SUMMARY STATEMENT

PROGRAM CONTACT: *(Privileged Communication)*
[redacted]
[redacted]

Release Date: 02/24/2026
Revised Date:

Application Number: 1R44EY131547-01

Principal Investigators (Listed Alphabetically):
[redacted] (Contact)
[redacted]
[redacted]

Applicant Organization: [redacted]

Review Group: ZRG1 BTSS-E (15)
Center for Scientific Review Special Emphasis Panel
Small Business: Bioengineering, Technology and Surgical Sciences

Meeting Date: 01/22/2026
Council: JAN 2026
Requested Start: 07/01/2026

Opportunity Number: PA-24-246
PCC: EYS -SO

Project Title: Lipid Nanoparticle-Mediated Gene Therapy for Inherited Retinal Dystrophy: From Preclinical Validation to IND-Enabling Studies

SRG Action: Impact Score:33
Next Steps: Visit https://grants.nih.gov/grants/next_steps.htm
Human Subjects: 10-No human subjects involved
Animal Subjects: 30-Vertebrate animals involved - noass. conditions noted
Participant Sex:
Participant Race and Ethnicity:
Participant Age:
0-No human subjects

Project Year	Direct Costs Requested	Estimated Total Cost
1	298,450	369,878
2	945,620	1,172,568
3	889,340	1,102,781
TOTAL	**2,133,410**	**2,645,227**

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

1R44EY131547-01 [redacted]

RESUME AND SUMMARY OF DISCUSSION: The vote reflected a split among committee members. Summary of split: the choice of lipid nanoparticle delivery over established AAV vectors was considered a significant risk by some reviewers who questioned whether the potential advantages justified the additional development timeline, while others viewed the non-viral approach as a strength that could overcome AAV limitations including immunogenicity and cargo size constraints.

- The unmet need for effective treatments for inherited retinal dystrophies beyond those addressable by AAV vectors was considered significant.
- The lipid nanoparticle platform was considered innovative but carries risk given the established success of AAV in ocular gene therapy.
- The preclinical approach using well-characterized animal models was considered rigorous.
- Concerns about the manufacturing scale-up pathway and the timeline to IND filing were noted.
- Commercialization was assessed as adequate but dependent on successful demonstration of LNP advantages over AAV.

DESCRIPTION (provided by applicant): This Fast-Track SBIR project proposes to develop and validate a novel lipid nanoparticle (LNP) delivery system for gene therapy targeting inherited retinal dystrophies that cannot be addressed by current AAV-based approaches due to cargo size limitations or immunogenicity concerns. The innovation enables delivery of full-length therapeutic transgenes up to 12 kb directly to retinal photoreceptors, overcoming the ~4.7 kb packaging limit of AAV vectors. Phase I will complete formulation optimization and demonstrate therapeutic gene expression in two validated mouse models of retinal degeneration, with advancement contingent on achieving expression levels sufficient for functional rescue. Phase II will conduct IND-enabling studies including GLP toxicology in non-human primates, manufacturing process development, and preparation of regulatory submissions. Preliminary data demonstrate successful LNP-mediated delivery of reporter genes to photoreceptors in wild-type mice with expression persisting for 16 weeks post-injection, and initial efficacy data in the rd12 mouse model showing partial rescue of electroretinogram responses.

PUBLIC HEALTH RELEVANCE: Inherited retinal dystrophies affect approximately 200,000 Americans and represent a leading cause of childhood and adult-onset blindness for which limited treatment options exist. While AAV-based gene therapy has shown promise, the majority of causative genes exceed AAV packaging capacity. The proposed LNP platform could enable gene therapy for these currently untreatable conditions, potentially preserving vision in patients who would otherwise progress to blindness.

CRITIQUE 1

Significance: 2

Investigator(s): 2

Innovation: 3

Approach: 5

Environment: 2

Overall Impact: This application proposes development of an LNP-based gene therapy platform for inherited retinal dystrophies. The unmet need is clear and the non-viral approach is innovative. However, the choice to pursue LNP over the established AAV platform introduces significant risk. The preclinical data are promising but preliminary, and the Approach has notable weaknesses in the manufacturing and regulatory timeline. The team is qualified and the environment is strong.

