Unique Drug And Oxygen Delivery Systems

NOVALIQ

AN INTEGRATED PIPELINE OF OPHTHALMIC PRODUCTS BASED ON EYESOL™ DELIVERY TECHNOLOGY

In this piece, Dieter Scherer, PhD, Chief Scientific Officer, Novaliq, describes two of the company's most advanced products. NovaTears® OTC is ready to be marketed as a wetting agent for the ocular surface and for stabilisation of the tear film for the relief of dry-eye and irritated-eye symptoms, and CyclASol®, a clear formulation of Cyclosporin A, which has completed a Phase I clinical trial. Both products use Novaliq's semifluorinated alkane technology, EyeSol®.

Novaliq GmbH, based in Heidelberg, Germany, is a drug delivery company developing a superior generation of ocular formulations for poorly soluble drugs. These patented ocular formulations are based on semifluorinated alkanes (SFAs), which can be easily applied in the form of eye drops or as an eye spray.

Since its establishment in 2007, Novaliq has obtained five rounds of funding totaling US$42.2 million (£28 million) from its major shareholder, Dievini Hopp Biotech Holding, a venture capital company focusing on biopharmaceutical companies in Europe.

BUSINESS STRATEGY

Novaliq's strategy is to establish a portfolio of consumer and prescription products in the field of ophthalmic diseases including evaporative dry-eye disease. These multi-dose products are intended to cover unmet medical needs with one major advantage of being preservative free.

MECHANISMS OF ACTION & TECHNOLOGY

Novaliq's technology platform is based on highly purified SFAs. These biocompatible liquids can dissolve poorly soluble drugs and have excellent wetting properties.

Their amphiphilic profile makes SFAs ideal for the production of purely physical active drug solutions or homogenous suspensions for ocular applications.

PRODUCT PIPELINE

Novaliq GmbH currently has several product candidates with excellent market potential in various stages of development (see Figure 1).

THE TECHNOLOGY

EyeSol® is Novaliq's proprietary ophthalmic drug delivery technology based on SFAs. For the treatment of complicated retinal detachment, these compounds have been used in patients intra-ocularly as temporary endotamponades for more than 10 years. They are well tolerated and have an excellent safety profile. SFAs are chemically and biologically inert and thus do not cause ocular tissue irritation.

PHYSICAL PROPERTIES

Their extraordinary spreading properties support the drug distribution on the corneal surface. In addition, their low viscosity and low surface tension result in much smaller droplet size compared with water leading to improved administration, superior kinetics and reduction of systemic side effects.

Due to their amphiphilic nature, SFAs can dissolve poorly water soluble compounds or create stable ophthalmic suspensions. As a non-aqueous system, they do not require preservatives and support the long term stability of the formulation.

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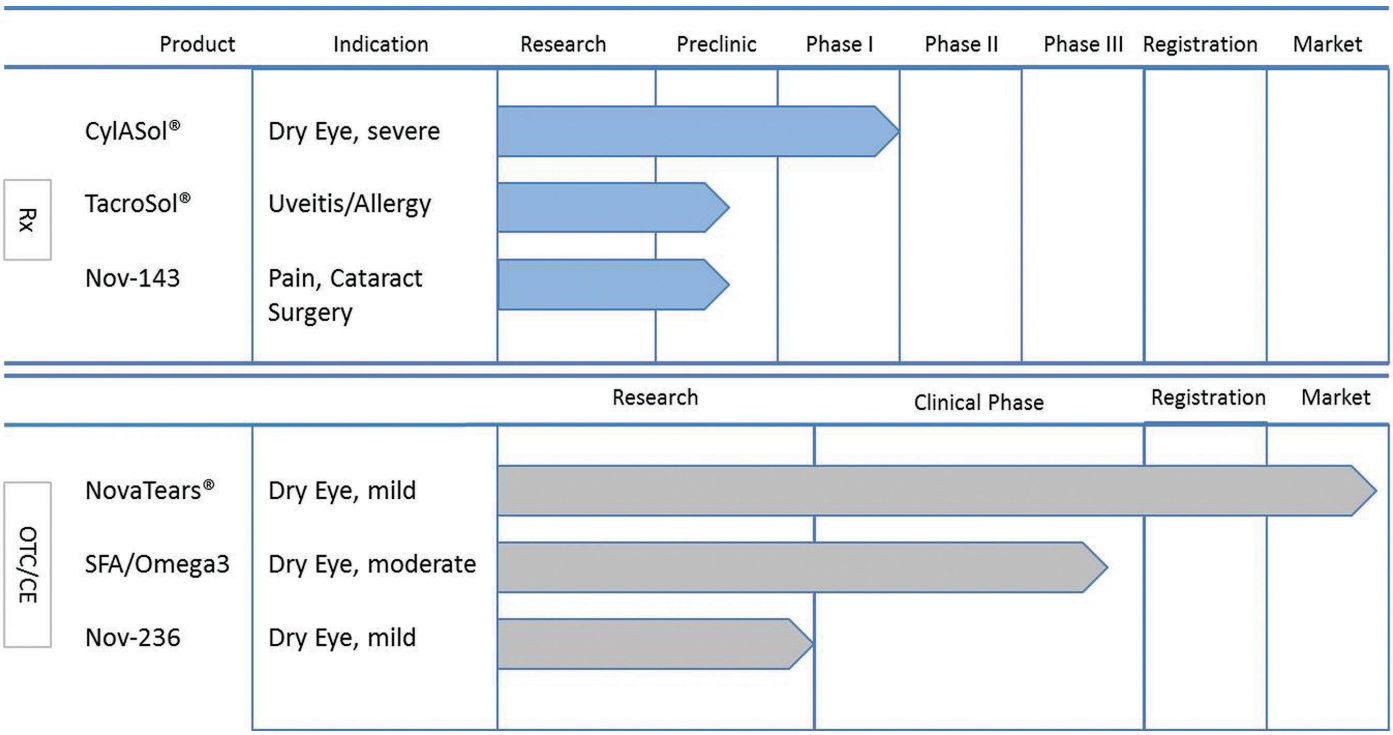

