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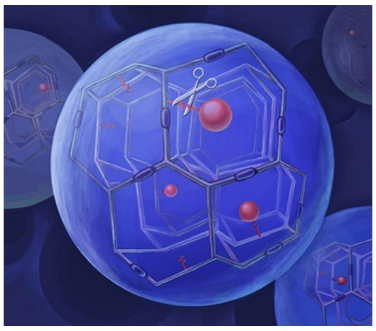


Hydrogel Microspheres with ?-eliminative Linker Technology

Based on public information

Developer(s)

ProLync, Inc.

Originator

https://prolynxinc.com

United States

ProLynx is a biotechnology company that specializes in developing long-acting drug delivery systems. Their technology involves attaching therapeutic agents to proprietary linkers that degrade at a controlled rate, allowing for the sustained release of drugs over extended periods. This approach is designed to reduce the frequency of dosing and improve patient compliance.

Sponsor(s)

No sponsor indicated

Partnerships

Daiichi Sankyo

https://www.daiichisankyo.com/

Bayer HealthCare LLC

https://www.bayer.com/en/

GlaxoSmithKline

https://www.gsk.com/

Technology information

Type of technology

Polymer-based particles, PEGylated hydrogel and beta-eliminative cross-linker

Administration route

Subcutaneous, Intravenous, Intratumoral

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Topoisomerase 1 inhibitors (TOP1i)

Development Stage

Phase II

Regulatory Approval

Not provided

Description

ProLynx's platform leverages custom-synthesized chemical linkers to conjugate therapeutic molecules to carrier systems, thereby enabling controlled and sustained drug release. The biodegradable nature of these linkers, which degrade at predefined rates determined by their molecular architecture, facilitates predictable and prolonged therapeutic efficacy. This technology is versatile, accommodating a broad spectrum of therapeutic modalities, including small molecules, peptides, and proteins.

Technology highlight

1) Drug release in the Prolynx formulation is mediated by β-eliminative linkers, which undergo a rate-controlled elimination reaction. 2) Each linker within the library incorporates a unique “modulator” that independently regulates the drug release kinetics, irrespective of enzymatic influence. 3) The carrier system is composed of circulating macromolecules, such as polyethylene glycol (PEG), fabricated into 40 µm porous PEG-hydrogel microspheres. 4) To synchronize drug release with the degradation of the polymeric matrix, slower-cleaving linkers are integrated into the hydrogel crosslinks.

Technology main components

1) One or more API 2) Cross linker - it has a functional group that reacts with the reactive polymer and a moiety that cleaves by elimination under physiological conditions also comprising a functional group that reacts with one or more polymers. 3) PEGlated hydrogel microspheres 4) Gel-forming solvent (eg: water, alcohols, acetonitrile, or tetrahydrofuran)

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

Not provided

API co-administration

Not provided

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

A large-scale aseptic manufacturing of injectable microsphere is proposed. This unit is capable of preparing up to ~2 L of high-quality 50 µm diameter hydrogel microspheres/day.

Tentative equipment list for manufacturing

• Reflux Condensers • Magnetic Stirrer • Centrifuge • Filtration Equipment (vacuum filters) • Rotary Evaporator • pH Meter • Oven or Drying Chamber • Cryogenic Freezer

Manufacturing

Manufacturing process requires ISO Class 5 or 7 environment. The manufacturing process includes: • Reflux Apparatus - Crosslinking of Polymers and Incorporation of Drugs • Filtration and Centrifugation Equipment • Spectroscopic Instruments

Specific analytical instrument required for characterization of formulation

• Size Exclusion Chromatography (SEC) • Dynamic Light Scattering (DLS) • Mechanical Testing

Clinical trials

D15-11073

Identifier

NCT02646852

Link

https://clinicaltrials.gov/study/NCT02646852

Phase

Phase I

Status

Completed

Sponsor

ProLynx LLC

More details

This is a Phase I, open-label, two-arm, dose escalation study of PLX038 intravenous infusion administered to patients with refractory or relapsed solid tumors. This study will explore two different dosing schedules: Arm 1, once every 3 week (q3w), and Arm 2, once weekly for 2 consecutive weeks of a 4-week cycle.

