3RD ANNUAL

Nano-rare Patient Colloquium 2025

World-class Precision Medicine Centers:

Catalysts for Change in Nano-rare Disease Care

Sarah M. Glass, PhD
Chief Operating Officer

Treating Nano-Rare Patients Requires a Specific Regulatory and Clinical Approach

- Individual patients are treated under FDA ‘authorized’ Individualized ASO Research INDs
- n-Lorem is the regulatory sponsor of each IND
  - Not the same as a commercial drug development pathway
- Physicians are highly motivated, but most institutions are unfamiliar with n of 1 research studies
- Trial design pioneered by n-Lorem is a modified cross-over design which allows patients to be their own control
  - Compares baseline to on-treatment data within the same patient

Individualized ASOs: Funding Challenges Require Creative Solutions

- n-Lorem commits $1.2M for every patient's ASO program
  - n-Lorem must fundraise to support ASO program costs for all patients
  - As a non-profit, >88% of our funds go to patient costs
  - ASO Design and Discovery is rapid and cost effective; the majority of costs are incurred during ASO Development and Manufacturing
  - n-Lorem cannot fund the activities associated with carrying out the treatment protocol - different than commercial trials
- Institutions and physicians are responsible for finding approaches to fund the treatment administration and associated costs
  - Novel and unique operational, financial and risk-related challenges
  - Funding paths include:
    - Philanthropic / Research funds, Grants, Insurance, Patient support of fundraising, Federal/ State aid

Objectives

Raise awareness to the community of the requirements for institutions and physicians

Highlight key barriers and challenges for Institutions and Patients / Families with potential solutions

Share best practices and recommendations

3RD ANNUAL

Nano-rare Patient Colloquium 2025

I. Requirements of each Physician and Institution

Raise awareness to the patient community of the requirements for institutions and physicians

Physician and Institution Requirements for Collaboration Begin Upon Patient Acceptance

- Physician submits application
- Progress at every step by all parties as well as funding impacts overall program timelines

Pre-ASO Discovery Activities Set the Foundation for the Collaboration between the Institution and n-Lorem

Consent patient to research protocol, collect samples, **generate required cell line for ASO discovery**

Maintain clinic visits with patient to **collect pre-treatment data**

Develop and obtain **IRB approval** for a research protocol to collect patient cells

Execute **Material Transfer Agreement** for data and sample sharing with n-Lorem

Meet semi-annually with n-Lorem and communicate progress to the patient

As ASO Discovery Advances at n-Lorem, Parallel Activities at the Site are Initiated

Collect pre-treatment **baseline data**

Begin institutional review of **Treatment Evaluation Agreement (TEA)**

Identify individualized patient **treatment goals** and present to **STAR committee**

Begin securing necessary **funding / institutional support** for treatment

Meet quarterly with n-Lorem and communicate progress to the patient

Initiation of ASO Development Means a Clinical Candidate has been Identified: One Step Closer to Patient Dosing

Continue collecting pre-treatment **baseline data**

Continue securing **funding** / **institutional support** for treatment

Collaborate to develop treatment **protocol** and **informed consent form**

Provide **clinical content** for IND

Meet monthly with n-Lorem and communicate progress to the patient

The FDA is Supportive: Detailed Logistics are Finalized to Enable Patient Dosing

Complete **REDCap training** and attend remote **site initiation visit**

Meet bi-weekly with n-Lorem and communicate progress to the patient

Submit research study for **IRB approval**

Fully execute TEA to enable drug shipment

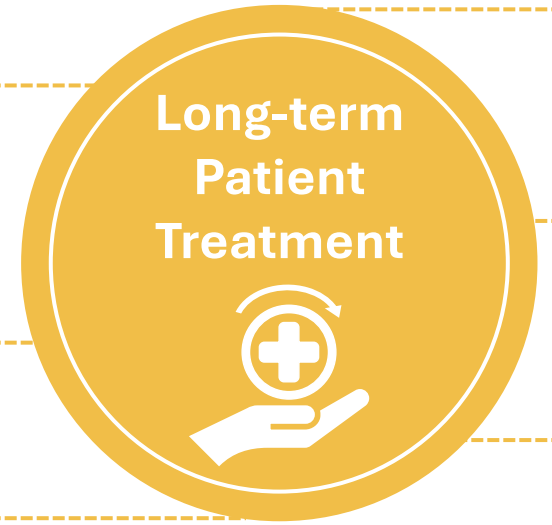
Schedule **patient's first and subsequent doses** and surrounding assessments

Meeting Long-term Regulatory Requirements and Supporting the Ongoing Treatment Decision

