ABIONYX

# General Meeting of Shareholders

## 28 June 2022

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# Agenda

1. Abionyx
2. CER-001
3. COVID-19
4. LCAT Deficiency
5. Sepsis induced Acute Kidney Injury
6. Uveitis

# 1. Abionyx

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# A seasoned management team specialized in HDL and Ophthalmology

**Cyrille Tupin**
CEO

**Connie Keyserling**
Peyrottes, M.S.
Senior VP Clinical Development & Operations

**Ronald Barbaras,**
Ph.D.
Senior VP R&D

**Margit Holzer,**
Ph.D.
Senior VP Bio-production

**Pierre-Paul Elena,**
Ph.D.
Scientific Director

**Yann Quentric,**
M.S.
CEO Iris

**Karen Viaud, M.S.**
Senior VP Pre-clinical studies

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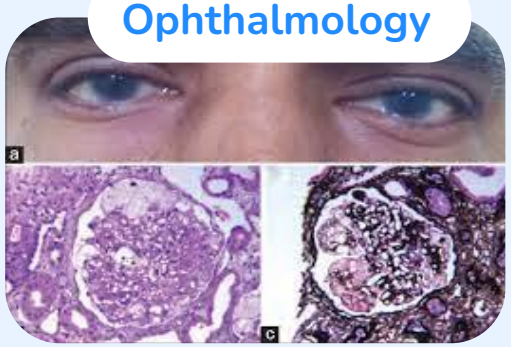
# Abionyx Vision and Mission Statement

**Re-inventing the bio-HDL for the benefit of patients with rare or severe diseases**

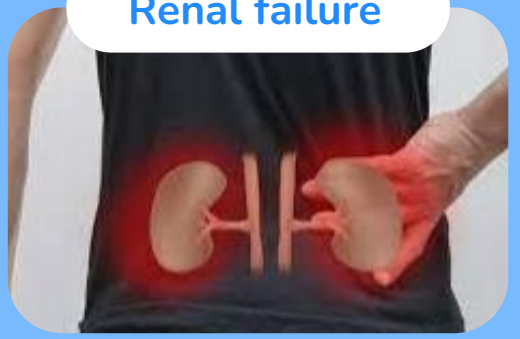
Covid

Sepsis

Ophthalmology



Renal failure



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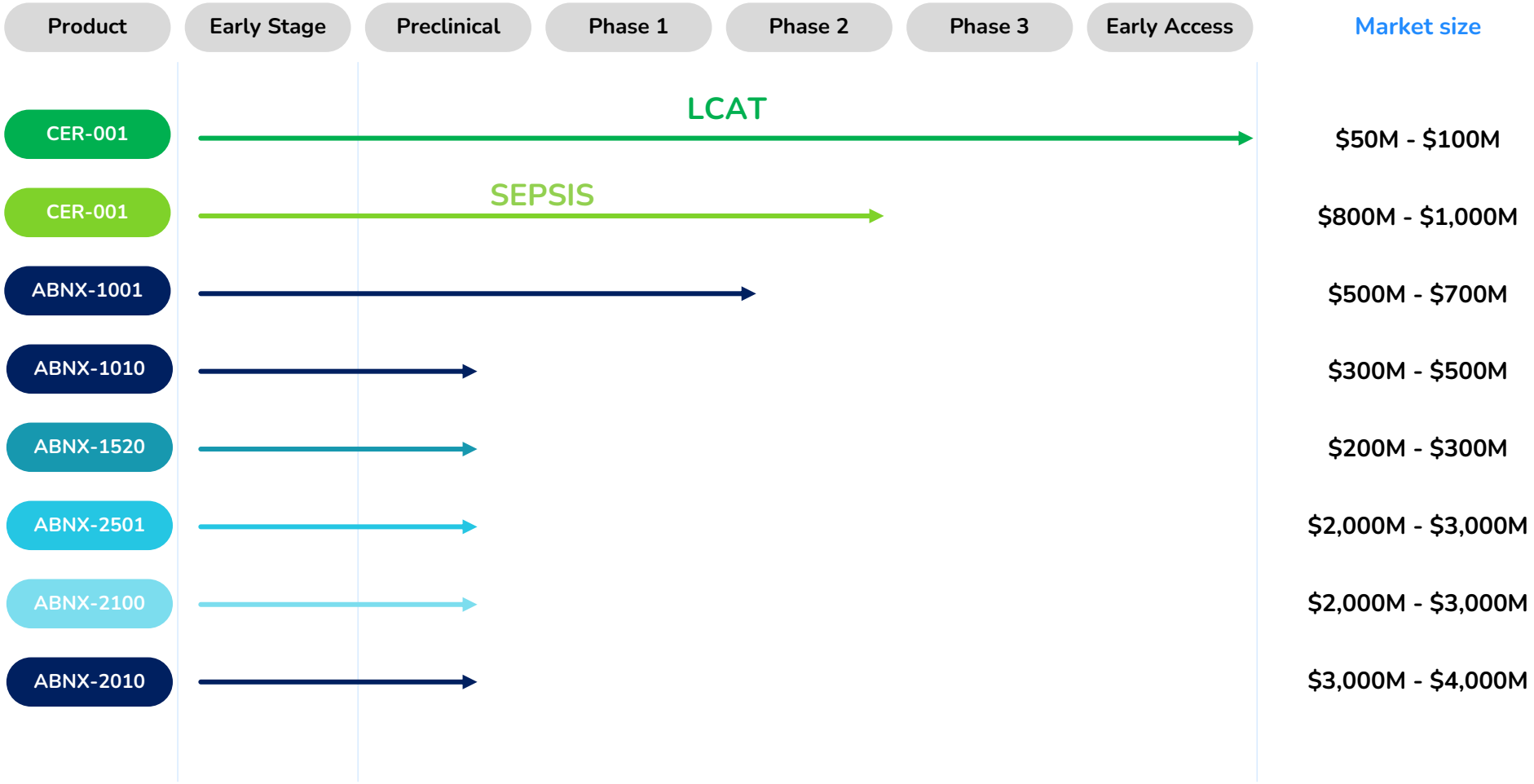
# Indications under investigation