Purpose

A Phase I Study of PLX038 in Patients With Advanced Solid Tumors

Interventions

Intervention 1

PLX038

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-03-01

Anticipated Date of Last Follow-up

2023-07-11

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2023-02-01

Actual Completion Date

2023-07-01

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Patients must have histologically (or cytologically)-confirmed diagnosis of solid tumor, refractory after standard therapy for the disease or for which conventional systemic therapy is not reliably effective or no effective therapy is available. * Aged ≥ 18 years. * ECOG Performance Status of 0 or 1. * Adequate clinical laboratory values defined as: * absolute neutrophil count ≥ 1.5 × 10\^9/L * platelets ≥ 100 × 10\^9/L * hemoglobin ≥ 9.0 g/dL (transfusions permissible) * plasma creatinine ≤ 1.5 × upper limit of normal (ULN) for the institution or calculated clearance ≥ 60 mL/min (Cockcroft-Gault formula) * bilirubin ≤ 1.5 × ULN * alanine transaminase (ALT) and aspartate transaminase (AST) \< 2.5 × ULN (\< 5 x ULN if documented hepatic metastases)

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

40

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "Once every 2 weeks and every 3 weeks "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intravenous

Use case

Treatment

Key resources

Not provided

TOPOLOGY

Identifier

NCT06162351

Link

https://clinicaltrials.gov/study/NCT06162351

Phase

Phase II

Status

Recruiting

Sponsor

Institut Curie

More details

Single arm phase II study for with primary objective to evaluate the efficacy of PLX038 on response rate for patients with pretreated, metastatic or locally advanced triple negative breast cancer.

Purpose

A Study to Evaluate the Efficacy and Toxicities of PLX038, in Patients With Locally Advanced or Metastatic Triple-negative Breast Cancer

Interventions

Intervention 1

PLX038

Countries

France

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-04-17

Anticipated Date of Last Follow-up

2024-05-16

Estimated Primary Completion Date

2025-08-19

Estimated Completion Date

2026-03-19

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Willing and able to comply with the protocol and provide written informed consent prior to study-specific screening procedures. * Age ≥ 18 years. * Females and males with cytologically or histologically confirmed breast carcinoma (either the primary or metastatic lesions). * Locally advanced or metastatic disease that is not amenable to curative treatment. * Triple negative breast cancer (both ER and PR \<10%, HER2-negative or HER2-low). * Measurable disease (per RECIST version 1.1). * Prior therapy (administered in the neoadjuvant, adjuvant and/or metastatic setting) with an anthracycline, taxane and sacituzumab-govitecan (unless not medically appropriate or contraindicated for the patient). * Received a minimum of two prior cytotoxic chemotherapy regimens for local

Health status

Not provided
Other health status: Breast carcinoma

Study type

Interventional (clinical trial)

Enrollment

44

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "once every3 weeks "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intravenous

Use case

Treatment

Key resources

Not provided

POP-ART

Identifier

NCT06337630

Link

https://clinicaltrials.gov/study/NCT06337630

Phase

Phase I

Status

Not yet recruiting

Sponsor

Institut Curie

More details

Phase I with a dose finding cohort, followed by expansion cohorts in pre-specified tumor types.

Purpose

A Study on Tuvusertib (Oral ATR Inhibitor) in Combination With PLX038 (Topo1 Inhibitor) in Patients With Advanced Solid Tumors

Interventions

Intervention 1

PLX038 + Tuvusertib

Countries

France

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-06-15

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-03-22

Estimated Primary Completion Date

2025-06-15

Estimated Completion Date

2029-02-15

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Willing and able to comply with the protocol and provide written informed consent prior to study-specific screening procedures. * Age ≥ 18 years. * Locally advanced or metastatic solid cancer that is not amenable to curative treatment. * Measurable disease (per RECIST version 1.1). * Received a minimum of one and a maximum of six prior cytotoxic chemotherapy regimens for locally advanced or metastatic cancer. * Resolution of chemotherapy and radiation therapy related toxicities to NCI-CTCAE version 5.0 Grade 1 or lower severity, except for stable sensory neuropathy (≤ Grade 2), alopecia (any grade), presence of clinically managed chronic autoimmune AEs from prior immune therapy. * Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. * Adequate orga

