Overview of Featured Projects

LHON Collective's **Vision Hope Now** campaign is a global initiative dedicated to accelerating progress toward a cure and improving the lives of those affected. By partnering with the Milken Institute, leading clinicians, and researchers to create a landscape analysis and opportunity map, a clear, coordinated path forward has emerged to advance LHON research. The following are featured projects highlighting how LHON Collective will execute on each of the goals.

Goal 1 Biological & Data Resources

1a: LHON Biorepository and iPSC Library

A $100,000 annual investment over three years will establish and expand a vital LHON biorepository in partnership with COMBINEDBrain. This funding will directly support the collection of patient blood samples and the process of reprogramming them into induced pluripotent stem cells (iPSCs) from 6+ people each year.

By making these critical human cell lines available to the scientific community, this initiative will complement existing animal models and create a more robust, translational research ecosystem to accelerate therapeutic development for LHON. Revenue generated from these distributions will be reinvested by LHON Collective to produce more iPSC lines so this becomes a self-sustaining project.

1b: LHON Natural History and Biostatistics Program

A $75,000 annual investment will expand LHON Collective's established Data Collection Program, which already includes over 250 enrolled individuals affected by or at risk for LHON. Funding will support participant recruitment, longitudinal follow-up, data management, quality assurance, and integration of clinical information and participant-submitted genetic testing reports. Regular participant updates create a robust natural history dataset that captures the progression of LHON over time.

This investment will also support a formal natural history study, generating evidence to define disease progression, identify clinical trial endpoints, and strengthen future regulatory and clinical trial submissions.

Ways to Give

Follow the Journey

LHON Collective

Goal 2 Scientific Models

2a: Mitochondrial Gene Editing Models

A **$125,000 investment ($25,000 annually over five years)** will enable a specialized team at a premier research laboratory in Cambridge, UK, focusing on LHON. This initiative will advance work in mitochondrial gene editing, beginning with the validation and enhancement of an LHON mouse model to drive targeted therapeutic advancements.

This investment benefits from a multiplier effect by activating matching contributions and becomes a catalyst for LHON focus that builds on programs supported by the UK government, a major non-profit, and other philanthropic funders. This leveraged financial model ensures that donor support is amplified to strengthen preclinical tools and fast-track the development of effective treatments.

2b: Patient-Derived Cell Models

A $100,000 annual investment will support researchers in developing next-generation human models for LHON using patient-derived induced pluripotent stem cells (iPSCs). Funding will accelerate the creation of retinal ganglion cells, optic nerve, glial cells, and other advanced human cellular models that address critical gaps in LHON research.

By supporting the development and broad availability of these research models, this initiative will complement existing animal models and strengthen the translational research ecosystem. More representative human models will enable researchers to better understand disease mechanisms, identify therapeutic targets and biomarkers. Promising treatments can then be better evaluated before they enter clinical trials, accelerating the development of new therapies for LHON.

Goal 3 Therapeutic Discovery

3a: Collaborative Research Awards

LHON Collective seeks to launch a series of collaborative awards that will foster research across institutions and disease mechanisms to understand why some individuals with LHON mutations develop vision loss while others remain unaffected. By investigating genetic, metabolic, and environmental factors that confer resilience, institutions and researchers can identify new therapeutic targets and uncover protective mechanisms that may prevent or restore retinal ganglion cell degeneration. **These awards will consist of Discovery ($25,000), Targeted ($50,000), and Catalytic ($100,000)** funding levels that span research across early-stage hypotheses, translational validation, and proof-of-efficacy stages of development. The insights generated from this work will advance therapies and help address unanswered questions in LHON.

3b: AI-Driven Therapeutic Repurposing

The goal is to fund collaborations with leading technology platforms to identify potential efficacy of repurposed therapeutics. The leading drug-repurposing technology platforms today have a great depth of understanding of the medicines themselves, but need to be trained on the most current characterization of rare diseases, such as LHON.