RARE DISEASES | RENAL DISEASES | OPHTHA MONO RETINAL DISEASES | OPHTHA MONO CORNEAL DISEASES | OPHTHA COMBO RETINAL DISEASES | OPHTHA COMBO CORNEAL DISEASES

# A strategy focused on rapid access to market

## Diversify the medical franchises

| | Pillar 1 | Pillar 2 | Pillar 3 |
|---|---|---|---|
| FRANCHISE | **RENAL** | **OPHTALMOLOGY** | **CRO** |
| STRENGTHS | • ODD in a rare disease (LCAT renal)<br>• Totally financed phase 2 trial in sepsis<br>• High potential in other inflammatory diseases | • ODD in a rare disease (LCAT ophtha/Fish-eye disease) | • World leadership in PK and preclinical ophthalmology<br>• Unique expertise in clinical ophthalmology: 70 products to market<br>• Very strong relationships with world KOL |
| OBJECTIVES | • NDA in LCAT<br>• MAA in LCAT | • 3 phase 2 within 36 months | • Increase the portfolio to 400+ customers |

# 2. CER-001, A unique recombinant bio-HDL

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# CER-001 : one of the most advanced therapeutic bioproduct

- **A bioengineered complex comprising natural human HDL protein and apolipoprotein A-I (apoA-I) with all the known biological properties of natural HDL**

- **A safety profile allowing administration at very high doses and frequencies**

- **Commercially viable manufacturing process with stability of 5 years**

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# Bio-HDL: a safe bioproduct with more than 900 patients treated intravenously for up to 18 months

**Historical data leading to excellent safety profile (900 patients)**

| Study | Number of subjects | Indication / doses | Conclusion |
|---|---|---|---|
| Single Ascending Dose | 32 | Healthy Volunteers<br>0.25 to 45 mg/kg | Safety and pharmacokinetic established |
| SAMBA (PoC) | 9 | Familial Primary Hypoalphalipoproteinemia<br>8 mg/kg 20 doses over 26 weeks | Pharmacodynamics established |
| CHI SQUARE (P2) | 507 | Acute Coronary Syndrome<br>3, 6, 12 mg/kg/week for 6 weeks | Good tolerability of infusions<br>No demonstration of efficacy on atheroma |
| CARAT (P2) | 301 | Acute Coronary Syndrome<br>3 mg/kg/week for 10 weeks | Good tolerability of infusions<br>No demonstration of efficacy on atheroma |
| MODE (P2) | 23 | Homozygous Familial Hypercholesterolemia<br>8 mg/kg 12 doses over 24 weeks | Reduction of carotid atherosclerosis at 6 months |
| EXPRESS (P2) | 12 | Heterozygous Familial Hypercholesterolemia<br>8 mg/kg/week for 6 weeks | No demonstration of efficacy on atheroma |
| TANGO (P3) | 30 | Familial Hypoalphalipoproteinemia<br>8 mg/kg 19 doses over 24 weeks | Good tolerability of infusions<br>No demonstration of efficacy on atheroma |

**New phase Phase 2 study**

| | | | |
|---|---|---|---|
| RACERS (P2) | 20 | **Sepsis-induced Acute Kidney Injury**<br>5, 10, 20 mg/kg BID 8 doses over 6 days | Ongoing |

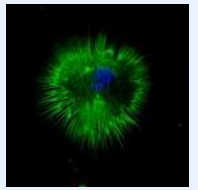
# Bio-HDL : 3 major efficacy impacts for Ophthalmology