Health status

Not provided

Other health status: Previously treated advanced or metastatic cancer

Study type

Interventional (clinical trial)

Enrollment

92

Allocation

Not provided

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)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key resources

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
- Non-removable

Release properties

1) Drug release is governed by a rate-controlled β-elimination mechanism. The drug release rate is directly proportional to the degree of ionization at physiological pH 2) The API is covalently linked to the hydrogel matrix via a cleavable linker. 3) Hydrolysis of this linker liberates the API, increasing plasma drug concentration and the half-life of the drug. Various acidity of the functional group added to the API controls the rate of release from the hydrogel. 4) The controlled release profile is attributed to the slower degradation rate of the hydrogel matrix.

Injectability

A 25 to 30-gauge needle is used for subcutaneous injections. Insert the needle at an angle of 45° or 90° depending on the length of the needle and/or depth of the subcutaneous layer.

Safety

Phase II studies of PLX038 show that it is safe and effective in previously treated advanced breast cancer. It is a conjugated active metabolite of Irinotecan.

Stability

The structure and integrity of hydrogel remain stable in physiological conditions of pH and temperature.

Storage conditions and cold-chain related features

Not provided

Potential application(s)

Therapeutic area(s)

Other(s) : "Ocular disorders and achondroplasia"

Pain management

Oncology

Use case(s)

Treatment

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker

Frequency of administration

Monthly, Once every 2 weeks

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults

Genders

- All

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

No

Comment

Not provided

Potential associated API(s)

Exenatide

Class(es)

Antidiabetic

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Diabetes

Foreseen user group

Not provided

Foreseen duration between application(s)

Once a week

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi)

Class(es)

PEG-PARP inhibitor

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Oncology

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Topoisomerase 1 inhibitors (TOP1i)

Class(es)

Antineoplastic agent - Topoisomerase 1 inhibitor

Development stage

Phase II

Clinical trial number(s)

NCT06162351

Foreseen/approved indication(s)

Advanced Breast Cancer

Foreseen user group

Women more than 18 years old who are previously treated with chemotherapy

Foreseen duration between application(s)

Every three weeks

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Interleukin 15 (IL-15)

Class(es)

Immunotherapy

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 but the PK study shows that the t1/2 (half life) is approximately 5 days

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

C-type natriuretic peptides (CNP)

Class(es)

Modified type C natriuretic peptide (CNP) analog

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Achondroplasia

Foreseen user group

Not provided

Foreseen duration between application(s)

Every 2 weeks and once monthly

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Hydrogels with biodegradable crosslinking

Brief description

Hydrogels that degrade under appropriate conditions of pH and temperature by virtue of crosslinking compounds that cleave through an elimination reaction are described. The hydrogels may be used for delivery of various agents, such as pharmaceuticals.

Representative patent

US11454861B2

Category

Formulation

Patent holder

Prolynx LLC

Exclusivity

Not provided

Expiration date

August 30, 2039

Status

Active

Description

Slow-release conjugates of SN-38

Brief description

Conjugates of SN-38 that provide optimal drug release rates and minimize the formation of the corresponding glucuronate are described. The conjugates release SN-38 from a polyethylene glycol through a β-elimination mechanism.

Representative patent

US10342792B2

Category

Not provided

Patent holder

Prolynx LLC

Exclusivity

Not provided

Expiration date

June 14, 2038

Status

Active

Description

Prodrugs and drug-macromolecule conjugates having controlled drug release rates

Brief description

The present invention provides methods and compositions that permit controlled and prolonged drug release in vivo. The compounds are either prodrugs with tunable rates of release, or conjugates of the drug with macromolecules which exhibit tunable controlled rates of release.

Representative patent

US9387254B2

Category

Not provided

Patent holder

Prolynx LLC

Exclusivity

Not provided

Expiration date

March 21, 2034

Status

Active

Description

Conjugates of somatostatin analogues

Brief description

Conjugates of carriers and hydrogels for controlling the biological half-life of somatostatin and its analogs are disclosed.