LHON Collective plans to **invest $100,000 / year** in an LHON-specific model incorporating the most current definition of LHON and underlying cellular mechanics. The expected output may identify up to 20 repurposed therapeutic candidates to then be prioritized by leading LHON clinical researchers. Subsequent annual funding will focus on assessing human benefit. By leveraging AI, the LHON community can help advance promising therapies toward preclinical and clinical development faster than traditional discovery approaches and offer a proof-point for other rare diseases.

3c: Optic Nerve Protection and Restoration

This funding aims to expand the frontier of optic nerve research with a specific focus on translating advances into LHON. While much of the current progress in optic nerve regeneration is driven by studies in larger diseases such as glaucoma, this initiative will encourage researchers to explore how these approaches can apply to LHON and other rare optic neuropathies. With **an initial investment of $50,000 per year**, the program will support a partnership with the RReSTORe Consortium, that builds on other NIH and ARPA-H funded research to consider novel approaches of protecting and recovery of function.

The research will focus on identifying both shared and distinct biological mechanisms across optic nerve diseases, determining where existing restorative strategies may be effective for LHON and where tailored, disease-specific approaches are required. The insights generated from this work will provide critical preliminary data to support a larger funding proposal to the NIH. Ultimately, this effort seeks to lay the groundwork for a more effective and potentially disease-agnostic framework for restoring optic nerve function, aiming to accelerate meaningful therapeutic advances for individuals affected by LHON.

Goal 4 Community and Scientific Engagement

4a: LHON Community Conference

Funding will support the 2027 LHON Conference. Over the years, this has proven to be one of the most impactful ways to build a strong LHON community. **Sponsorship of $50,000** will bridge the gap of conference expenses not covered by registration fee revenue. This will enable successful delivery of the event and financial support for LHON community members who would otherwise be unable to attend.

4b: Scientific Engagement and Partnership Development

A $15,000 annual investment supports volunteers from LHON Collective to bring expertise and lived experience to key scientific symposia, industry gatherings, and translational research forums where new technologies, therapeutic platforms, and collaborative opportunities are emerging. By establishing a presence in broader ophthalmology, neuroscience, mitochondrial disease, and biotechnology communities, LHON Collective is raising awareness of the unmet needs of individuals living with LHON, building relationships with leading researchers and companies, and identifying opportunities to apply existing technologies to our rare disease.

As LHON often lacks the visibility needed to attract scientific and commercial interest, strategic engagement at these events is critical to positioning the disease as a compelling area for innovation and investment. This initiative aims to foster cross-disease collaboration, catalyze new research partnerships, and expand the network of investigators and organizations working to accelerate the development of treatments for LHON.

4c: Global Scientific Strategy Summit

Milken Institute helped facilitate the first LHON Scientific Retreat in Portugal, which proved to be an important catalyst for researchers outside of LHON to join LHON-focused experts from around the world in exploring gaps, prioritizing research, and encouraging collaboration. **A $125,000 investment** will support the second invitation-only LHON Scientific Strategy Summit, bringing together experts in mitochondrial biology, ophthalmology, neuroscience, gene therapy, optic nerve regeneration, artificial intelligence, and related fields. Building on learnings from the inaugural summit, this collaborative forum will evaluate relevance of emerging technologies, foster new partnerships, and focus research priorities to accelerate LHON scientific progress.

By bringing together expertise from within and beyond the LHON community, the summit will develop a coordinated roadmap for future research, attract new investigators, and advance the most promising opportunities for therapeutic development.

Goal 5 Funding Progressive Innovation

Sustainable Research Fund

This model transforms philanthropic giving into a sustainable engine for innovation. This initiative establishes **an initial $500,000 investment** vehicle enabling LHON Collective to co-invest directly in the expansion of innovative therapeutic approaches. Specifically, these funds will be used to enable new trials as well as LHON sleeves of already established clinical trials for broader mitochondrial or vision-related conditions.

As LHON is a rare disease, many research programs do not prioritize an LHON cohort unless additional funding is provided. By carefully deploying this catalytic capital with expert input, we can move forward with potential treatment options that may otherwise never reach our community. When these co-invested trials achieve commercial success, returns have the potential to provide revenue that is recycled into progressive therapeutic approaches, creating self-sustaining funding for future scientific advancements.