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Review

UK & EUROPE SPECIAL

BIOTECH STARTUPS

EDITION

**OPTIMISING GI
TREATMENTS
WITH AN
EFFECTIVE
DRUG
DELIVERY
PLATFORM**

ESOCAP



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CEO

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Consider an instance where you've suffered from a sore throat that stopped you from comfortably swallowing, let alone relishing, your favourite food or beverage. While the uneasiness would be infuriating for a few days, you could quickly recover with minimal medication. However, 1 in 2000 people suffer from a disease known as eosinophilic esophagitis (EoE) that causes them incessant trouble in swallowing and induces recurring abdominal pain and oesophageal food impaction and vomiting. Among infants and toddlers, EoE also leads to poor growth, malnutrition, and weight loss. What's more, the treatment of EoE is not even remotely simple as the cure for a sore throat. Repetitive endoscopies, strict diet management and therapy, and administering off-label topical steroids are the go-to treatments for affliction.

Akin to EoE, diseases such as Barrett's oesophagus and gastroesophageal reflux disease (GERD) are difficult to treat because both physicians and the pharmaceutical industry are in dire need of a drug that can be administered directly to the oesophagus. But, as physicians know, the anatomical and functional characteristics of the oesophagus create an ultra-short transit time of any medication from mouth to stomach, and hinders effective absorption of its constituents into the oesophageal lining.

OPTIMISING GI TREATMENTS WITH AN EFFECTIVE DRUG DELIVERY PLATFORM

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Our platform will be valuable for biopharmaceutical companies already working in gastroenterology, immunology or oncology, as well as for contract manufacturers





Our technology offers maximum flexibility, as multiple relevant drug substances, including biologics and further innovative compounds, can be incorporated into the thin film, making the smart drug delivery platform applicable to various clinical indications

With a clear comprehension of the challenges that both patients and care providers face when tackling such diseases, Switzerland-based EsoCap has developed the world's first solution for effective local oesophagus therapy. The FDA recognised the unique drug delivery system and granted the Orphan Drug Designation status to treat EoE, enabling targeted and long-lasting local therapy. The proof of principle in humans has been established, and the unique targeted application platform to treat the upper gastrointestinal tract is currently under clinical validation with the ongoing ACESO phase II trial in EoE in Europe. However, to understand how the solution has revolutionised the treatment of oesophageal diseases, one must first comprehend how the company overcame the challenges posed by the task.

Innovation with Humble Origins

The story of EsoCap began in 2017 with a conversation between two great minds at the Center of Drug Absorption and Transport of the University of Greifswald. Prof. Dr Werner Weitschies, a visionary in drug development, had formulated a brand new way of treating diseases in the upper gastrointestinal (GI) tract. With immense know-how in the behaviour of drugs and dosage forms in the GI tract and new formulation concepts for oral and topical drug delivery, Prof. Dr Weitschies presented his idea for an innovative drug delivery system to Dr Werner Tschollar—the President of the board. Soon after, both joined forces to patent the technology and conceptualise an organization centred on it.

By 2019, the EsoCap team had conducted and successfully passed the proof of functionality for the delivery system at the University of Greifswald. All healthy volunteers in the study were able to successfully swallow

the product without experiencing marked discomfort or even pain when swallowing. The detailed study procedure was published in the Journal of Controlled Release (J Krause et al., J Control Release 2020; 327:1-7) and recently in Pharmaceutics (C Rosenbaum et al., Pharmaceutics 2021; 13, 828).

“We have been conducting work on the absorption of drugs by the mucosa of the gastrointestinal tract. Topical treatment in the upper gastrointestinal tract is extremely difficult to achieve due to ultra-short transit times with less than two seconds from the mouth to the stomach. Our invention addresses the need for targeted local delivery of drugs in the esophagus,” says Prof. Dr Werner Weitschies.

Dr Weitschies's breakthrough in the drug delivery mechanism centred on a unique platform designed to assist in the precarious treatment of the upper gastrointestinal tract. Unlike conventional drug delivery methods such as tablets, capsules, and viscous fluids, the EsoCap technology ensures that the drug adheres to the oesophageal mucosa for at least 15 minutes for maximum treatment efficiency.

A Simple Yet Highly Effective Solution

EsoCap's innovative application technology consists of a drug-loaded thin-film rolled up in a capsule that unravels and sticks to the oesophageal mucosa when swallowed. This ensures local drug delivery and prolonged mucosal contact as the film slowly dissolves and delivers the active pharmaceutical ingredient (API) locally.