Representative patent

US10413594B2

Category

Not provided

Patent holder

Prolynx LLC

Exclusivity

Not provided

Expiration date

June 22, 2024

Status

Active

Supporting material

Publications

** Henise, J. et al. A Platform Technology for Ultra-Long Acting Intratumoral Therapy. Sci Reports 14:14000. doi:org/10.1038/s41598-024-64261-8. (2024) **

Intratumoral (IT) therapy is a powerful method of controlling tumor growth, but a major unsolved problem is the rapidity that injected drugs exit tumors, limiting on-target exposure and efcacy. We have developed a generic long acting IT delivery system in which a drug is covalently tethered to hydrogel microspheres (MS) by a cleavable linker; upon injection the conjugate forms a depot that slowly releases the drug and “bathes” the tumor for long periods. We established technology to measure tissue pharmacokinetics and studied MSs attached to SN-38, a topoisomerase 1 inhibitor. When MS~SN-38 was injected locally, tissues showed high levels of SN-38 with a long half-life of ~ 1 week. IT MS~SN-38 was ~ tenfold more efcacious as an anti-tumor agent than systemic SN-38. We also propose and provide an example that long-acting IT therapy might enable safe use of two drugs with overlapping toxicities. Here, long-acting IT MS~SN-38 is delivered with concurrent systemic PARP inhibitor. The tumor is exposed to both drugs whereas other tissues are exposed only to the systemic drug; synergistic anti-tumor activity supported the validity of this approach. We propose use of this approach to increase efcacy and reduce toxicities of combinations of immune checkpoint inhibitors such as αCTLA-4 and αPD-1

** Carreras, C. et al. <a href="https://prolynxinc.com/pdf/Carreras_BC2024.pdf" rel="noopener noreferrer" target="_blank" style="color: rgb(248, 117, 0); background-color:**

**rgb(255, 255, 255);">Long-Acting Poly(ADP-ribose) Polymerase Inhibitor Prodrug for Humans. Bioconjugate Chem 35(4), 551-558. (2024) https://pubs.acs.org/doi/10.1021/acs.bioconjchem.4c00112 **

Poly(ADP-ribose) polymerase inhibitors (PARPi) have been approved for once or twice daily oral use in the treatment of cancers with BRCA defects. However, for some patients, oral administration of PARPi may be impractical or intolerable, and a long-acting injectable formulation is desirable. We recently developed a long-acting PEGylated PARPi prodrug, PEG~talazoparib (TLZ), which suppressed the growth of PARPi-sensitive tumors in mice for very long periods. However, the release rate of TLZ from the conjugate was too fast to be optimal in humans. We prepared several new PEG~TLZ prodrugs having longer half-lives of drug release and accurately measured their pharmacokinetics in the rat. Using the rates of release of TLZ from these prodrugs and the known pharmacokinetics of free TLZ in humans, we simulated the pharmacokinetics of the macromolecular prodrugs and released TLZ in humans. From several possibilities, we chose two conjugates that could be administered intravenously every 2 weeks and maintain TLZ within its known therapeutic window. We describe situations where the PEG~TLZ conjugates would find utility in humans and suggest how the intravenously administered long-acting prodrugs could in fact be more effective than daily oral administration of free TLZ

** Fontaine, S. D., Carreras, C. W., Reid, R. R., Ashley, G. W., & Santi, D. V. (2023). A Very Long-acting Exatecan and Its Synergism with DNA Damage Response Inhibitors. Cancer research communications, 3(5), 908–916. https://doi.org/10.1158/2767-9764.CRC-22-0517 **

Exatecan (Exa) is a very potent inhibitor of topoisomerase I and anticancer agent. It has been intensively studied as a single agent, a large macromolecular conjugate and as the payload component of antigen-dependent antibody–drug conjugates. The current work describes an antigen-independent conjugate of Exa with polyethylene glycol (PEG) that slowly releases free Exa. Exa was conjugated to a 4-arm 40 kDa PEG through a β-eliminative cleavable linker. Pharmacokinetic studies in mice showed that the conjugate has an apparent circulating half-life of 12 hours, which reflects a composite of both the rate of renal elimination (half-life ~18 hours) and release of Exa (half-life ~40 hours). Remarkably, a single low dose of 10 μmol/kg PEG-Exa—only approximately 0.2 μmol/mouse—caused complete suppression of tumor growth of BRCA1-deficient MX-1 xenografts lasting over 40 days. A single low dose of 2.5 μmol/kg PEG-Exa administered with low but efficacious doses of the PARP inhibitor talazoparib showed strong synergy and caused significant tumor regression. Furthermore, the same low, single dose of PEG-Exa administered with the ATR inhibitor VX970 at doses of the DNA damage response inhibitor that do not affect tumor growth show high tumor regression, strong synergy, and synthetic lethality.