## Elimination of lipid disorders : *"Scavenger"*

- **Non-cellular interactions**
  - Removal of toxic lipids (LPS) and lipid deposits (LCAT)
- **Cellular interactions**
  - Lipid elimination (atherosclerosis)
  - Lipid reorganization (glomerulopathy, kidney)

## Endothelial protection : "Vascular protection"

- **Stabilize intercellular junctions**
- **Cytoskeletal rearrangement**
- **Antioxidant**
- **Vasodilator**
- **Anti-apoptotic (limits programmed cell death)**



## Systemic anti-inflammatory

- Macrophage-induced inflammation
- Endothelial Inflammation
- Targeting of the complement

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# No direct competition: CER-001 is the only recombinant HDL in development

| Code | Product | Company | Status | Patients | Completion |
|---|---|---|---|---|---|
| CSL-112 | Human derived HDL (purified endogenous from plasma) | CSL | Phase 3 ongoing | 17'000 ACS patients | June 2023 |
| ETC-216<br>MDCO-216 | ApoA-I Milano (mutated form of ApoA-I) phospholipid complex | The Medicine Company<br>now Novartis | Terminated after Phase 2 PoC | 126 ACS | July 2017 |
| CER-001 | Recombinant HDL (unmutated ApoA-I) | Abionyx | Phase 2 | 20 AKI patients | June 2022 |

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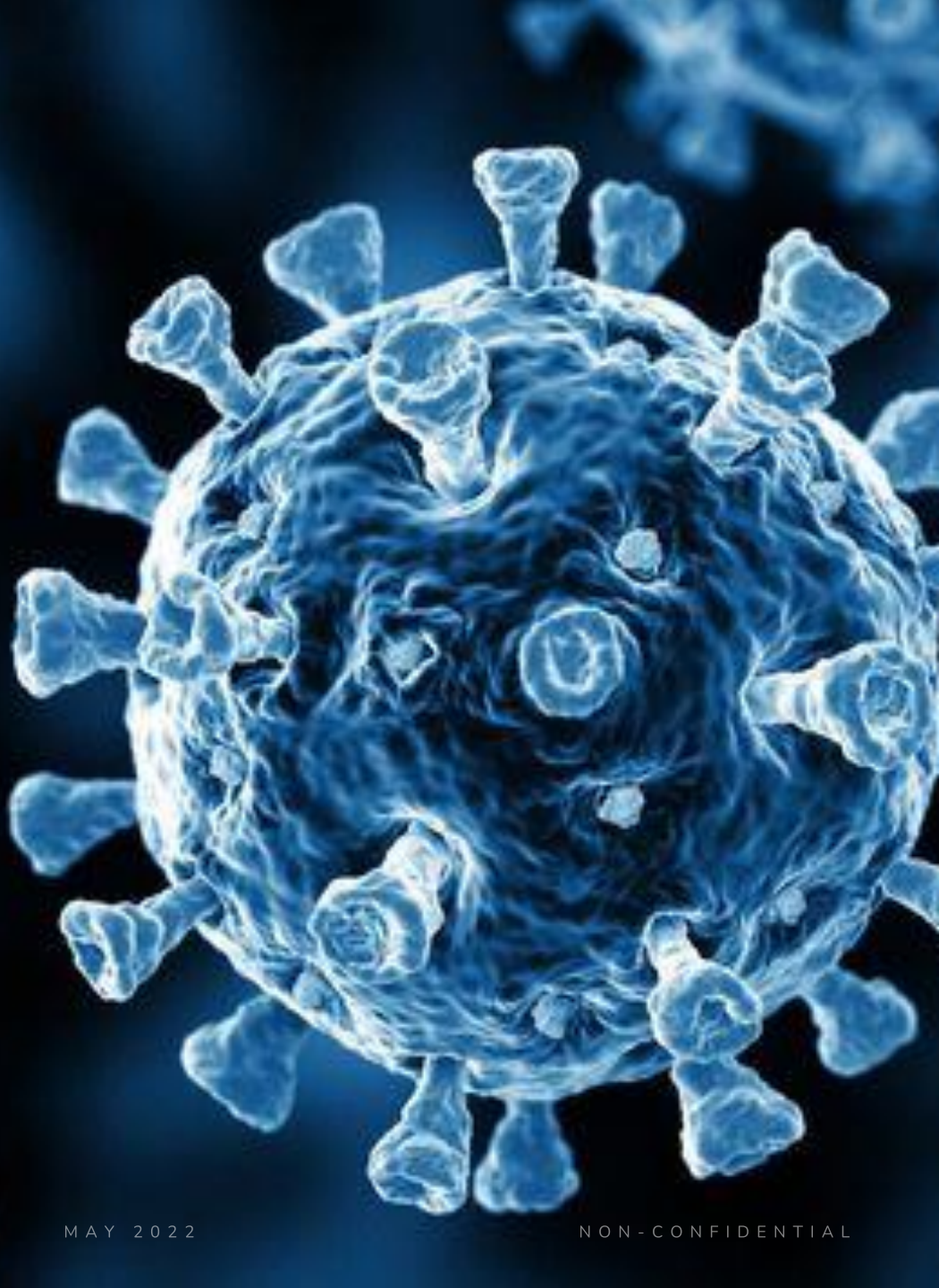
# 3. COVID-19