“From the patient's perspective, administering the drug is as easy as swallowing a capsule,” says Isabelle Racamier, CEO of EsoCap. The EsoCap technology consists of a capsule containing a thin film loaded with an API. The technology offers maximum flexibility, as multiple

relevant drug substances, including biologics and other innovative compounds, can be incorporated into the thin film, making the drug delivery platform applicable to various clinical indications, including approved APIs and APIs under development. This flexibility gives EsoCap an approach that has potential in treating a range of different oesophageal disorders such as GERD and Barrett's oesophagus, a risk factor for GERD patients potentially leading to oesophageal cancer. Along with EoE, EsoCap is also researching GERD and Barrett's disease as priority indications, as these are areas of high unmet medical need.

The drug delivery platform comprises a slit capsule, a rolled-up thin film, a sinker, and a connecting thread. The film has a length of approximately 25cm to ensure that the drug is administered over the entire length of the oesophagus. The slit in the capsule allows the end of the rolled film to be threaded through and attached to a retainer outside the capsule, which is attached to a capsule holder. A sinker is also an integral part of the product since it increases the weight of the capsule and thereby avoids buoyancy in the mouth while swallowing. Thanks to a connecting thread, EsoCap doesn't unroll in the mouth and throat during swallowing. The patient swallows the capsule with a specially designed drinking device filled with water. Upon swallowing, the slit film unrolls and sticks to the mucosa, where it dissolves slowly while releasing the drug substance.

This simplistic yet ingenious technology can treat several diseases in the oesophagus and potentially help over 370 million patients worldwide. Moreover, the solution's flexibility and simplicity allow it to effectively deliver drugs needed in gastroenterology, immunology, oncology, rare diseases, and more. A study conducted by Prof. Evan S. Dellon titled ‘Viscous Topical is More Effective than Nebulised Steroid Therapy for Patients with Eosinophilic Esophagitis’ has

proven that prolonged contact time with the oesophagus mucosa is directly related to higher drug efficacy. “Our technology offers maximum flexibility, as multiple relevant drug substances, including biologics and further innovative compounds, can be incorporated into the thin film, making the smart drug delivery platform applicable to various clinical indications,” adds Isabelle.

Gaining Attention from the Pharmaceutical Industry

What sets EsoCap leagues ahead of competitors and a source of excitement for many healthcare experts worldwide is its ability to locally administer drugs to the oesophagus and how it prevents side effects in patients. For example, orodispersible budesonide tablets cause candidiasis among more than 10 per cent of patients because the tablet melts in the mouth, although the administration site is the oesophagus. Additionally, the company has a robust IP and has approved Orphan Drug Designation in lead indication.

The promising potential of EsoCap's technology has garnered a lot of attention from experts across the world. EsoCap has collaborated with distinguished specialists in gastroenterology, surgery, immunology, and pathology in various conferences, and has received acclaim for its innovative technology. EsoCap also hosted a well attended virtual Investigators' Meeting for the ACESO study on March 18, 2021, to showcase the huge market potential of the platform. The ACESO trial is a multicenter, randomized, double-blinded, placebo-controlled clinical Phase II trial evaluating the efficacy, tolerability, and safety of ESO-101 in adult patients with active EoE, where patients are treated once daily for 28 days. For the phase II study, EsoCap is currently recruiting 42 patients with the rare disease EoE at 14 centres in four countries. The trial's primary objective is to evaluate efficacy based on histological response. Secondary objectives include efficacy based on further histology parameters and clinical symptoms, efficacy based on clinical response assessed by patient-reported outcomes, efficacy based on endoscopic response, patient-reported treatment satisfaction, as well as evaluation of tolerability and safety.

The organisation is keen on engaging in a partnership with a prominent biopharmaceutical company in 2022. “We are currently demonstrating clinical feasibility in EoE with the ACESO phase II trial. We use the data from the trial, and other applications in Barrett and reflux, to put together a deal with a major biopharmaceutical company,” says Isabelle. EsoCap's unique innovative drug delivery platform is set to be a game changer in the treatment of complex oesophageal diseases. “Our platform will be valuable for biopharmaceutical companies already working in gastroenterology, immunology or oncology, as well as for contract manufacturers.” [LS](#)