



Cis-UCA Eye Drops for the treatment of Dry Eye

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Herantis Pharma Plc

- Drug development company formed through Hermo Pharma Ltd's acquisition of 99% of shares in Laurantis Pharma Ltd in Apr 2014
- Focus in products for the treatment of inflammatory and CNS diseases
- Expertise in early clinical development
 - Preclinical research
 - Early clinical research
 - Clinical Proof-of-Concept
- Completed a successful IPO in June 2014

Herantis portfolio (drug candidates)

Drug candidate	Indication	Preclin	Phase 1	Phase 2	Phase 3	Launch
Cis-UCA Eye Drops	Dry Eye	▲	▲	▲		
CDNF neuroprotective factor	Parkinson's disease	▲	*			
Lymfactin®	Secondary lymphedema	▲	*			
Cis-UCA Emulsion Cream	Atopic dermatitis**	▲	▲	▲		
CDNF neuroprotective factor	Amyotrophic lateral sclerosis (ALS)**	▲				

*This stage of clinical development in planning and scheduled

**Currently not one of the main products of the Company. The next steps are pending later decisions. Not a funding priority.

Cis-UCA Eye Drops: Overview

- Positioning: Superior efficacy and safety in Dry Eye Syndrome
- In murine Dry Eye model, more efficacious than Restasis® - the only FDA-approved drug for the treatment of Dry Eye Syndrome (sales >\$900 million)
 - “Best product we have tested in our dry eye animal model” – ORA, a leading CRO in ophthalmology
 - Phase 1 data suggest clear improvement over safety profile of Restasis®
- Efficacy data from a phase 2 study in the USA expected by Q3/2015

Cis-urocanic Acid (cis-UCA)

- Endogenous small-molecule component of human and animal skin
- Formed in the upper layers where histidine is deaminated to trans-UCA, and trans-UCA is photoisomerised into cis-UCA by UV irradiation of the skin

Ocular anti-inflammation rationale



- Cis-UCA is an anti-inflammatory and cytoprotective agent for human corneal and conjunctival cells
- Cis-UCA suppresses secretion of inflammatory cytokines (e.g. IL6, IL-8) from UVB-stimulated human corneal epithelial cells
- Cis-UCA suppresses the JNK signaling pathway, and protects corneal epithelial cells from UVB-induced apoptosis

Illustration is not related to the text on this page.