1. Significance:

Strengths

- Inherited retinal dystrophies represent a significant unmet clinical need with limited treatment options.
- Many causative genes exceed AAV cargo capacity, creating a clear rationale for alternative delivery platforms.

Weaknesses

- For genes that fit within AAV capacity, the advantage of LNP over established AAV approaches is not clearly articulated.

2. Investigator(s):

Strengths

- The team includes strong expertise in retinal gene therapy, lipid nanoparticle formulation, and regulatory science.
- The PI has a strong publication record in ocular drug delivery.

Weaknesses

- The PI has not previously led an IND-enabling program, which is a central deliverable of Phase II.

3. Innovation:

Strengths

- LNP delivery to photoreceptors is genuinely novel and could enable treatment of conditions currently beyond reach of AAV.
- The ability to deliver transgenes up to 12 kb is a significant advantage over AAV.

Weaknesses

- AAV-based ocular gene therapy has an established regulatory pathway and clinical track record. Choosing an unproven platform introduces substantial risk.
- The redosing advantage of LNP over AAV is theoretical and has not been demonstrated in the retina.

4. Approach:

Strengths

- The use of well-characterized mouse models (rd12, Cep290) for preclinical validation is appropriate.
- The Phase I go/no-go criteria are clearly defined with quantitative thresholds.

Weaknesses

- The manufacturing process development plan lacks detail. The transition from lab-scale to GMP production of LNP formulations is a known challenge not adequately addressed.
- The GLP toxicology study in non-human primates is described at a high level without sufficient detail on endpoints, group sizes, or the specific toxicology CRO.
- The timeline from Phase I completion to IND filing appears compressed given the complexity of CMC development for LNP products.
- Durability of expression beyond 16 weeks has not been demonstrated, raising questions about the therapeutic window.

5. Environment:

Strengths

- The university partnership provides access to GLP-compliant vivarium facilities and established retinal imaging capabilities.
- The contract manufacturing organization has prior experience with LNP products.

Commercialization Plan (Phase II and Fast-Track Only):

- The market analysis is reasonable given the orphan indication.
- Revenue projections assume successful IND filing which remains a significant milestone.

Vertebrate Animals:

Acceptable

Budget and Period of Support:

Recommend as Requested

CRITIQUE 2

Significance: 1

Investigator(s): 3

Innovation: 2

Approach: 4

Environment: 3

Overall Impact: The application addresses a significant unmet need with an innovative non-viral gene delivery platform. The preliminary data are encouraging though incomplete. The team has relevant expertise but the organizational capacity for IND-enabling work needs strengthening. The approach is scientifically sound but the regulatory and manufacturing pathway needs more development.

1. Significance:

Strengths

- Clear unmet need for gene therapy approaches that overcome AAV size limitations.
- The potential to treat currently untreatable inherited blindness is compelling.

2. Investigator(s):

Strengths

- Strong scientific expertise in LNP formulation and retinal biology.

Weaknesses

- Limited prior experience with GLP studies and IND submissions may present challenges in Phase II.
- The team would benefit from additional regulatory affairs expertise.

3. Innovation:

Strengths

- LNP delivery to photoreceptors is truly novel and addresses a real limitation of current gene therapy.
- The potential for redosing without immune responses is scientifically exciting.

4. Approach:

Strengths

- Well-designed preclinical studies with appropriate animal models.
- Clear go/no-go criteria with quantitative benchmarks.

Weaknesses

- The CMC development plan for LNP manufacturing at GMP scale needs significantly more detail.
- The 16-week expression data, while encouraging, may not be sufficient to support a single-injection therapeutic model.
- The NHP toxicology study design should be more fully described.

5. Environment:

Strengths

- Strong academic research environment with appropriate facilities.

Weaknesses

- The company is early-stage with limited infrastructure for IND-enabling activities.

Commercialization Plan (Phase II and Fast-Track Only):

- Adequate market analysis. Orphan drug designation pathway is appropriate.
- Partnership strategy for clinical development is described but not yet formalized.

