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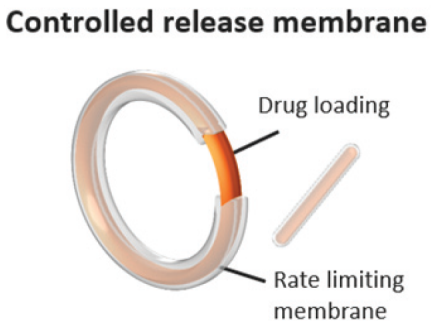


Ethylene Vinyl Acetate Implant (VitalDose®)

Developer(s)

Celanese Corporation

Originator

https://www.celanese.com/

United States of America

Celanese Corporation, formerly known as Hoechst Celanese, is an American technology and specialty materials company headquartered in Irving, Texas. It is one of the leading global producers of high-performance engineered polymers that are used in a variety of high-value applications.

Sponsor(s)

No sponsor indicated

Partnerships

Population Council
https://popcouncil.org/

Bachem, ltd
https://www.bachem.com/

Nanoform Finland Ltd
https://nanoform.com/en/

Glaukos Corporation
https://www.glaukos.com/en-uk/

Alessa Therapeutics, Ltd
https://alessatherapeutics.com/

John Hopkins University
https://www.jhu.edu/

The Gates Foundation
https://www.gatesfoundation.org/

Technology information

Type of technology

Polymeric implant

Administration route

Intratumoral, ocular insert, intrathecal, Subcutaneous, Intra-vitreal, Topical (Vaginal), Transdermal

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

travoprost

Development Stage

Marketed

Regulatory Approval

Approved by USFDA on 14 December 2023 for open-angle glaucoma (OAG) or ocular hypertension (OHT)

Description

VitalDose is a polymer-based microporous long-acting implant for systemic and local drug delivery. It has a high drug-loading capacity and supports small molecules, peptides, monoclonal antibodies, and iRNA therapeutics. The implant maintains plasma concentrations for months to years, depending on the API’s pharmacokinetics. Available in rod, ring, and film configurations, it enables versatile clinical applications.

Technology highlight

1) Contraceptive Sustained Release implant (6 months-5 years) 2) Biodurable design made using hydrophobic polymer 3) Customizable design 4) <70% API loading 5) Zero Order Kinetics 6) Refillable, replaced and retrieved 7) Low off-targeting toxicities 8) 40% vinyl acetate serves as a drug matrix while 18% vinyl acetate forms the rate control membrane

Technology main components

1. Polymer Matrix (30–100 wt%) – Core polymers include poly(lactic-co-glycolic acid), polyolefins, polyvinyl chloride, polycarbonates, polysulfones, styrene-acrylonitrile copolymers, polyurethanes, silicone polyether-urethanes, polycarbonate urethanes, and silicone polycarbonate-urethanes. Example: Ateva 4030AC. 2. Excipients—Radiocontrast agents, hydrophilic compounds, bulking agents, plasticizers, surfactants, crosslinking agents, flow aids, colorizing agents (e.g., chlorophyll, methylene blue), antioxidants, stabilizers, lubricants, antimicrobial agents, and preservatives. 3. Surfactants—One or more nonionic, anionic, and/or amphoteric surfactants. 4. API—Small molecules, proteins, or iRNA therapeutics. 5. Bromelain Powder

Information on the raw materials sourcing, availability and anticipated price

iDose TR 75 mcg intraocular implant is around 13,950 USD/implant

Delivery device(s)

Sterile single-dose Implant inserter

APIs compatibility profile

API desired features

Water-soluble molecules

Water-insoluble molecules

Small molecules

VitalDose EVA implants target specific pharmacological classes, including estrogen hormones, tetracycline antibiotics, and antiviral agents. The platform primarily delivers small molecules acting as allosteric agonists or inhibitors. Therapeutic agents that are used for treating solid tumor, ocular inflammation, glaucoma, psychiatric disorders, and osteoporosis are also targeted for VitalDose EVA implant.