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biomedicines

# Compassionate use program in COVID-19

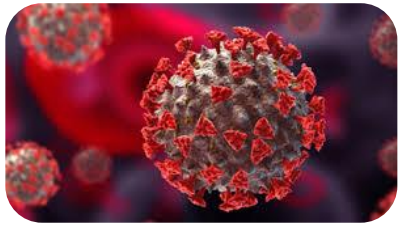
COVID-19 is associated with respiratory symptoms characterized by acute lung injury, rapidly progressing to acute respiratory distress syndrome

The pulmonary dysfunction is rapidly accompanied by a major "cytokine storm" when inflammatory cytokines are released abundantly into the bloodstream leading to host tissue damage (https://doi.org/10.1016/j.immuni.2020.04.003)

Decreased levels of total cholesterol, LDL and HDL have been observed in patients with COVID-19 infections. In addition, major changes in HDL proteome and decreased HDL functionality has been observed in severe COVID-19 patients (https://doi.org/10.1038/s41598-021-81638-1)

Hypothesis: lipid abnormalities could be modified by pharmacological agents that increase plasma ApoA-I and HDL levels and increase the number of functional, anti-inflammatory HDL particles

**Compassionate Access Authorization for CER-001 in COVID-19**



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# 4. LCAT Deficiency

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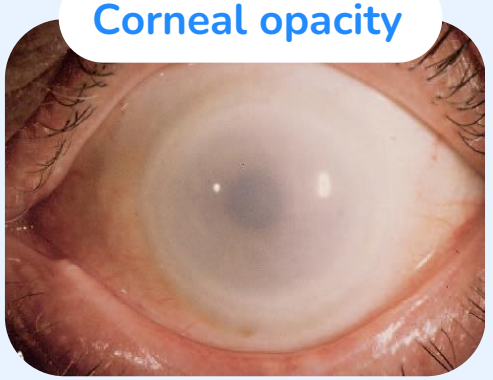
# Emblematic ultra-rare disease for nephrologists: LCAT deficiency

**A severe systemic disease affecting mainly the kidneys but also the cornea**

- Diminished plasma HDL
- Corneal opacities
- Hypertriglyceridemia
- Proteinuria
- Chronic and end-stage renal failure related to glomerural deposits of abnormal lipoproteins (3rd or 4th decade)
- Presence of LpX (proteoliposome: PL, CNE, TG & Albumin)

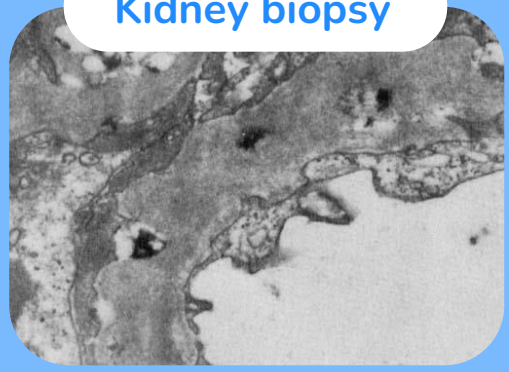
**A severe disease with no existing treatment to demonstrate proof of efficacy of CER-001**

## Corneal opacity



Corneal opacity in patient with LCAT deficiency (Viestenz et al, 2002),

## Kidney biopsy



Kidney biopsy of patient with LCAT deficiency. Capillary lumen (lower right), thickened basement membrane with lipid-filled vacuoles. and fusion of foot processes can be seen (Frohlich et al, 1978).

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# Clinical Proof-of-Concept in ophthalmology

Pr. Faguer

**The ability of ApoA-I to decrease corneal opacification** in Fish-Eye Disease opens the way for interventional studies evaluating a bio-HDL in patients developing corneal lipid deposits of different origins (lipid keropathy, corneal dystrophy…)

# Positive clinical results in a renal indication that is also ophthalmologic for a bio-HDL

- ATUn at the Toulouse-Rangueil Hospital to treat LCAT deficiency, an ultra-rare disease with both renal and ophthalmic manifestations (Fish-Eye Disease)
- A patient with severe progressive renal failure
  ready to receive dialysis and suffering from significant lipid deposits in the cornea
- In addition to avoiding dialysis, patient's clear vision was restored, demonstrating the systemic mechanism of action of CER-001 to remove lipids from the cornea, a breakthrough innovation in ophthalmology