Figure 1: Novaliq's Pipeline of Prescription Only and Over-the-Counter Products.

NOVATEARS®

NovaTears® OTC, the first product based on Novaliq's proprietary EyeSol® Technology, is an innovative multi-dose, non-aqueous, non-blurring and preservative-free topical eye drop formulation for lubrication of the ocular surface. It is intended for use as a wetting agent for the ocular surface and for stabilisation of the tear film for the relief of dry-eye and irritated-eye symptoms. Due to its significantly reduced surface and interface tension NovaTears® has a superior wettability compared with all other available eye drop technologies. NovaTears® has been classified as a class IIa medical device and received CE mark approval in Europe in July 2013.

NOVATEARS® POSITIVE CLINICAL RESULTS

In an observational clinical study, NovaTears® OTC eye drops showed excellent clinical performance and safety in patients with hyperevaporative dry-eye disease. The study (NT-001), which placed NovaTears® OTC eye drops in 30 patients with symptoms of mild-to-moderate evaporative dry-eye disease, was successfully completed in July 2014 and demonstrated efficacy and safety in relief of dry-eye symptoms.

The primary objective of the open, prospective, uncontrolled post-market clinical follow-up study (treatment survey) was to confirm whether NovaTears® was able to lubricate the ocular surface successfully, stabilise the eye's tear film, and relieve adverse symptoms associated with dry-eye disease. Additionally, local tolerability and safety of NovaTears® was assessed when used in accordance with its approved labelling.

Tear film stability improved over the study period (measured using industry-standard Schirmer I and TFBUT tests), tear osmolarity remained unchanged and assessment by a subjective dry-eye questionnaire revealed that patient symptom severity decreased after use of NovaTears® over a 5-7 week period.

Corneal staining (measured using the Oxford Grading Scheme) indicated less corneal damage after treatment, as demonstrated by patient shift towards Grade 0 at follow-up. No changes were observed in either visual acuity or intraocular pressure,

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indicating that use of NovaTears® eye drops is safe.

Novaliq is currently preparing NovaTears® for market entry in several geographic regions with dedicated ophthalmic partners. (NovaTears® is not approved for marketing or distribution in the US.)

CYCLASOL®

Based on Novaliq's proprietary Eyesol® technology, CyclASol® is the only Cyclosporin A ophthalmic solution.

> ""Based on Novaliq's proprietary Eyesol® technology, CyclASol® is the only Cyclosporin A ophthalmic solution"

CyclASol® is developed as a clear solution in multi-dose, preservative free bottles for patients with dry-eye syndrome and has demonstrated long term stability plus preclinical data indicating superior wettability, pharmacokinetics and biocompatibility compared with conventional emulsions.

CyclASol® is the second Novaliq product with positive data in humans, for the first time addressing poorly soluble pharmaceutically relevant APIs. In July 2014, Phase I clinical study was successfully completed.

CYLASOL® CYS-001 CLINICAL STUDY SUMMARY

CYS-001, a two-arm, double-blind, randomised, placebo-controlled, cross-over Phase I study investigated the safety, local tolerability and systemic exposure of Cyclosporin A compared with a placebo (perfluorobutylpentane) following single and multiple ocular doses of CyclASol and Placebo solution in healthy volunteers.

Objectives of the 18-patient trial were to investigate safety, local tolerability and systemic exposure of CyclASol® (Cyclosporin A solution) eye-drops and vehicle following single and multiple ocular doses in healthy volunteers. No drug-related signs or symptoms of ocular discomfort or irritation were reported; in particular no dryness, grittiness, burning, stinging, tiredness, blurred or foggy vision, redness, watery eyes, eye mucus or crusting. In slit-lamp examinations, no subjects revealed any clinically abnormal signs of the anterior and posterior eye structures. With dosing of up to four drops per eye per day, no systemic levels of Cyclosporin A were detected after any dose or at any time point when using a highly sensitive assay with a LLOQ as low as 0.1 ng/ml. Novaliq has a granted patent position in most relevant markets. (CyclASol® is not approved for marketing or distribution in the US.)

CyclASol® is the first clear Cyclosporin A solution in clinical trials to treat dry-eye syndrome. Whilst conventional Cyclosporin A formulations are emulsions, CyclASol® is the first and only 0.05% clear Cyclosporin A solution based on Novaliq's proprietary EyeSol® platform technology.

- CyclASol® eye drops are safe and well-tolerated
- No burning or other adverse effects
- Available in preservative-free multi-dose bottles
- Excellent spreading and wettability
- Superior biocompatibility
- Proven long-term stability
- Broad patent protection.

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