Nucleic acids

Suitable vaccines include whole viral particles, recombinant proteins, subunit proteins (gp41, gp120, gp140), DNA vaccines, plasmids, bacterial vaccines, and polysaccharides such as extracellular capsular polysaccharides, along with other vaccine vectors. Similarly, nucleic acids may include RNA- or DNA-based molecules such as oligonucleotides, aptamers, ribozymes, DNAzymes, and small interfering RNAs (siRNA), including messenger (mRNA), transfer (tRNA), ribosomal (rRNA), and interfering (iRNA) RNAs.

Proteins

Suitable proteins or peptides may include adrenocorticotropic hormone, angiotensin, β-endorphin, bombesin, calcitonin, calcitonin gene-related polypeptide, cholecystokinin-8, colony-stimulating factors, desmopressin, endothelin, enkephalin, erythropoietins, gastrins, glucagon, human atrial natriuretic polypeptide, interferons, insulin, growth factors, growth hormones, luteinizing hormone-releasing hormone, melanocyte-stimulating hormone, muramyl-dipeptide, neurotensin, oxytocin, parathyroid hormone, peptide T, secretin, and somatomedins.

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

50-75 wt%

API co-administration

2 different APIs : Not provided

LogP

Min: -6.9 Max: 5

Scale-up and manufacturing prospects

Scale-up prospects

Celanese produces 60,000 metric tons of vinyl acetate annually at its Nanjing facility and plans to expand production by 10,000 metric tons per year. Additionally, Celanese and Nanoform are collaborating to enhance biologics delivery through small implants using the VitalDose platform. Meanwhile, Celanese and Glaat Pharmaceuticals have partnered on formulation development and and clinical trial setup.

Tentative equipment list for manufacturing

HAAKE™ Rheomix OS Mixers

Manufacturing

Manufacturing Process of EVA Implants (Hot Melt Extrusion(HME) /Fusion Deposition 3D Modeling) i) Mixing Processes (One or more of the following) 1. Melt mixing 2. Extrusion 3. Batch mixing 4. Roll milling ii) Melt Processing Techniques at 210°C (One or more of the following) 1. Compression molding 2. Injection molding (injection phase and holding phase) 3. Blow molding 4. Vacuum forming 5. Calendaring 6. Extrusion 7. Spinning 9. Film formation The API and ground EVA polymer are dry blended and are fed into HME to yield the final product form.

Specific analytical instrument required for characterization of formulation

UV/Vis absorption spectroscopy using Cary 1 split beam instrument

Clinical trials

GC-010

Identifier

NCT03519386

Link

https://clinicaltrials.gov/study/NCT03519386

Phase

Phase III

Status

Completed

Sponsor

Glaukos Corporation

More details

Phase III study to compare the safety and efficacy of intraocular implants containing travoprost at two different elution rates versus Timolol Maleate Ophthalmic Solution, 0.5% (timolol) in reducing elevated intraocular pressure in subjects with open-angle glaucoma (OAG) or ocular hypertension (OHT).

Purpose

Randomized Study Comparing Two Models of a Travoprost Intraocular Implant to Timolol Maleate Ophthalmic Solution, 0.5%

Interventions

Intervention 1

G2-TR intraocular implant containing travoprost

Potential application(s)

travoprost

Intervention 2

Sham surgery + active-comparator eye drops

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-07-26

Anticipated Date of Last Follow-up

2024-11-12

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2022-04-05

Actual Completion Date

2024-04-02

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: * Diagnosed with open-angle glaucoma or ocular hypertension. * C/D ratio ≤ 0.8 * Zero to three preoperative ocular hypotensive medications Exclusion Criteria: * Active corneal inflammation or edema. * Retinal disorders not associated with glaucoma.