Annals of Internal Medicine

LATEST ISSUES IN THE CLINIC JOURNAL CLUB MULTIMEDIA CME / MOC AUTHORS / SUBMIT

Letters | July 2021

**Administration of the High-Density Lipoprotein Mimetic CER-001 for Inherited Lecithin–Cholesterol Acyltransferase Deficiency**

Stanislas Faguer, MD, PhD, Magali Colombat, MD, PhD, Dominique Chauveau, MD, PhD, ... View all authors

Beyond its role in prevention of glomerular complement deposition, CER-001 may also exert beneficial action in familial LCAT deficiency by restoring systemic levels of competent HDL, acting at early steps of reverse cholesterol transport (not demonstrated here), and by acting as a fully active agent of innate immunity. In [illegible] HDL can [illegible] complement activation and cholesterol crystal–induced inflammation. In familial LCAT deficiency, low HDL cholesterol levels within tissues may have potentiated complement activation by abnormal LpX lipoproteins, which have a lipid-rich surface mimicking bacterial membranes (5).

The clear improvement of the patient's blurred vision at the end of follow-up and previous data showing the role of apoA-I in the development of corneal clouding and blurred vision lays the groundwork for interventional studies evaluating CER-001 in patients who develop lipid corneal deposits from other causes (such as secondary lipid keratopathy or inherited corneal dystrophy). We hope that this case report will draw attention to CER-001 as a novel, immediately available treatment option for patients with familial LCAT deficiency and that this will provide further data for the use of CER-001 in this disorder.

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# Treatment of CER-001 in severe FLD patient improved kidney function and lipoprotein profile

- Double Orphan Drug Designation received from FDA and EMA
- Named compassionate treatment with CER-001 of an Italian patient with LCAT deficiency was authorized by the Friuli Venezia Giulia Regional Ethical Committee, (Opinion CEUR-2020-EAP-012-ASUFC) in February 2020.
- The worsening of kidney function in the patient was slowed by CER-001 infusions. Kidney biopsy showed a reduction of lipid deposits and a stabilization of the disease.
- The patient presented with dramatically low HDL-cholesterol, and abnormal prominent large lipoprotein complexes, named LpX, which are known to be toxic to the kidneys. Treatment with CER-001 led to a normalization of the lipoprotein profile, with a decrease of LpX in favour of normal-sized lipoproteins.
- Clarification of the mechanism of action: Incubation of podocyte cells with the patient's plasma collected at different time points before and during CER-001 treatment progressively led to less lipid accumulation in kidney cells, confirming that the drug-induced remodelling of plasma lipoproteins is responsible for the reduced cholesterol deposit in cells.

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# 5. Sepsis-Induced Acute Kidney Injury

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# Ongoing phase 2a study: RACERS

CVBF Consorzio per Valutazioni Biologiche e Farmacologiche

- Randomized, open-label, placebo-controlled, parallel-group study evaluating the safety and efficacy of CER-001 in ICU patients with sepsis and high risk of AKI (SOFA/ Sequential Organ Failure Assessment score)

- 20 patients randomized to receive 8 doses of CER-001 or placebo over 6 days
- Primary endpoint of the study: onset and severity of AKI according to KDIGO criteria, as well as safety and tolerability of dosing regimens to select the optimal dose of CER-001
- 2 highly committed Italian KOL experts: Prof. Loreto Gesualdo, Head of Unit of Nephrology, Dialysis and Transplantation and Prof. Salvatore Grasso: Head of Unit of Anesthesia and Intensive Care with potential recruitment from two additional units within the same hospital (Anesthesia and Resuscitation Unit and Urology Unit)
- Rationale: Latest publication (01/2021) demonstrating the major role of HDL in the survival of septic patients treated in the ICU and the correlation between the decrease in HDL level over the first 3 days and the survival of patients

**Interim results in April 2022**

**Initiation of a Phase 2a study**


Initiation of a Phase 2a study with CER-001 in patients with sepsis at high risk of developing acute kidney injury

- Clinical study in partnership with the University of Bari and the CBVF consortium and fully funded
- ATUn showed promising efficacy in severe kidney disease
- Evaluation of the clinical activity of CER-001 in the prevention of acute kidney injury in intensive care unit patients with sepsis
- A potentially modifying effect on the progression of the inflammatory cascade in sepsis

