Symphony Therapeutics

# NEW PRODUCT OPPORTUNITY

# OcuHeal™-UV400+

The First Ophthalmic UV-Protective Antioxidant Eye-drop

## Protect and Heal

## Executive Summary


UV exposure of ocular tissues has been linked to multiple disorders of the eye, some of which can lead to blindness (Turbert, 2020). These disorders are corneal pterygium (ocular surface growths), corneal blebs, corneal and scleral burns, cataract formation, corneal thinning, corneal ulcers, retinal burns, glaucoma and macular degeneration.

The World Health Organization (WHO) has reported that corneal blindness is a critical cause of blindness worldwide where either loss of transparency or distortion of the refractive surface causes vision impairment (WHO, 2022). Chronic exposure to UV can cause damage to the anterior pole of the eye, ranging from minor (pterygium) to serious photokeratitis. In the veterinary markets, UV damage to ocular tissues can lead to corneal opacity, pannus, cataracts and ocular carcinoma.

UV radiation from sunlight is categorized based on wavelength: UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm). More than 90% of UVB and 60% of UVA radiation is absorbed by the cornea, whereas the retina and deeper ocular tissues absorbed UV light in the range 300-800 nm, with the most phototoxic effect on the retina at wavelengths around ~430 nm ("blue light"). UV light that damages ocular tissues are primarily due to UVA and UVB (UVC is filtered out by the ozone layer), causing photochemical damage to cellular DNA due to the spontaneous production of reactive oxygen species. The production of reactive oxygen species elicits the production of pro-inflammatory species causing degeneration of critical ocular tissues. A clinical need exists for a pharmaceutically compliant ophthalmic product with UV-blocking properties and ideally, a product that can prevent and heal ocular tissue damage.

We have developed OcuHeal-UV400+, a lipid nanoparticle eye-drop product that contains a flavonoid, found abundantly in fruit and vegetables. IB0108 is a small molecule of molecular weight < 500 Daltons, has FDA GRAS status as an oral supplement, has anti-oxidant capabilities, is biocompatible to the ocular surface and blocks portions of UVA and UVB. When incorporated/encapsulated into Symphony's proprietary lipid nanoparticle technology (OcuHeal™), the entire UV light wavelength range from 200-550 nm are blocked, thus enhancing the properties of the UV-blocking molecule. Additionally, it's potent anti-oxidant and anti-inflammatory properties renders a healing and protective effect to the ocular surface.

We present data that demonstrates the UV-blocking properties of the product, distribution of the anti-oxidant throughout the eye and preclinical safety and tolerability. Manufacturing and sterilization processes have been developed to enable a sterile, ophthalmic product, stable at room temperature. OcuHeal-UV400+ sterile eye-drops are compliant to ophthalmic criteria with osmolality in the range 300-320 mOsm/L, a mean particle size in the range 70-100 nm, preservative-free and with viscosity in the range 60-100 centipoise.

The utility of this product as a preventive and curative measure to UV damage on the ocular surface is extraordinary.

**Currently, there are no ophthalmic UV-protective medications in either the veterinary or human markets.**

The OcuHeal-UV400+ technology is based on a proprietary platform technology, that has been wholly patented in 12 global jurisdictions. The UV-protective technology can be also be extended into an

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eyelid wipe to block damaging UV radiation. Currently, there are no biocompatible UV products to protect sensitive "around-the-eye" area from UV wearing of contact lenses or alleviation of irritation due to allergy and pollution.

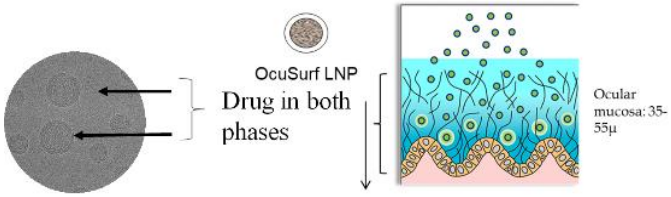
Due to deep and efficient permeation into ocular tissues and membranes, OcuHeal-UV400+ preservative-free eye-drop product may be considered for other eye-protective applications such as ocular lubrication due to digital strain, extended wearing of contact lenses or alleviation of irritation due to allergy and pollution.

## Introducing OcuHeal™

The OcuHeal-UV400+ is based on the OcuHeal™ platform technology, enabled for multiple small-molecule drugs (glucocorticosteroids, antibiotics, anti-glaucoma, immunosuppressant drugs).

OcuHeal platform technology is a liquid-crystalline, lipid nanoparticle drug delivery system designed to rapidly permeate tissues and thus, enhance bioavailability. The drug is dissolved in a lipid phase

High bioavailability; drug is dissolved in lipid cores and aqueous continuous phase; the drug-containing nano-sized lipid particles can permeate the ocular mucosa to permeate the corneal epithelial layer.




Hydrophobic drugs due to its low intrinsic solubility in water, can be fully dissolved in the lipid phase. Most hydrophobic drugs have low bioavailability due to their low solubility.

The lipid particles can be further functionalized to enhance cellular uptake.

## Competitive Advantage: Selection of the UV-Block Molecule for OcuHeal-UV400+

The UV-blocking molecules in commercial topical sunscreens were excluded due to their inherent toxicity to cells, cancer-causing potential and detrimental effect on cellular DNA. Additionally, organic sunscreen molecules cleave in the presence of UV and water, producing reactive oxidizing species. Thus, the ideal UV-block molecule should be reactive species quenching and effective UV-blocking, in the requisite UV wavelength range of 280-500 nm.

IB-0108 is a small molecule, plant-derived molecule with decades of safe human history as an oral supplement and with FDA GRAS status. Additionally, IB-0108 has been shown to be an effective anti-oxidant.

**To address the clinical need, we have developed an ophthalmic UV-blocking anti-oxidant eye-drop formulation based on the OcuHeal nano-lipid technology.**

## IP Position for OcuSurf-LNP

OcuHeal™ is trademark-pending. The patent portfolio has been fully patented in US, Canada, China, Japan, Singapore, New Zealand, Australia, India, South Africa, Europe. Patent life to 2035. Additional patent applications on design and use of UV-block and indications have been filed.

## Potential for Pipeline Utilizing Patented Platform

High potential for a pipeline of products, ocular, intranasal and dermal.

## About Symphony/ Contact Information

Symphony Therapeutics is a wholly-owned subsidiary of Integral BioSystems.

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## References

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WHO. (2022, June). *WHO Fact Sheets/Detail/UV Radiation*, pp. https://www.who.int/news-room/fact-sheets/detail/ultraviolet-radiation.