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

590

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Not provided

Frequency of administration

Other : "Single Dose "

Studied LA-formulation(s)

Implant

Studied route(s) of administration

Other(s) : "Intraocular "

Use case

Treatment

Key resources

Not provided

IDOS-402-IVIV

Identifier

NCT06582732

Link

https://clinicaltrials.gov/study/NCT06582732

Phase

Phase II

Status

Completed

Sponsor

Glaukos Corporation

More details

To evaluate the performance of the Travoprost Intracameral Implant by determining residual drug in explanted implants of the Travoprost Intracameral Implant and by determining aqueous humor concentrations of travoprost free acid at specified timepoints post administration through 24 months

Purpose

Performance of the Travoprost Intraocular Implant

Interventions

Intervention 1
Travoprost Intracameral Implant exchanged at Month 12
Potential application(s)

travoprost

Intervention 2

Travoprost Intracameral Implant exchanged at Month 3

Potential application(s)

travoprost

Intervention 3

Travoprost Intracameral Implant exchanged at Month 6

Potential application(s)

travoprost

Intervention 4

Travoprost Intracameral Implant exchanged at Month 24

Potential application(s)

travoprost

Intervention 5

Travoprost Intracameral Implant exchanged at Month 21

Potential application(s)

travoprost

Countries

Armenia

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-03-10

Anticipated Date of Last Follow-up

2024-09-19

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2023-11-02

Actual Completion Date

2023-11-02

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: * Diagnosis of either open angle glaucoma (i.e. primary, pseudoexfoliation, or pigmentary glaucoma) or ocular hypertenson * Zero to three

topical intraocular pressure lowering medications at the time of Visit 1 (Screening) exam. * Best spectacle corrected visual acuity of 16 letters or more correctly read at 4 meters or better in each eye. * Open angle as defined by Shaffer grade ≥ 3 at slit-lamp at the planned implantation site Exclusion Criteria: * Traumatic, uveitic, neovascular, or angle-closure glaucoma; or glaucoma associated with vascular disorders * Active ocular inflammation, infection or edema * Clinically significant dystrophy (e.g., bullous keratopathy, Fuch's dystrophy) or clinically significant guttata

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

210

Allocation

Not provided

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "Single Dose "

Studied LA-formulation(s)

Implant

Studied route(s) of administration

Other(s) : "Intraocular "

Use case

Treatment

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
- Monolithic

Release properties

VitalDose is a continuous drug delivery system that releases therapeutic agents from an ethylene vinyl acetate (EVA) membrane at a steady, low-dose rate, with sustained release lasting up to three years. In intratumoral administration, the drug exhibits modified kinetics, allowing for a gradual and controlled release directly into the tumor microenvironment, optimizing therapeutic efficacy while minimizing systemic exposure.

Injectability

VitalDose is a liquid formulation and can be injected using a standard injection device with a standard 21-25 gauge needle or even thinner depending on the formulation characteristics.

Safety

In the Phase 3 clinical trial of iDose, the Travoprost VitalDose implant was evaluated for safety. Among the patients who received the implant, 2.6% experienced systemic serious adverse events (SAEs), while 0.5% experienced ocular SAEs. The most common side effects were iritis, ocular hyperemia, reduced visual acuity, and increased intraocular pressure (IOP).

Stability

The API in the EVA implant demonstrated stability over a period of 6 months.

Storage conditions and cold-chain related features

Store at 2°C to 25°C (36°F to 77°F). Do not freeze

Potential application(s)

Therapeutic area(s)

Contraception
Multipurpose technology : "rare diseases, ophthalmology, women’s health, CNS, infectious diseases, and endocrinology applications"
Oncology
HIV

Use case(s)

Pre-Exposure Prophylaxis (PrEP)
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 6 months, Yearly

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

- Female
- Cisgender female
- Transgender female
- All

Pregnant individuals

No

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

Beta blocking agents

Class(es)

Beta Blocker - Opthalmology

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Glaucoma

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

travoprost

Class(es)

Prostaglandin analogues

Development stage

Marketed

Clinical trial number(s)

NCT03519386

Foreseen/approved indication(s)

Open-Angle Glaucoma, Ocular Hypertension

Foreseen user group

Adults < 18years old

Foreseen duration between application(s)

Single dose

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Approved by USFDA on 14 December 2023 for open-angle glaucoma (OAG) or ocular hypertension (OHT)

Dexamethasone

Class(es)

Synthetic Corticosteroids

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Ocular hypertension

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

goserelin

Class(es)