Provide data to n-Lorem and resolve queries in a timely fashion through **REDCap**

Maintain IRB approval and continuing review throughout life of study

Meet with n-Lorem monthly



Carryout treatment in accordance with protocol

Report safety data and adverse events to n-Lorem in accordance with regulatory guidelines

Provide **drug accountability** records to n-Lorem

3RD ANNUAL

Nano-rare Patient Colloquium 2025

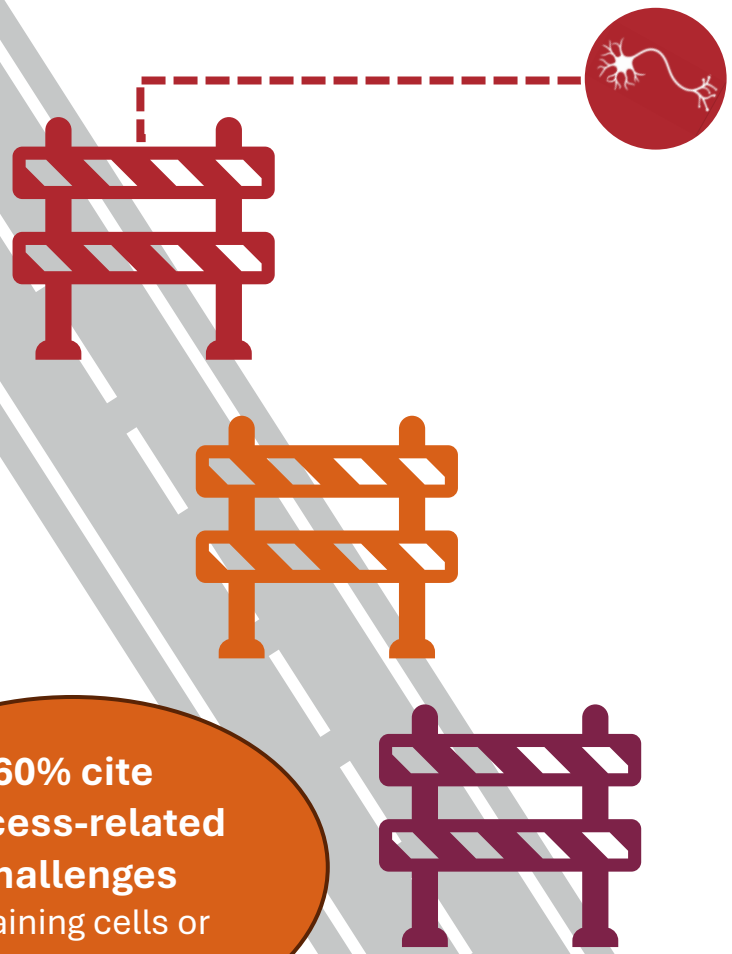
II. Key Barriers and Challenges

Highlight key barriers and challenges for Institutions and Patients / Families with potential solutions

Compelling Evidence for Consistent Challenges Across Institutions

- Obtained input from 26 investigators and co-investigators across 26 unique clinical sites who are actively working with n-Lorem at various stages
  - 14 / 26 respondents are physicians are treating patients currently
  - 12 / 26 respondents are supporting programs at various stages of Discovery and Development
- Key challenge areas assessed: Process, Funding, Patient Management, Institutional Support

Key Challenges Facing Physicians and Institutions



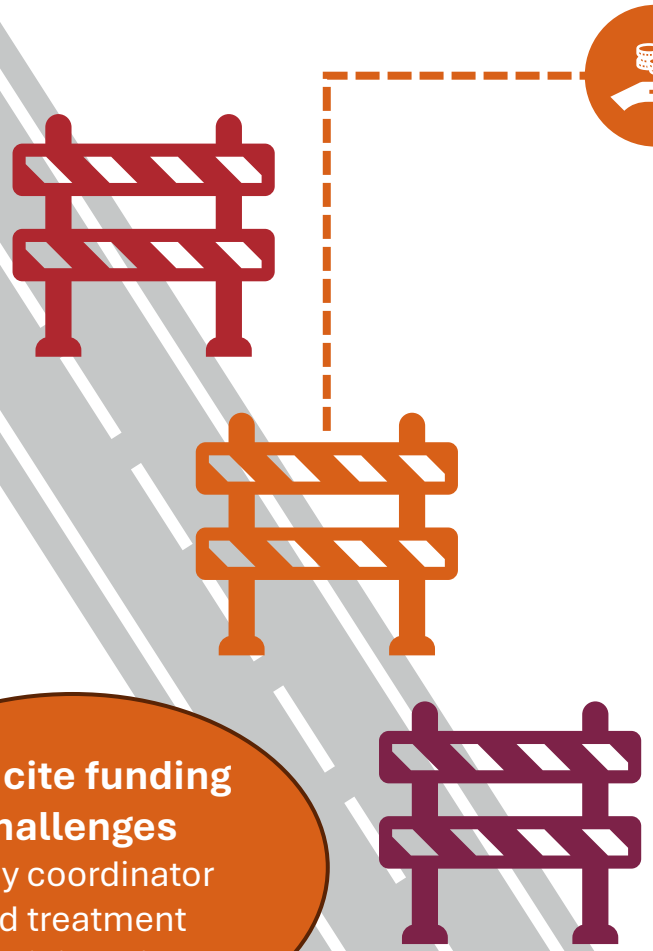
60% cite process-related challenges obtaining cells or IRB approvals