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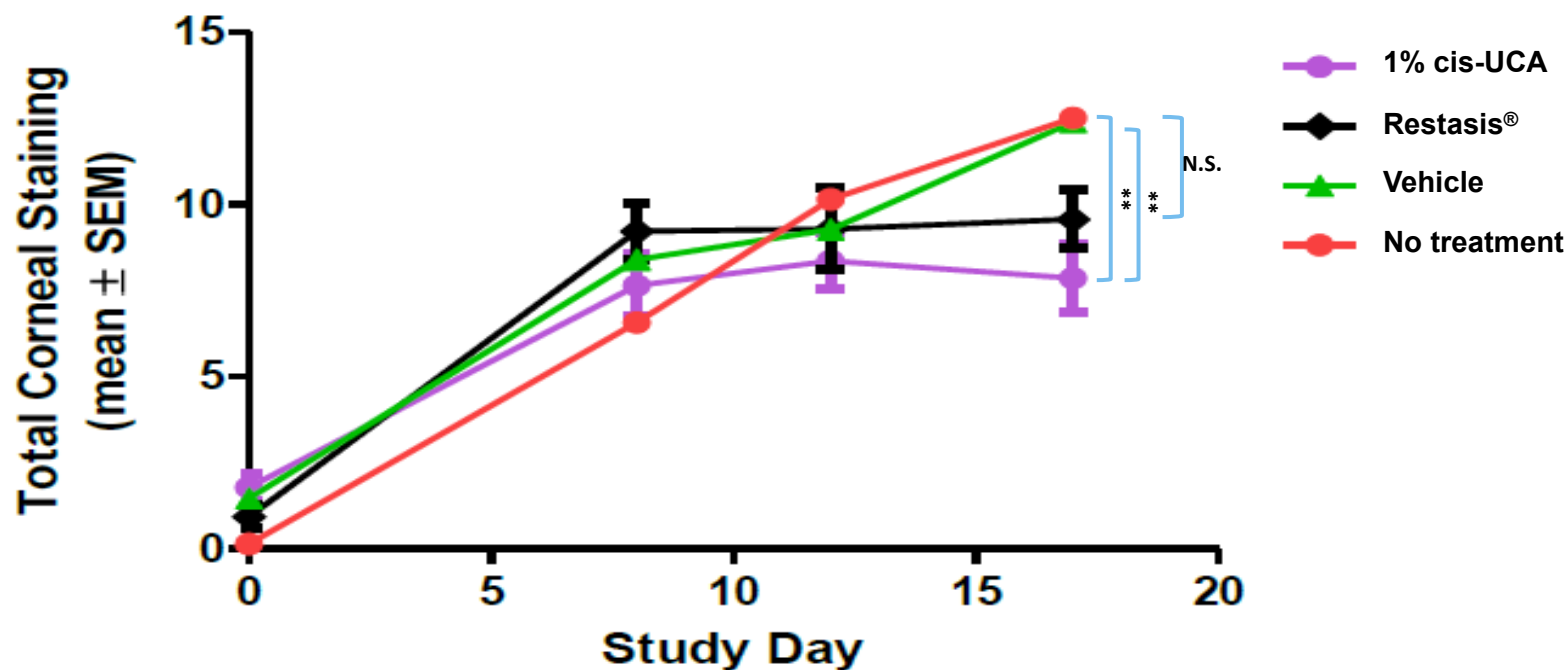
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Cis-UCA Eye Drops: Preclinical and clinical data

- Pre-clinical studies suggest cis-UCA eye drops has the potential to be the first ever eye drop product having/providing:
 - Reduced corneal fluorescein staining in the murine model for experimental dry eye: Superior compared with Restasis® as a positive control
 - Strong safety profile in toxicological and safety pharmacology studies
 - Long-term applicability
 - Ability to be formulated in a variety of strengths for use across several eye diseases
- Clinical data in Phase 1 study (N=37):
 - Excellent local and systemic safety when administered thrice daily in both eyes for 14 days
 - No effects on eye function
 - Very low systemic absorption