** Schneider, E. L., Carreras, C. W., Reid, R., Ashley, G. W., & Santi, D. V. (2022). A long-acting C-natriuretic peptide for achondroplasia. Proceedings of the National Academy of Sciences of the United States of America, 119(30), e2201067119.https://doi.org/10.1073/pnas.2201067119 **

The C-natriuretic peptide (CNP) analog vosoritide has recently been approved for treatment of achondroplasia in children. However, the regimen requires daily subcutaneous injections in pediatric patients over multiple years. The present work sought to develop a long-acting CNP that would provide efficacy equal to or greater than that of vosoritide but require less frequent injections. We used a technology for

half-life extension, whereby a drug is attached to tetra-polyethylene glycol hydrogels (tetra-PEG) by β-eliminative linkers that cleave at predetermined rates. These hydrogels-fabricated as uniform ~60-μm microspheres-are injected subcutaneously, where they serve as a stationary depot to slowly release the drug into the systemic circulation. We prepared a highly active, stable CNP analog-[Gln6,14]CNP-38-composed of the 38 C-terminal amino acids of human CNP-53 containing Asn to Gln substitutions to preclude degradative deamidation. Two microsphere [Gln6,14]CNP-38 conjugates were prepared, with release rates designed to allow once-weekly and once-monthly administration. After subcutaneous injection of the conjugates in mice, [Gln6,14]CNP-38 was slowly released into the systemic circulation and showed biphasic elimination pharmacokinetics with terminal half-lives of ~200 and ~600 h. Both preparations increased growth of mice comparable to or exceeding that produced by daily vosoritide. Simulations of the pharmacokinetics in humans indicated that plasma [Gln6,14]CNP-38 levels should be maintained within a therapeutic window over weekly, biweekly, and likely, monthly dosing intervals. Compared with vosoritide, which requires ~30 injections per month, microsphere [Gln6,14]CNP-38 conjugates-especially the biweekly and monthly dosing-could provide an alternative that would be well accepted by physicians, patients, and patient caregivers.

** Schneider, E. L., Henise, J., Reid, R., Ashley, G. W., & Santi, D. V. (2016). Hydrogel Drug Delivery System Using Self-Cleaving Covalent Linkers for Once-a-Week Administration of Exenatide. Bioconjugate chemistry, 27(5), 1210–1215. https://doi.org/10.1021/acs.bioconjchem.5b00690 **

We have developed a unique long-acting drug-delivery system for the GLP-1 agonist exenatide. The peptide was covalently attached to Tetra-PEG hydrogel microspheres by a cleavable β-eliminative linker; upon s.c. injection, the exenatide is slowly released at a rate dictated by the linker. A second β-eliminative linker with a slower cleavage

rate was incorporated in polymer cross-links to trigger gel degradation after drug release. The uniform 40 μm microspheres were fabricated using a flow-focusing microfluidic device and in situ polymerization within droplets. The exenatide-laden microspheres were injected subcutaneously into the rat, and serum exenatide measured over a one-month period. Pharmacokinetic analysis showed a t1/2,β of released exenatide of about 7 days which represents over a 300-fold half-life extension in the rat and exceeds the half-life of any currently approved long-acting GLP-1 agonist. Hydrogel-exenatide conjugates gave an excellent Level A in vitro-in vivo correlation of release rates of the peptide from the gel, and indicated that exenatide release was 3-fold faster in vivo than in vitro. Pharmacokinetic simulations indicate that the hydrogel-exenatide microspheres should support weekly or biweekly subcutaneous dosing in humans. The rare ability to modify in vivo pharmacokinetics by the chemical nature of the linker indicates that an even longer acting exenatide is feasible.