Obtaining the required cell line for n-Lorem's Discovery process:

- Requires an IRB approved research protocol which many physicians do not have
- Requires patient consent to sample collection which includes a blood draw or skin punch biopsy
- Timeline to generate cells can take between 3 to 12 months
- Cost to generate cells can be upwards of $10,000

Delays to the cell line generation process can significantly impact n-Lorem timelines

Key Challenges Facing Physicians and Institutions



88% cite funding challenges
study coordinator and treatment administration

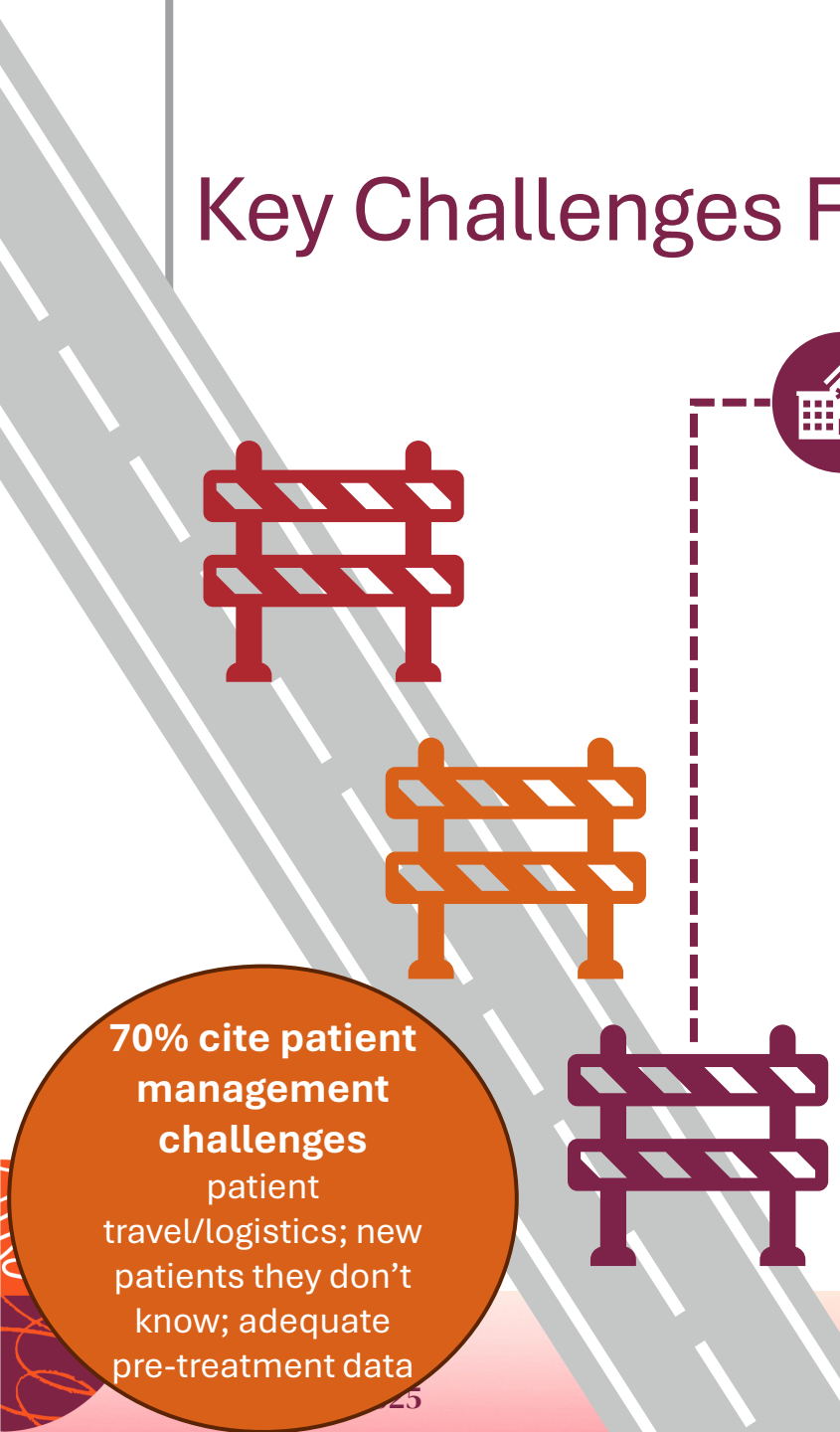
Securing necessary funding for treatment:

- Physician Time
- Pharmacy Costs
- Coordinator Time / Costs
- Treatment Costs (ex. Intrathecal administrations, hospital stays)
- Assessment costs

Collective goal to limit costs to patients, but physicians are limited by the constraints of their institution's infrastructure and policies

- Ability to use Philanthropic / Research Funds
- Ability to bill insurance

Key Challenges Facing Physicians and Institutions



Securing institutional support for working with n-Lorem:

- Data Ownership
- Publication Rights
- General support for n of 1 research studies which are unique

These terms are included in the Treatment Evaluation Agreement and **negotiation to date has taken between 3 months to 2 years** and significantly delay treatment timelines

70% cite patient management challenges
patient travel/logistics; new patients they don't know; adequate pre-treatment data

85% cite institutional support challenges
funding, n of 1 studies, contracting

3RD ANNUAL

Nano-rare Patient Colloquium 2025

Despite these challenges, the number of physicians and institutions collaborating with n-Lorem to treat patients continues to grow.

n-lorem FOUNDATION

3RD ANNUAL

Nano-rare Patient Colloquium 2025

n-Lorem Efforts to Enable Success Across Institutions

n-lorem FOUNDATION

Setting New Physicians and Institutions up for Success

Upfront site feasibility assessment before application submission helps to ensure physician / institutional readiness and commitment

Physician education to ensure a thorough understanding of the process and responsibilities ahead

Accept application submissions **by physicians** committed to fulfilling a long-term commitment to the patient program

Initiate Treatment Evaluation Agreement (TEA) reviews **early** in the process

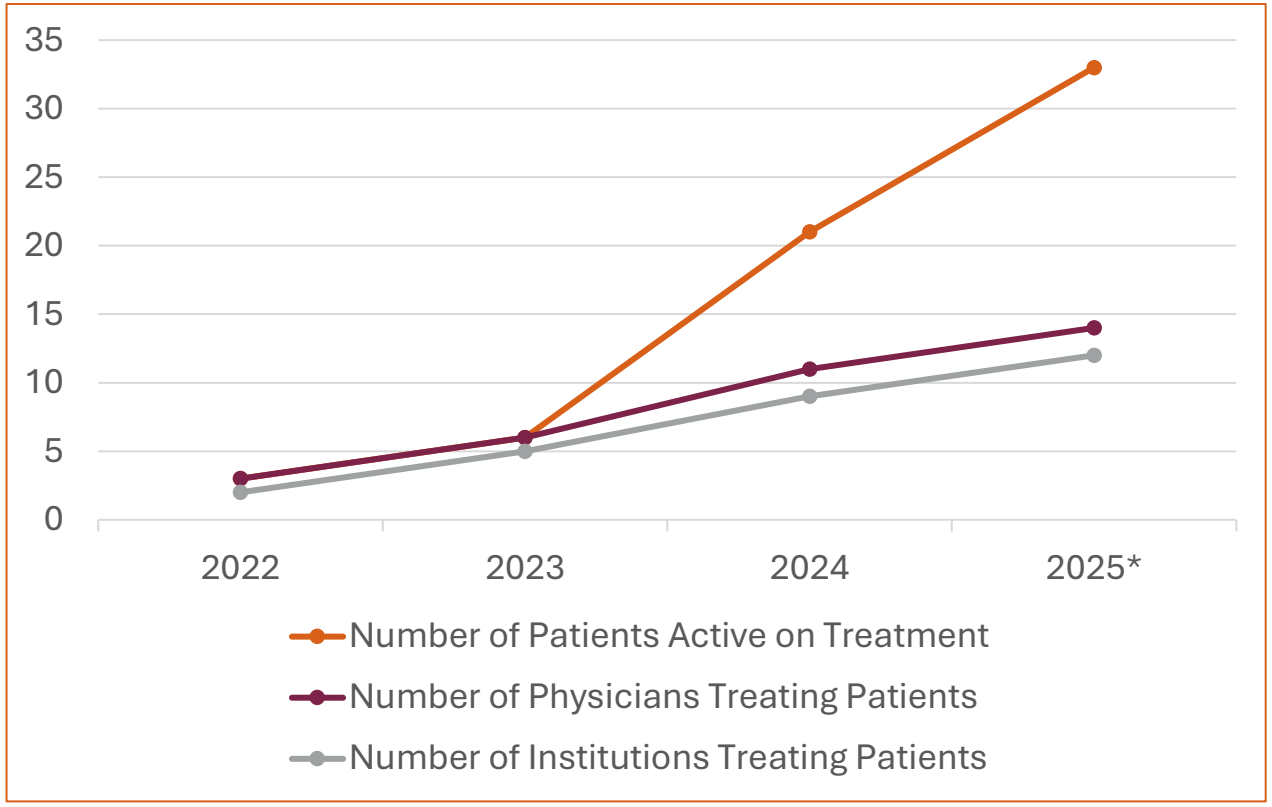
Setting Physicians and Institutions up for Success:
Addressing the Resource Challenge