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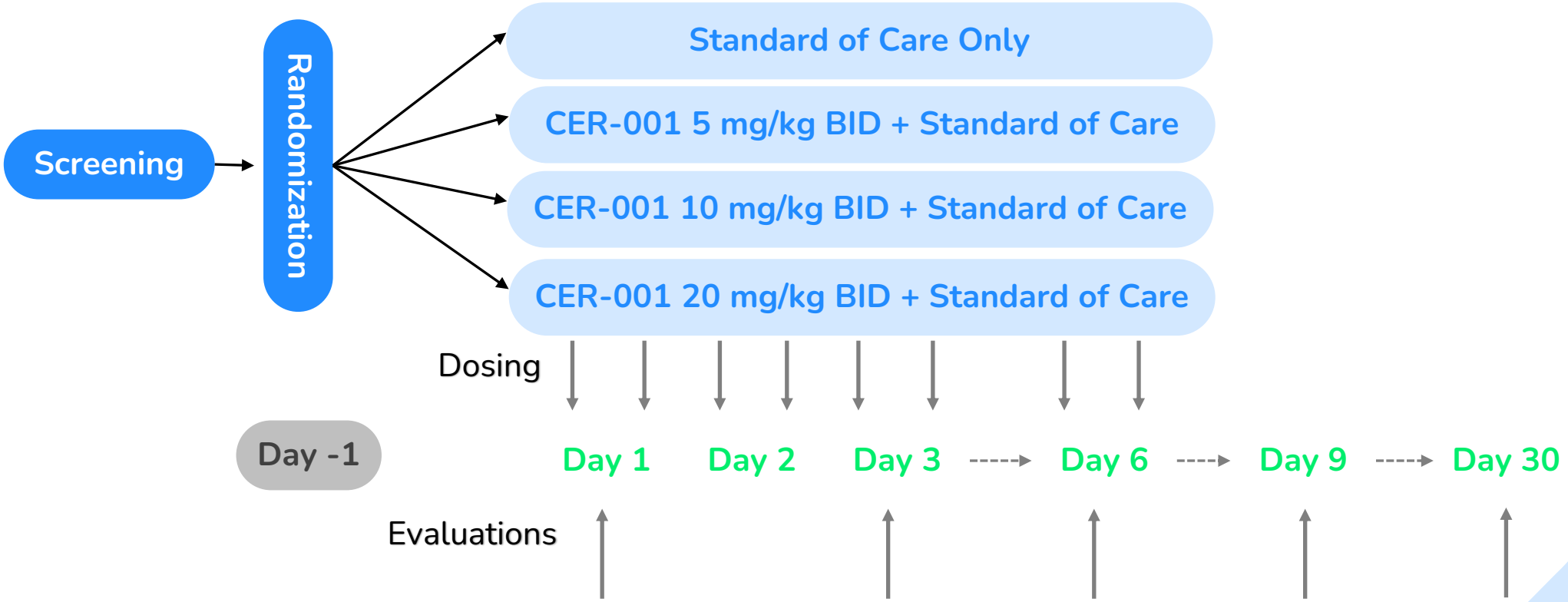
# RACERS Study

## Treatment protocol - 5 patients per group



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# Positive Interim Results from Phase 2a Clinical Trial Evaluating CER-001 in the Treatment of Septic Patients at High Risk of Developing Acute Kidney Injury

- Rapid reversal of cytokine storm in septic patients
- Enhanced resolution of biomarkers for inflammation including leukocytosis compared to standard of care
- No treatment-related serious side effects

