral systems that can ease the burden of daily adherence have not yet been developed. Here we describe an oral dosage form composed of distinct drug-polymer matrices which achieved week-long systemic drug levels of the antiretrovirals dolutegravir, rilpivirine and cabotegravir in a pig. Simulations of viral dynamics and patient adherence patterns indicate that such systems would significantly reduce therapeutic failures and epidemiological modelling suggests that using such an intervention prophylactically could avert hundreds of thousands of new HIV cases. In sum, weekly administration of long-acting antiretrovirals via a novel oral dosage form is a promising intervention to help control the HIV epidemic worldwide.

** Foltin, R. W., Zale, S., Sykes, K. A., Nagaraj, N., Scranton, R. E., & Comer, S. D. (2022). A novel long-acting formulation of oral buprenorphine/naloxone produces prolonged decreases in fentanyl self-administration by rhesus monkeys. Drug and alcohol dependence, 239, 109599. https://doi.org/10.1016/j.drugalcdep.2022.109599 **

We evaluated the efficacy of this formulation in reducing intravenous (i.v.) fentanyl self-administration by three male and three female rhesus monkeys. Buprenorphine HCl and naloxone HCl were co-formulated using an 11:1 ratio of buprenorphine:naloxone in a controlled-release gastric residence formulation administered in an oral capsule (LYN-013). Naloxone was included to determine the feasibility of combining naloxone with buprenorphine in the formulation as an abuse deterrent. Complete fentanyl dose-response functions were determined during each session. The efficacy of single doses of 56/5, 112/10 and 168/15 mg buprenorphine/naloxone in reducing fentanyl self-administration was examined over 13 days. LYN-013 significantly decreased the rate of responding for fentanyl for 3 days and significantly reduced total intake of fentanyl for 8 days. Time to maximal buprenorphine levels (Tmax) ranged between 56 and 68 h for all 3 doses. The maximal buprenorphine level (Cmax) following 168 mg was 2.3 ng/ml which was significantly greater that those observed for 56 mg (1.22 ng/ml) and 112 mg (1.35 ng/ml). Finally,

the area-under-curves (AUCtau) were buprenorphine dose-dependently increased from 88 to 127-265 h*ng/ml. There were no signs of non-specific changes in behavior.

Additional documents

No documents were uploaded

Useful links

There are no additional links

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

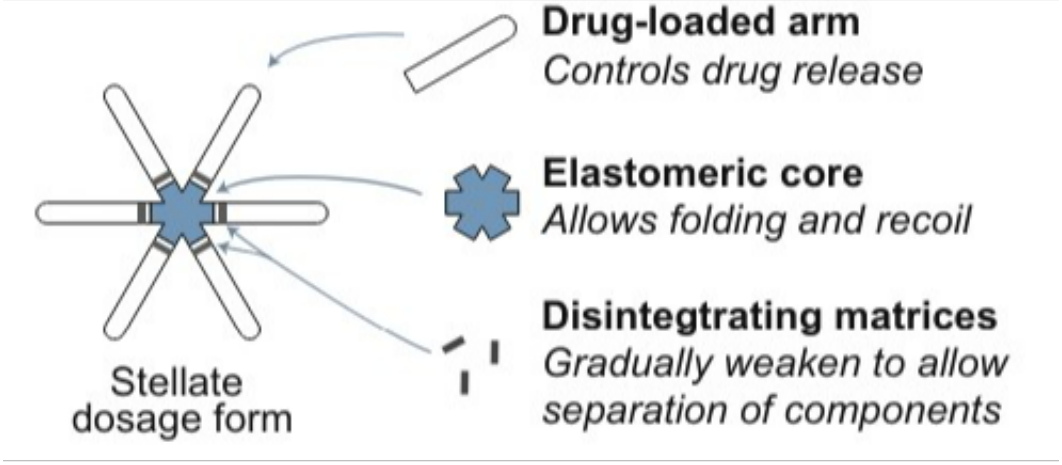
Work with MPP to expand access in LMICs

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



Drug-loaded arms control drug release, flexible elastomeric cores allow folding into a capsule and deployment in the stomach, disintegrating matrices control breakdown and passage out of the stomach

Kanasty, R., Low, S., Bhise, N., Yang, J., Peeke, E., Schwarz, M., ... & Bellinger, A. M. (2019). A pharmaceutical answer to nonadherence: Once weekly oral memantine for Alzheimer's disease.