- **Reduce physician and institution workload** by:
  - Authoring, submitting, and maintaining every IND
  - Building a custom REDCap for every patient
  - Facilitate all drug storage, shipment and treatment logistics to the greatest extent possible
- Provide support to physicians **applying for grants** to fund treatment costs
- Continue to research **insurance coverage** and better under landscape; pursue and participate openly
- Explore the **use of CROs** / centralized clinical trial units
- Explore supporting institutions using **other financial approaches**

An Increasing Network of Physicians and Institutions have Become Early Adopters

Year	# of Patients Active on Treatment	# of Physicians Treating Patients	# of Institutions Treating Patients
2022	3	3	2
2023	6	6	5
2024	21	11	9
2025*	33	14	12

*As of September 30, 2025



Expanding Distribution of Institutions Engaged with n-Lorem

Active patient treatment locations

Locations with initiated sites (ready to treat)

* Several locations/ sites are not represented here, as they are early in the initiation process.

3RD ANNUAL

Nano-rare Patient Colloquium 2025

V. Best Practices and Recommendations

Share best practices and recommendations

Share best practices and recommendations

Physicians / Institutions Considering Collaborating with n-Lorem

- ✓Start early: Institutional administration, legal approvals, sources of funding
- ✓Ensure commitment of patients and institution to treatment at your institution prior to application submission
- ✓Clear and consistent communication with patients and / or n-Lorem, our commitment is to do the same
- ✓Incorporate n-Lorem's timelines into your patient's overall treatment plan
  - disease progression and/or alternative treatment options considered against timelines

Share best practices and recommendations

Patients / Families Seeking Treatment and a Committed Physician

- ✓Identify a physician/ institution that you / your family could routinely visit and maintain continuity of care
  - Many pre-treatment and on-treatment clinic visits required in person, some overnight
  - Moving institutions after program acceptance can significantly delay or prevent ability to receive treatment
- ✓When seeking a physician, ensure they can support long-term treatment with n-Lorem ASO treatment
  - Not all physicians currently treating patients can treat additional patients
  - Each new patient and new ASO requires individual level funding and support from institution

Share best practices and recommendations

Patients / Families Preparing for Treatment or Actively Being Treated

- ✓Obtain clear understanding of patient financial responsibilities early in process
- ✓Participate fully in required clinical outcome assessments as described in protocol
  - These have been authorized by the FDA and approved by the IRB
- ✓Share openly with your physician any clinical observations, even if outside of protocol assessments
  - Unexpected improvements may necessitate the addition of novel assessments

Conclusions

Institutions and physicians tackle a broad range of tasks that are a) new to them and b) required to pursue patient treatment.

While there are barriers for Institutions and Patients / Families, progress is exemplified by the number of patients successfully being treated today.

Best practices enable more efficient on-boarding and broader interest in treating the nano-rare.

Treating Nano-Rare Patients with Experimental Medicines is Achievable

- We **applaud the pioneer physicians and institutions** who are treating or are committed to trying to treat
- We are **all early adopters** and are navigating a field that is rapidly evolving together
- **Early engagement** by all parties with institutional stakeholders adds efficiency and higher likelihood of success to the process
- The network of physicians working with n-Lorem **continues to increase** each year
- We look forward to enhancing existing and forging new institution collaborations in the coming year!

3RD ANNUAL

Nano-rare Patient Colloquium 2025

n-lorem FOUNDATION

Thank you!