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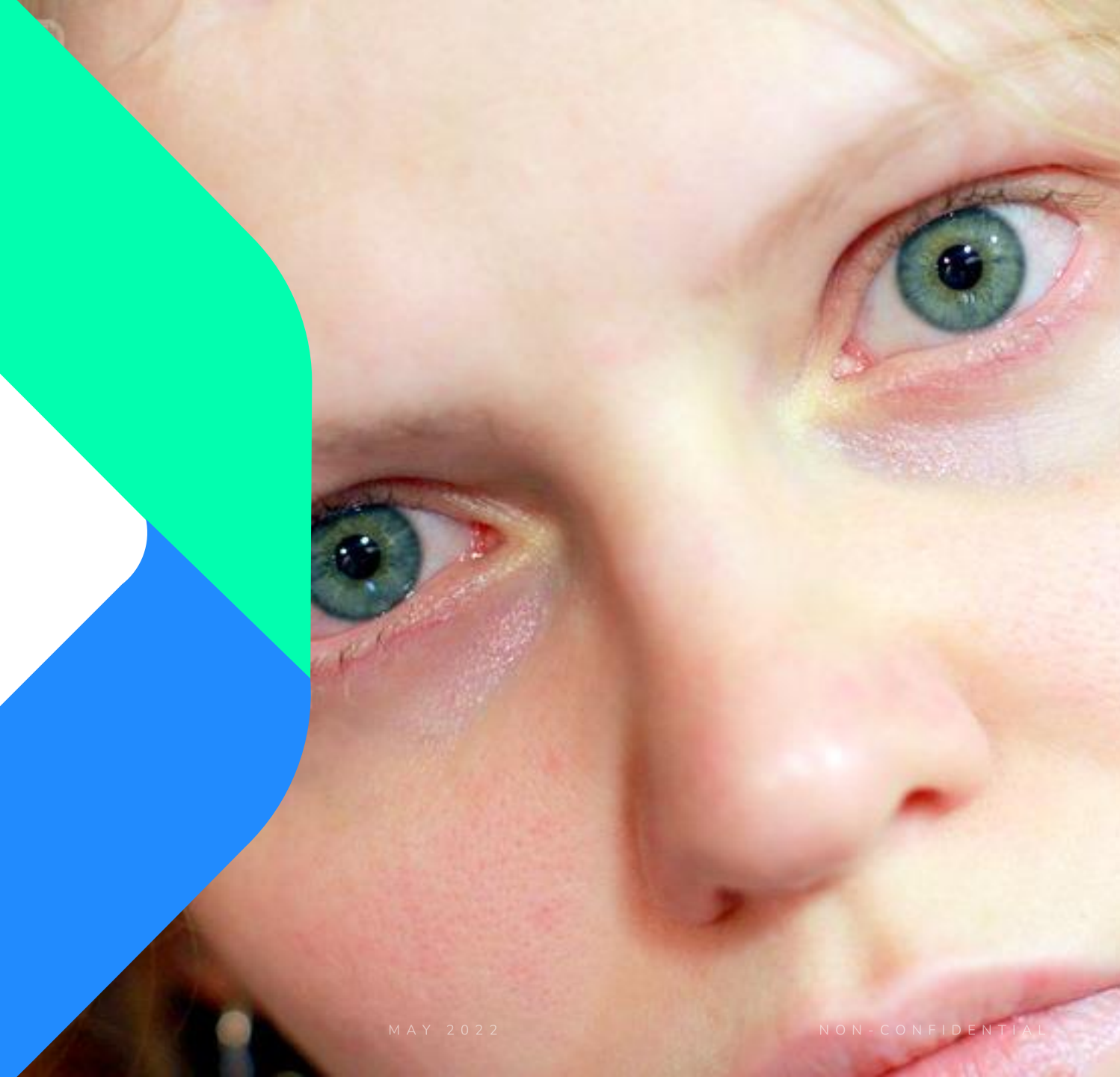
# 6. Uveitis



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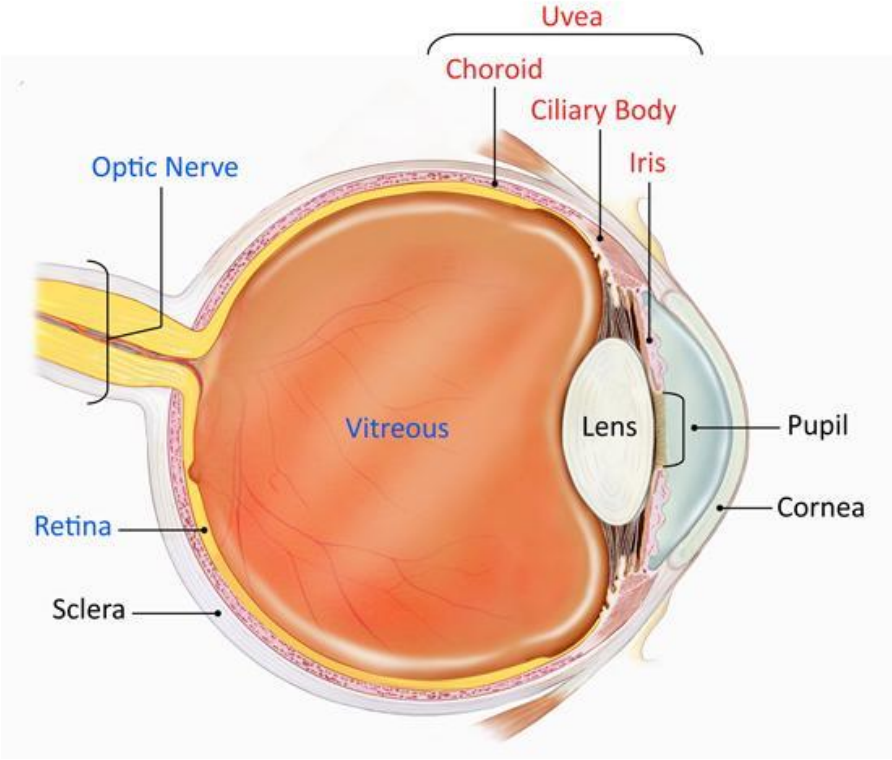
# Uveitis is a systemic inflammatory disease affecting the uvea