Gonadotropin releasing hormone analogues

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Solid Tumors

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

trastuzumab

Class(es)

HER-2 Inhibitors

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Solid Tumors

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Implantable Device for Sustained Release of a Macromolecular Drug Compound

Brief description

An implantable device for delivery of a macromolecular drug compound is provided. The device comprises a core having an outer surface and a membrane layer positioned adjacent to the outer surface of the core. The core comprises a core polymer matrix within which is dispersed a drug compound having a molecular weight of about 0.5 kDa or more, the polymer matrix containing a hydrophobic polymer. Further, the membrane layer comprises a membrane polymer matrix within which the macromolecular drug compound is optionally dispersed. The concentration of the macromolecular drug compound in the core is greater than the concentration of the macromolecular drug compound in the membrane layer.

Representative patent

US20190358167A1

Category

Device

Patent holder

Celanese EVA Performance Polymers Corporation

Exclusivity

Not provided

Expiration date

May 20, 2039

Status

Active

Description

Injection Molded Medical Devices Made From A High Molecular Weight Polyethylene

Brief description

A high molecular weight polyethylene polymer is formulated so that the polymer is capable of being injection molded. The polyethylene polymer has a Viscosity Number of greater than about 400 ml/g and has a melt flow rate of greater than about 0.9 g/10 min. The polyethylene polymer is of high purity and is particularly well suited for producing medical products.