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3

Significance: 2

Investigator(s): 2

Innovation: 2

Approach: 3

Environment: 2

Overall Impact: This is a well-conceived application proposing a novel approach to a significant unmet need in inherited retinal disease. The LNP platform offers genuine advantages over AAV for large-gene delivery. While risks exist, particularly in manufacturing and regulatory development, the scientific foundation is strong and the proposed work could generate data to advance this platform toward clinical translation.

1. Significance:

Strengths

- Clear and well-documented unmet need in inherited retinal dystrophies.
- The inability of AAV to deliver many causative genes creates a real therapeutic gap.

Weaknesses

- The application could more clearly distinguish which specific conditions would be targeted first.

2. Investigator(s):

Strengths

- Complementary expertise across LNP science, retinal biology, and device/drug development.
- Strong publication record and prior funding history.

3. Innovation:

Strengths

- The LNP approach is innovative and could open new therapeutic possibilities.
- Preliminary data demonstrating photoreceptor-targeted delivery are encouraging.

Weaknesses

- Long-term durability data are needed to fully validate the approach.

4. Approach:

Strengths

- Well-designed preclinical validation with appropriate models and endpoints.
- Phased approach with clear milestones is appropriate for the SBIR mechanism.
- Statistical analysis plans are adequate.

Weaknesses

- More detail on manufacturing process development would strengthen the application.

5. Environment:

Strengths

- Excellent research environment with access to specialized facilities.
- Strong institutional support documented.

Commercialization Plan (Phase II and Fast-Track Only):

- Credible commercialization plan with appropriate orphan drug strategy.

Budget and Period of Support:

Recommend as Requested

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: ACCEPTABLE.

PARTICIPANT SEX CODE: ACCEPTABLE

PARTICIPANT RACE AND ETHNICITY CODE: ACCEPTABLE

PARTICIPANT AGE CODE: ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Footnotes for 1R44EY131547-01; PI Name: [redacted]
NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-18-197 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-197.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

Center for Scientific Review Special Emphasis Panel

CENTER FOR SCIENTIFIC REVIEW

Small Business: Bioengineering, Technology and Surgical Sciences

ZRG1 BTSS-E (15)

01/22/2026

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-22-044 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-044.html, including removal of the application from immediate review.

CHAIRPERSON(S)

[redacted]
PROFESSOR
DEPARTMENT OF OPHTHALMOLOGY
UNIVERSITY OF IOWA
IOWA CITY, IA 52242

MEMBERS

[redacted]
ASSOCIATE PROFESSOR
DEPARTMENT OF BIOMEDICAL ENGINEERING
RICE UNIVERSITY
HOUSTON, TX 77005

[redacted]
PROFESSOR
SCHEIE EYE INSTITUTE
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PA 19104

[redacted]
ASSISTANT PROFESSOR
DEPARTMENT OF PHARMACOLOGY
VANDERBILT UNIVERSITY
NASHVILLE, TN 37232

[redacted]
ASSOCIATE PROFESSOR
DEPARTMENT OF CHEMICAL ENGINEERING
MIT
CAMBRIDGE, MA 02139

[redacted]
PROFESSOR
DEPARTMENT OF MOLECULAR BIOLOGY
UNIVERSITY OF TEXAS SOUTHWESTERN
DALLAS, TX 75390

[redacted]
ASSISTANT PROFESSOR

WILMER EYE INSTITUTE
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MD 21287

[redacted]
ASSOCIATE PROFESSOR
DEPARTMENT OF PHARMACEUTICAL SCIENCES
UNIVERSITY OF COLORADO
AURORA, CO 80045

[redacted]
PROFESSOR
DEPARTMENT OF GENETICS
WASHINGTON UNIVERSITY IN ST. LOUIS
ST. LOUIS, MO 63110

[redacted]
ASSOCIATE PROFESSOR
DEPARTMENT OF TOXICOLOGY
UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, NC 27599

[redacted]
ASSISTANT PROFESSOR
DEPARTMENT OF REGULATORY SCIENCE
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES, CA 90089

SCIENTIFIC REVIEW OFFICER

[redacted]
SCIENTIFIC REVIEW OFFICER
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

EXTRAMURAL SUPPORT ASSISTANT

[redacted]
EXTRAMURAL SUPPORT ASSISTANT
THE CENTER FOR SCIENTIFIC REVIEW
THE NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.