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

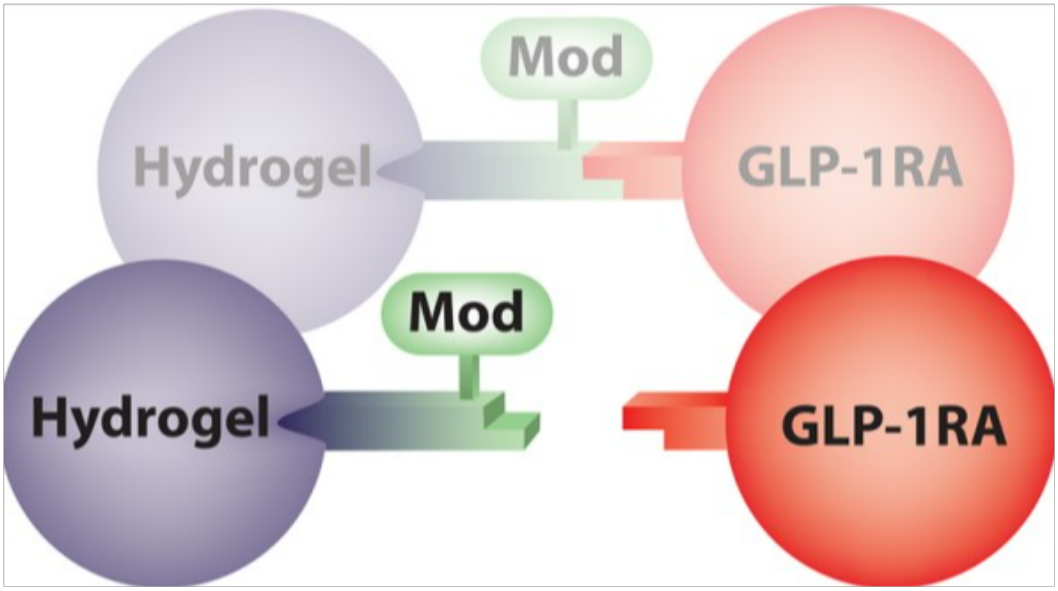
Work with MPP to expand access in LMICs

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

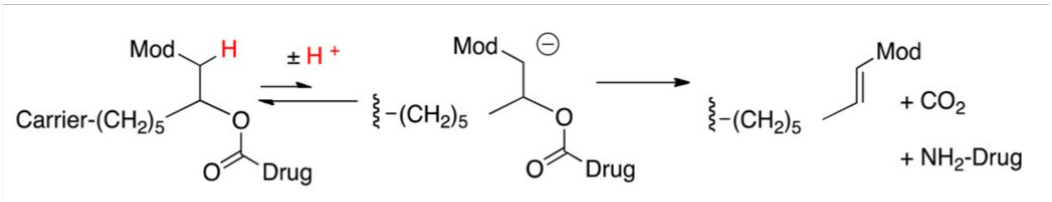
Comment & Information

Illustrations



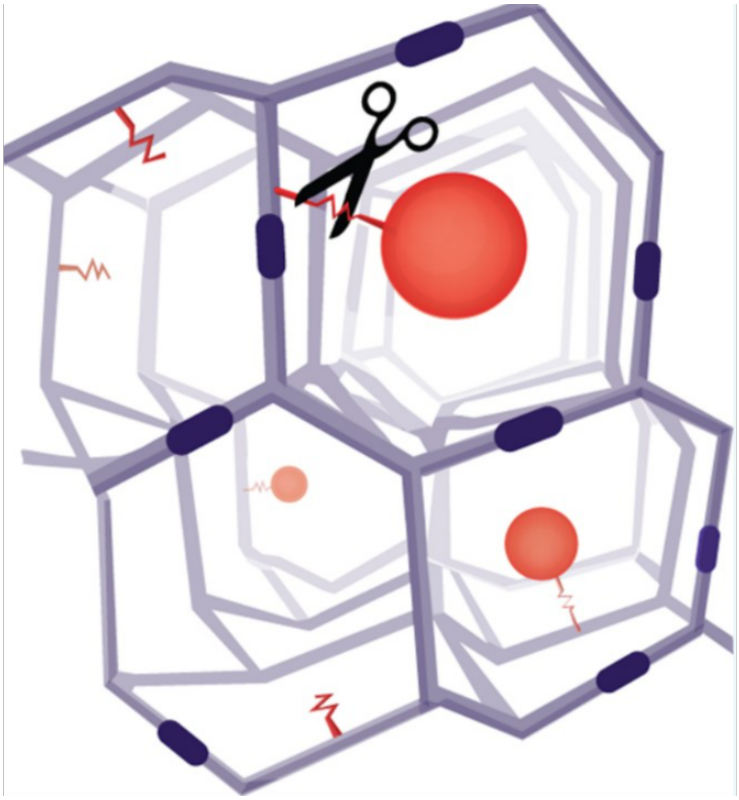
Dissociation of the API from the Hydrogel molecule attached to the cross-linker