Representative patent

US20240262942A1

Category

Device

Patent holder

Celanese International Corp

Exclusivity

Not provided

Expiration date

Not provided

Status

Pending

Supporting material

Publications

There are no publication

Additional documents

- VITALDOSE Published Report
- LEAP Workshop Summary

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

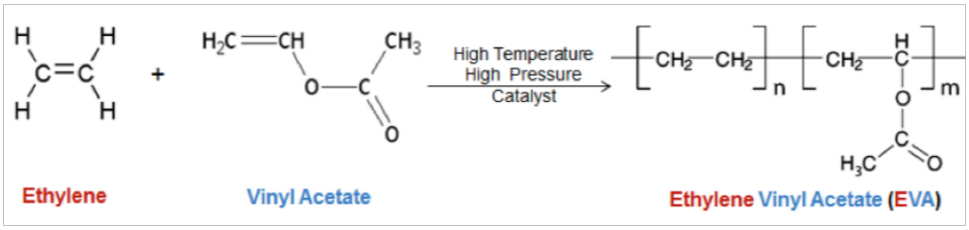
Work with MPP to expand access in LMICs

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

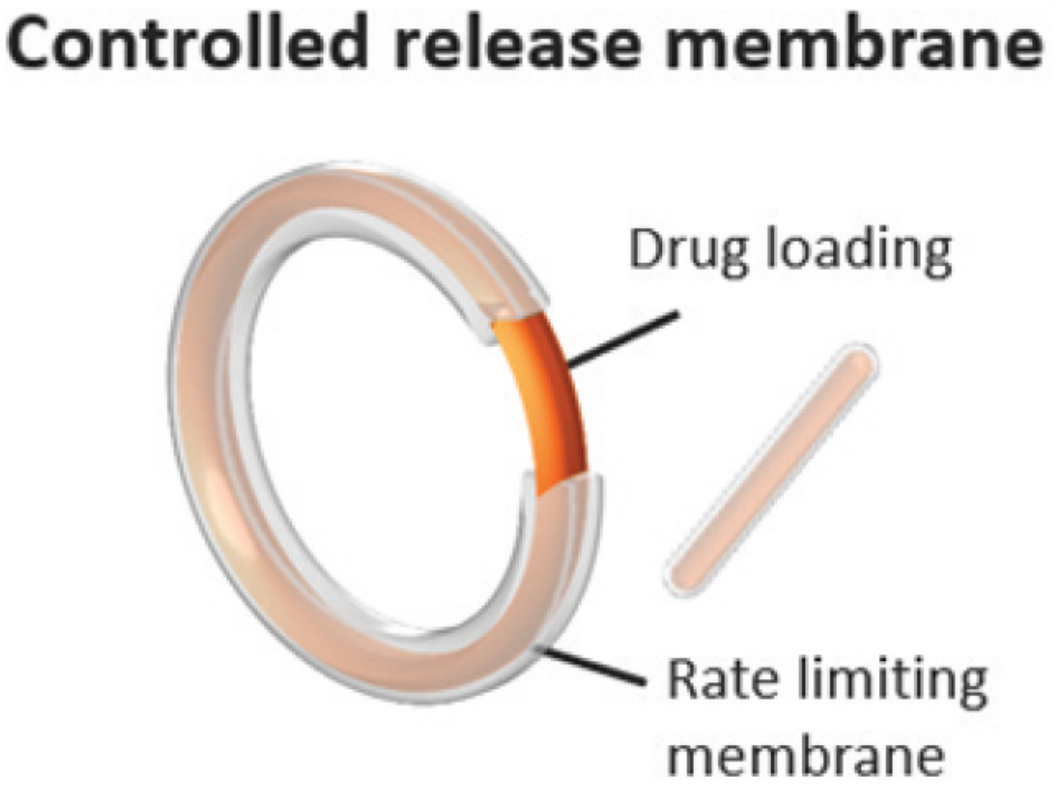
Comment & Information

Illustrations



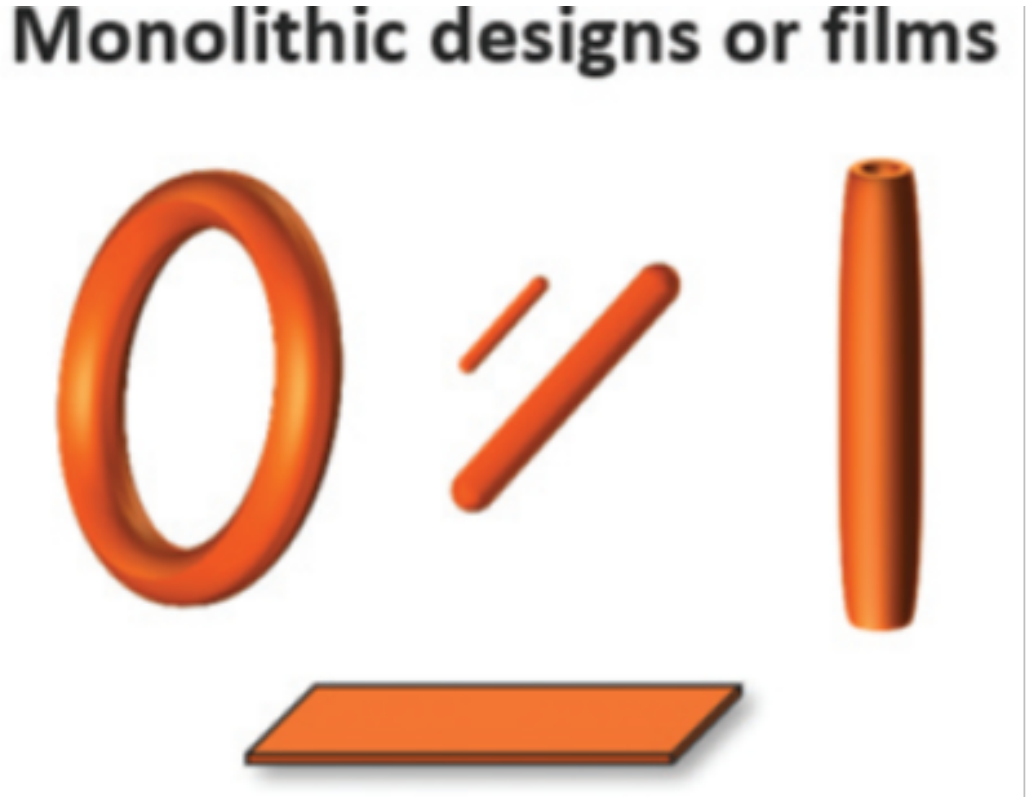
Ethylene Vinyl Acetate Synthesis

Zhang, B. (2015). Potential use of ethylene vinyl acetate copolymer excipient in oral controlled release applications: A literature review. Celanese. https://www.celanese.com/-/media/eva%20polymers/fi