Effects of Cis-UCA in a Murine Model of Dry Eye

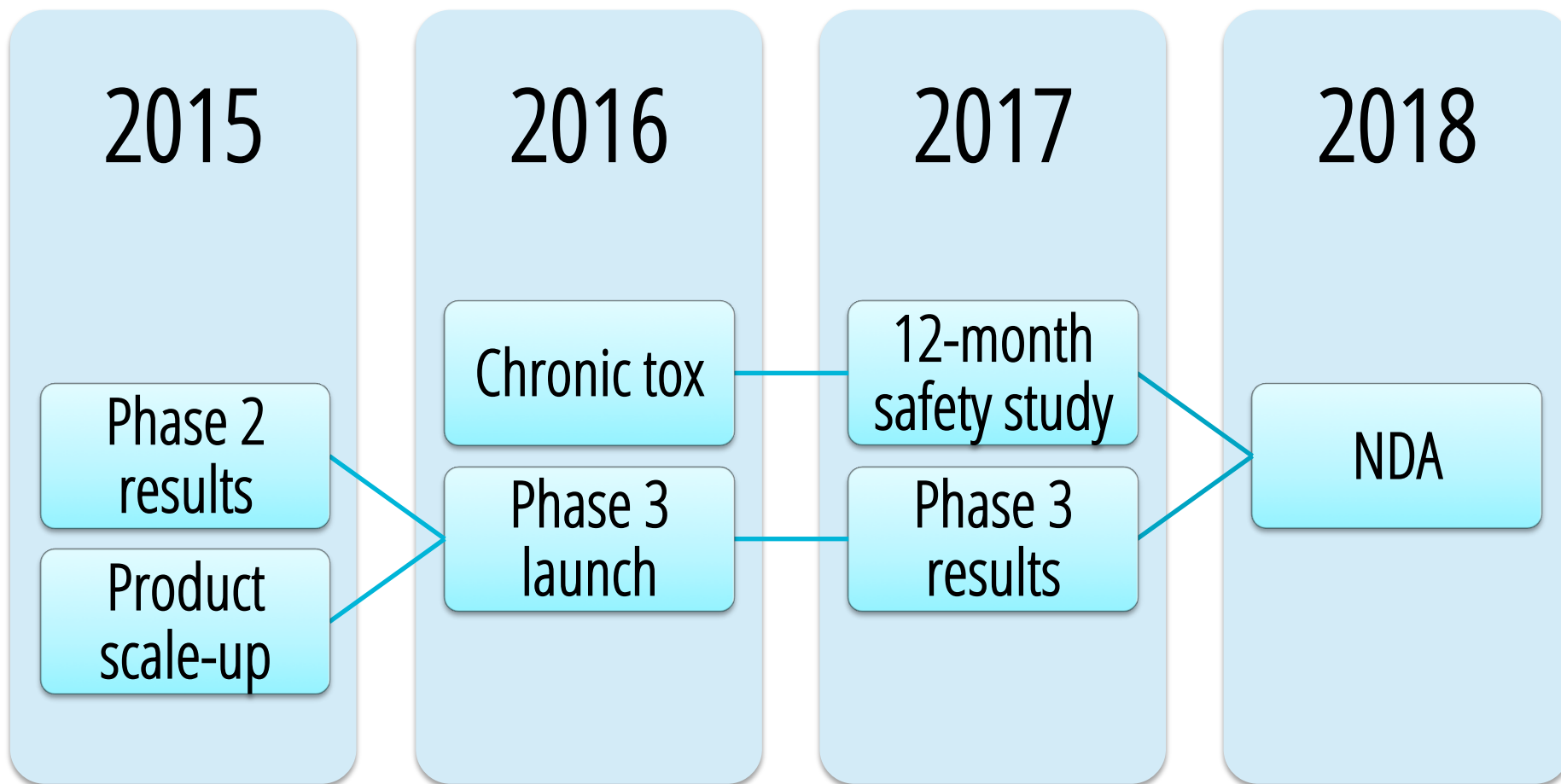


- 1% cis-UCA performed better than Restasis®, maintaining a two unit lower differentiation
- By day 17, 1% cis-UCA reduced staining significantly versus vehicle and “No treatment” group
- No statistical significance was found for Restasis® versus vehicle or versus the no treatment group