ProLynx, Inc. (n.d.). Technology. Retrieved August 16, 2024, from https://www.prolynxinc.com/technology.html



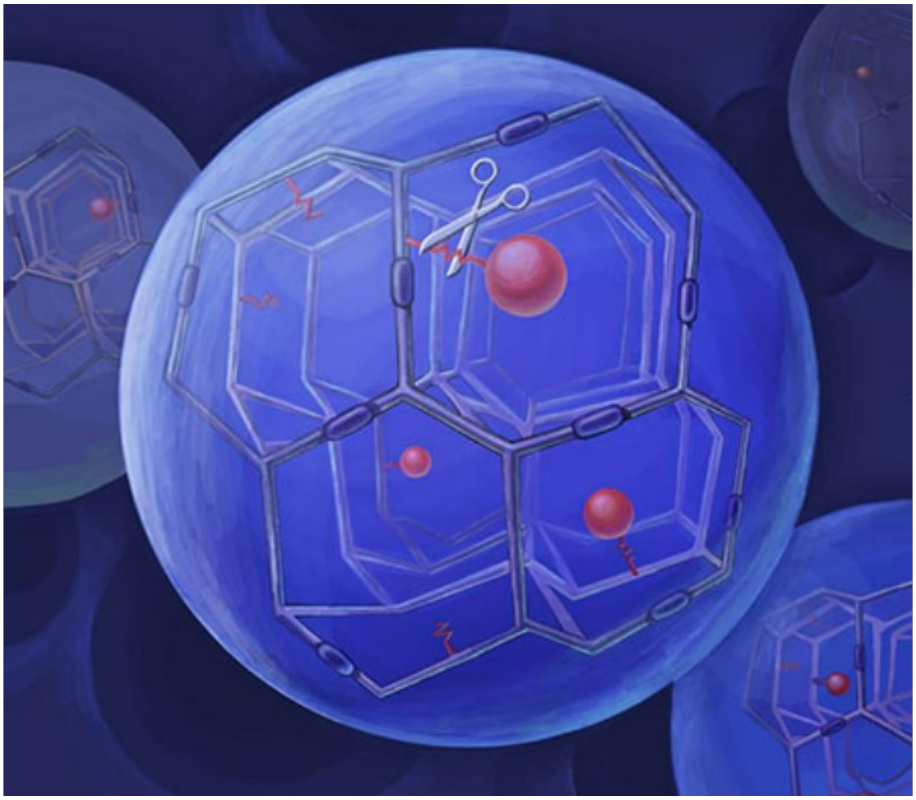
β- elimination of a macromolecular carrier that is attached to a linker that is attached to a drug via a carbamate functional group

Schneider, E. L., Henise, J., Reid, R., Ashley, G. W., & Santi, D. V. (2016). Hydrogel Drug Delivery System Using Self-Cleaving Covalent Linkers for Once-a-Week Administration of Exenatide.



Tetra-PEG hydrogel microspheres by a cleavable β-eliminative linker

Schneider, E. L., Henise, J., Reid, R., Ashley, G. W., & Santi, D. V. (2016). Hydrogel Drug Delivery System Using Self-Cleaving Covalent Linkers for Once-a-Week Administration of Exenatide.



Hydrogel with β- eliminative linker

ProLynx. (n.d.). ProLynx Incorporated. Retrieved August 21, 2024, from https://prolynxinc.com/