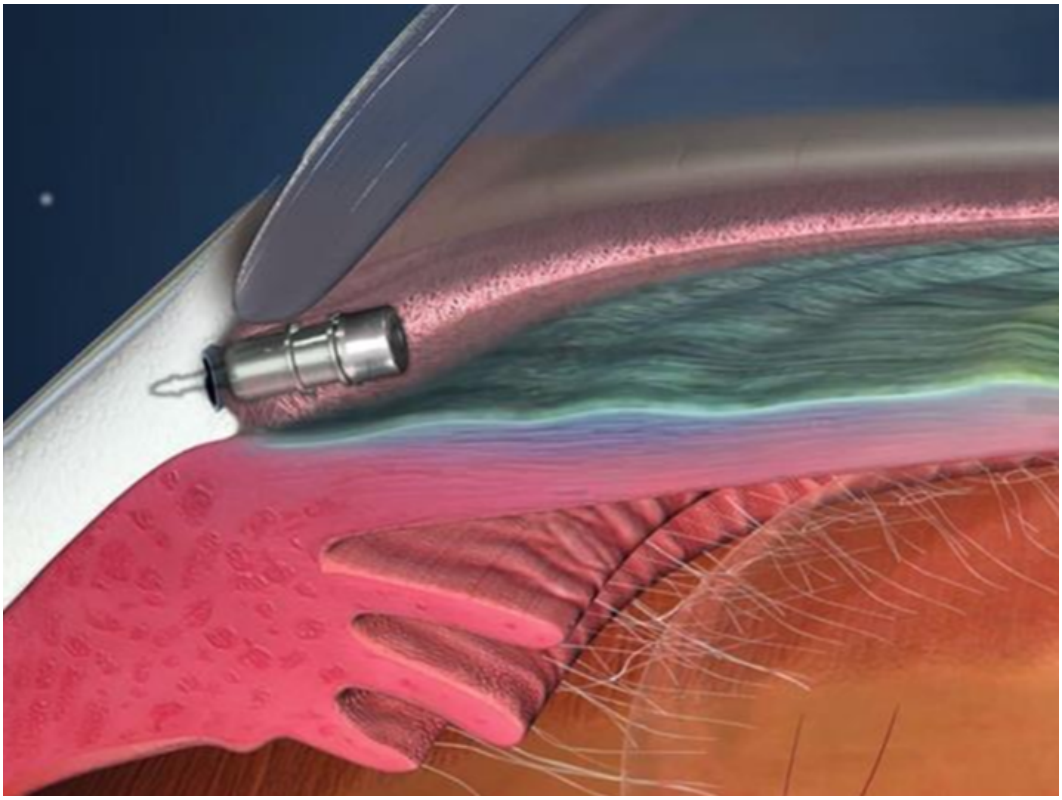
VitalDose EVA Implant with Core layer (reservoir) and a Membrane layer (raye limiting membrane)

Holmes, C., Chen, K., & Duke, B. (n.d.). Drug delivery platform - VitalDose® EVA implants for systemic & local delivery of therapeutics. Celanese. Retrieved from https://www.celanese.com/-/media/eva%2



Various Structural forms of EVA implant i.e, rings, rods and films

Holmes, C., Chen, K., & Duke, B. (n.d.). Drug delivery platform - VitalDose® EVA implants for systemic & local delivery of therapeutics. Celanese. Retrieved from https://www.celanese.com/-/media/eva%2



Intracameral VITALDOSE depot of Travoprost

Innovative Glaucoma Solutions. (2024). iDose TR prescribing information. iDose TR. https://www.idosetr.com/wp-content/uploads/2024/01/iDose-TR-Prescribing-Information.pdf

Sterile Single-dose inserter used for intracameral depot adminstration

Innovative Glaucoma Solutions. (2024). iDose TR prescribing information. iDose TR. https://www.idosetr.com/wp-content/uploads/2024/01/iDose-TR-Prescribing-Information.pdf