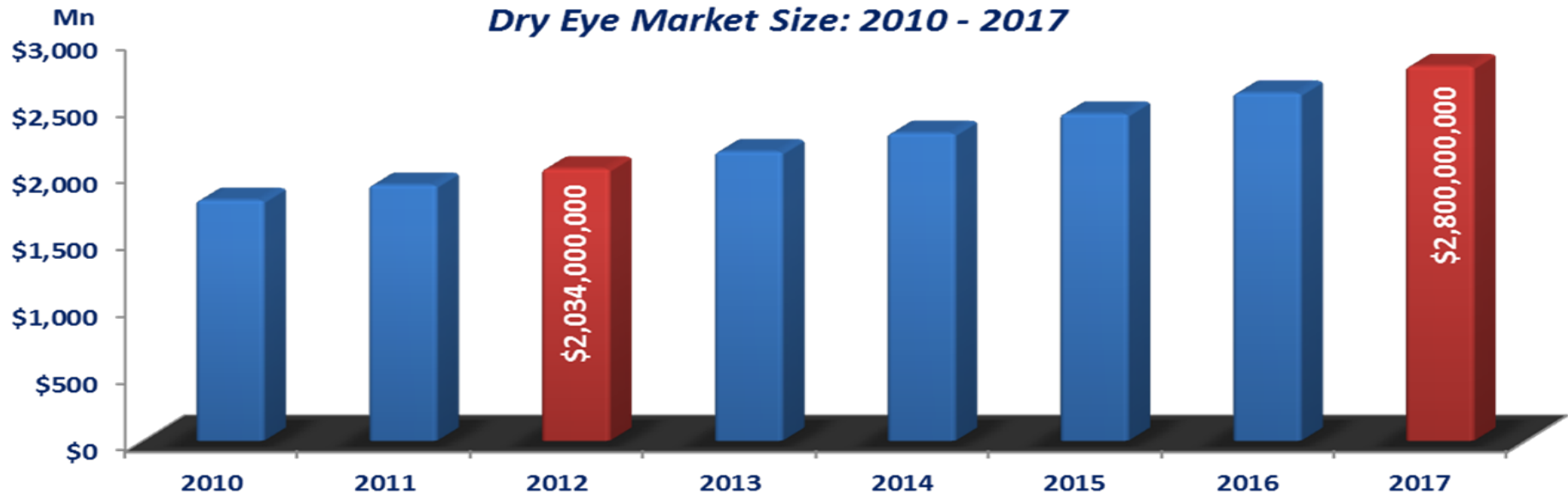
Phase 2 Study in Patients with Dry Eye kicked-off

- Phase 2 carried out in the USA with ORA Inc., a leading CRO in ophthalmology and Dry Eye expertise
 - IND cleared by the FDA
 - Randomized study, N=150
 - Vehicle vs. two different dose levels of Cis-UCA
 - 4 weeks treatment, co-primary endpoints for improvement of signs and symptoms
- First Patient In: December 2014, results available by Q3/2015
- Phase 2 study designed to lead directly to Phase 3 development and MAA

Cis-UCA Eye Drops: Target development schedule



Dry Eye market overview



- Datamonitor: Approximately 50 million adults suffer from dry eye across the seven major markets
- Current treatments include Allergan's Restasis®, the only FDA approved therapy for dry eye, as well as corticosteroid eye drops
- The dry eye market is expected to grow at a Compounded Annual Growth Rate (CAGR) of 6.3% over the next seven (7) years from \$2 billion in 2012 to \$2.8 billion in 2017 according to GlobalData

Cis-UCA Eye Drops: Business opportunities

- Significant market need in Dry Eye for a product treating both the symptoms and the disease, suitable for long term use
 - Allergan's Restasis® annual sales exceed 900 MUSD despite its weaknesses
- Large market opportunities in ophthalmology beyond Dry Eye
 - In animal models of Acute Inflammation and Allergic Inflammation, Cis-UCA has demonstrated good efficacy in preventing ocular surface inflammation
 - Effects of 0.5% Cis-UCA were comparable with potent antihistamine and corticosteroid eye drop products in suppressing conjunctival and eyelid hyperaemia in murine model of local eye irritation
 - Dose-dependent efficacy shown in murine allergic conjunctivitis model

Herantis is looking for a phase 3 development partner

- Existing data suggest cis-UCA Eye Drops are safe and efficacious
 - Even suitable for long term use
- Phase 2 clinical proof-of-concept data available in Q3/2015
 - Phase 3 being planned to lead to MAA in Dry Eye Syndrome in USA
 - Development program scheduled for NDA submission in Q4/2018
 - Market currently dominated by Restasis® with sales > 900 MUSD
- Cis-UCA drug substance is scalable to produce and easy to formulate
 - Excellent stability up to at least 24 months in formulation with no preservatives

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Thank you