Innovative Non-Viral Gene Therapies for the Treatment of Ocular Diseases
Innovative Non-Viral Gene Therapies for the Treatment of Ocular Diseases

**Company**
Clinical stage company developing innovative non-viral gene therapies using proprietary electrottransfection system

**Business Strategy**
Develop novel products for sight threatening indications with high unmet medical needs
Raising €30 Million Series B

**Value Proposition**
Innovative ocular delivery approach that sustains expression of therapeutic proteins in the eye for up to 6 months
Minimally invasive procedure: better safety, compliance and clinical outcomes

**Intellectual Property**
Broad IP portfolio (8 patent families)

**Management Team**
Strong management team with extensive clinical and drug development expertise in ophthalmology

**Current Investors**
[Images of current investors]
Management Team:
Global Ophthalmology Development & Gene Therapy Expertise

FRANCINE BEHAR-COHEN, MD, PhD
Founder

PATRICIA ZILIOX, PhD
President & CEO

RONALD BUGGAGE, MD
Chief Medical Officer

THIERRY BORDET, PhD
Preclinical Director

GINA PINTO, MBA
Finance & Admin. Director
The Need for New Treatment Approaches for Retinal Diseases

Intravitreal Injections
- Minimally Invasive
- Limited duration of effect
- Frequent re-administrations needed

Ocular Implants
- Moderately Invasive to Invasive
- Corticosteroid-related ocular side effects
- Foreign bodies introduced into the eye
- Frequent administrations (if biodegradable)

Viral Vector Gene Therapy
- Invasive subretinal surgery, potential damage to retina
- Entire retina not exposed to treatment
- Immunogenicity
- High Cost

Systemic Administrations
- Systemic side effects
- Poor compliance profiles
- Poor ocular bioavailability
- Requires medical/lab monitoring

All Current Treatments Approaches Have Limitations

EyeVensys Technology Key Competitive Advantages Over Existing Approaches
- Long duration of intraocular therapeutic protein expression, minimizing the need for frequent repeat administrations
- Easy, minimally invasive, safe administrations with reduced risk of retinal injury, systemic and ocular side effects
- Low cost, non-viral vector plasmids can encode a variety of therapeutic proteins with low risk of immunogenicity
Eyevensys Technology: An Innovative Drug Delivery Platform that Turns the Eye into a Biofactory

- Direct administration of plasmids into the ciliary muscle, using proprietary electrotransfection system
- Ciliary muscle cells become production site for therapeutic proteins encoded by plasmids
- Once produced, the protein is secreted into the choroid, vitreous and in the aqueous humor and reaches the back of the eye tissues
- Plasmid candidates designed to enable sustained therapeutic protein expression in the eye
## Targeting High Value Markets

<table>
<thead>
<tr>
<th>Diseases Targeted</th>
<th>Advantages over existing Treatments</th>
<th>Patient Prevalence Worldwide</th>
<th>Potential Market Value (US$ Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Orphan Retinal Diseases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinitis Pigmentosa</td>
<td>No treatment approved</td>
<td>~850K patients</td>
<td>$480M+</td>
</tr>
<tr>
<td><strong>Non Infectious Uveitis</strong></td>
<td>Reduced risk of side effects Improved compliance Convenience</td>
<td>1M patients</td>
<td>$600M+</td>
</tr>
<tr>
<td><strong>Retinal Diseases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry AMD</td>
<td>No treatment approved</td>
<td>&gt;16.4M patients</td>
<td>$2,000M+</td>
</tr>
<tr>
<td>Wet AMD, DME, RVO</td>
<td>Reduced patient and physician burden Convenience</td>
<td>~6M patients</td>
<td>$4,000M+</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>No neuroprotective treatment approved</td>
<td>~110M patients</td>
<td>Up to $3,800 M</td>
</tr>
</tbody>
</table>
## Eyevensys Technology Proof of Concept Validated in Animal Models

Technology validated in multiple animal models demonstrating safety and durability of expression with multiple proteins.

<table>
<thead>
<tr>
<th>1. Safety, Duration, Location of protein expression in rats, rabbits and primates</th>
<th>Reporter Proteins</th>
<th>• Green Fluorescent Protein</th>
<th>• Lucia Galactosidase</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Efficacy for Uveitis demonstrated in EIU and EAU Models</td>
<td>Anti-TNF Proteins</td>
<td>• hTNFR-Is</td>
<td>• hTNFR-Is/mIgG1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lenercept</td>
<td>• EYS606</td>
</tr>
<tr>
<td>3. Efficacy for Wet AMD demonstrated in Laser CNV Model</td>
<td>Anti-VEGF Proteins</td>
<td>• S-Flt1</td>
<td>• Aflibercept</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EYS609</td>
<td></td>
</tr>
<tr>
<td>4. Protection against Retinal Degeneration Demonstrated in LID, MNU, rd10, RCS, P23H Models</td>
<td>Neuroprotective Factors</td>
<td>• CNTF</td>
<td>• GDNF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EYS611</td>
<td></td>
</tr>
</tbody>
</table>

In animal models plasmid electrotransfection into the ciliary muscle enabled sustained and dose-dependent protein expression reaching the back of the eye for up to 9 months.
Prioritized Indication: Non-Infectious Uveitis (clinical Phase II)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Pre-Clinical</th>
<th>IND-Enabling</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>EYS606</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Infectious Uveitis (orphan)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EYS606 encodes a potent TNFα inhibitor, a recombinant fusion protein consisting of the extracellular domain of the human TNFα p55 receptor linked to the human IgG1 Fc.

EYS606 reduced the severity of disease and preserved the retina in the rat EAU model.

EYS606 decreased intraocular TNF-α levels and improves clinical and histological outcomes in uveitis rat models.
Additional Prioritized Indications: dry AMD and Retinitis Pigmentosa

**EYS611**
Retinal Degenerations (RP, dry AMD, Glaucoma)

**EYS611** is coding for a potent iron chelator with antioxidant and endogenous neuroprotective properties. Efficacy for preserving retina and safety demonstrated in animal models of dry AMD and RP

**EYS611 preserves the functionality of the retina as measured by ERG**

![Graph showing ONL thickness vs. Distance from optic nerve (µm)]

**Retinal function**
10 cd.s/m2_Photo amplitude b-wave

**ONL thickness**
- No LID
- LID
- EYS611
- NACA
- CA

**Amplitude (µV)**
- LID
- EYS611
- NACA
- CA
- No LID

**EYS611 preserves the survival of photoreceptors after light damage**

![Graph showing ONL thickness vs. Distance from optic nerve (µm)]

N-acetyl cysteine amide (NACA) is under development for RP. Carnosic acid (CA) is a natural antioxidant.
Board of Directors

**GARTH CUMBERLIDGE, PhD**  
Chairman of Board

**FRANK KALKBRENNER, MD, PhD**  
Managing Director  
Boehringer Ingelheim Corporate Venture Fund

**JERRY CAGLE PhD**  
Corporate Board Director  
Former Head of R&D Alcon

**OHAD HAMMER**  
Partner Pontifax

**CHAHRA LOUAFI**  
Investment Director and head of the fund for biotherapies and rare diseases at Bpifrance

**FRANÇOIS THOMAS MD**  
Venture Partner at Sofimac Innovation, Paris

**CATHERINE BOULE**  
Partner at Cap Décisif, a Paris-based seed Fund