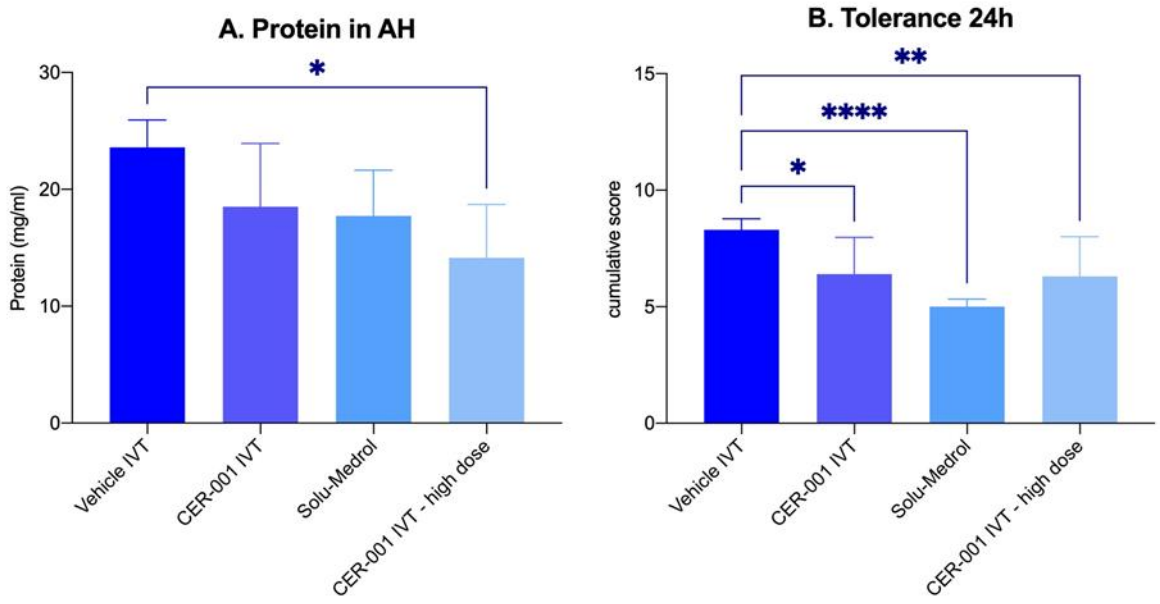

- Uveitis affects approximately 200 person per 100,000 in the western population
- More than half of all patients with uveitis develop complications related to their disease, and up to 35% of patients suffer severe visual impairment. Uveitis is believed to account for 5% to 10% of all causes of legal blindness in the United States and Europe
- The causes of uveitis are numerous including infections, trauma, non infectious systemic or ocular disease, and masquerade syndromes

Source: International Ophthalmology Clinics: Spring 2010 - Volume 50 - Issue 2 - p 1-17

# ABNX-1101: Effect on the modified McDonald-Shadduck score in the rabbit EIU model

**24 hours after the induction of inflammation and the treatment with CER-001:**

- Graph A reports the protein concentrations in the aqueous humor. In the intravitreal injection route, CER-001 strongly reduces the protein concentration and thus has an effect in LPS-induced uveitis.
- Graph B summarizes the cumulative slit lamp scores. For this evaluation, several concentrations of CER-001 showed a reduction in the signs of LPS-induced inflammation in this model of uveitis.




**In conclusion, CER-001 is effective in reducing signs of inflammation in the LPS intravitreal injection-induced model in a preclinical model.**

# The support of prestigious KOL in ophthalmology

- **Prof. Christophe Baudouin**, Professor of Ophthalmology in Paris, Head of the Ophthalmology Department at the Centre Hospitalier National d'Ophtalmologie de l'Hôpital des Quinze-Vingts (Paris), Director of the "S12" research team at the Institut de la Vision, and member of the prestigious international societies, American Society of Ophthalmology and Academia Ophthalmologica Internationalis, states: "The latest scientific work in the field shows that lipids and their metabolism are involved in many ocular pathologies, for example Meibomian gland dysfunction, and macular degeneration. By testing CER-001, a biomimetic HDL produced in France, in models of ocular pathology, we will be able to help choose the best ocular indication for this product, with the aim of providing patients with a new and effective treatment."

- **Prof. Catherine Creuzot-Garcher**, Professor of Ophthalmology in Dijon, Head of the Ophthalmology Department of the Dijon University Hospital, University Professor, co-leader of the Eye, Nutrition and Cellular Signaling team at the Dijon Scientific Center for Taste and Food, and Dr. Niyazi Acar (PhD), leader of the Eye, Nutrition and Cellular Signaling team at the Dijon Scientific Center for Taste and Food state: "Studying and developing the therapeutic potential of CER-001, a biomimetic HDL, in the treatment of eye diseases will allow us to better understand the role of lipids in the physiology and dysfunctions of the eye, particularly in the retina, and to provide our patients with an innovative solution for the future. "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# Why invest in ABIONYX

- One of the most advanced bioproduct with renewed IP (+20 yrs) including ophthalmology and biomanufacturing
- Several phase 2 trials and 1 MA by 2025
- A large portfolio of medical indications and bio/CRO activities that diversify the overall risks
- Committed teams, significant shareholders of the new company

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