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Application Requirements / Considerations

- Only US research physicians affiliated with a US institution capable of managing a Research IND can submit applications to n-Lorem.
- n-Lorem is focused on creating individual treatments for patients in the United States with nano-rare diseases caused by genetic mutations that affect approximately n=1-30 patients in the world. We encourage you to confirm the incidence of your patient's gene mutation to ensure the patient meets criteria for the n-Lorem Program before submission.
- Each patient must have a diagnosis and should have a full genomic analysis. Additionally, the type of change in genetic function must be understood, often this means that the patient is referred to a geneticist.
- n-Lorem is not able to accept patients who are currently involved in clinical trials or other experimental treatments.
- Application review timelines vary by gene complexity and thoroughness of the information provided. To ensure an efficient review of your application, please provide all requested information at the time of application submission or upon request.
- Please understand that ASO technology, like all drug discovery technologies, has limits and n-Lorem may not be able to help every patient.

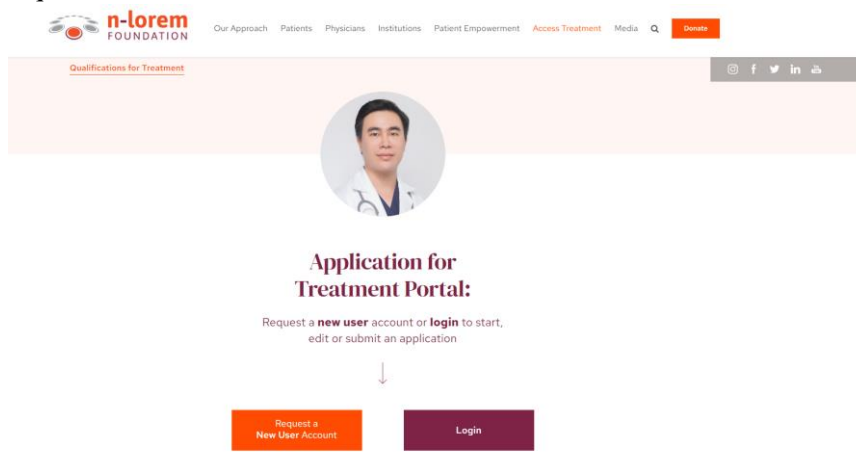
Troubleshooting:

- Note that the n-Lorem Application portal works best with Chrome, Edge, and Safari browsers.
- The email used to create an account is stored in the system, so that if a user tries to create another account with the same email, the user will be informed that an account already exists. If this has happened to you, please reset your password and use the previously established account.
- If you need help throughout the application process or have questions regarding where in the review process your application is, please reach out to applicationhelp@nlorem.org and your question will be routed to the appropriate individual for action.
- Videos cannot be uploaded into the application portal, if you would like to provide videos in support of your application, please reach out to applicationhelp@nlorem.org with a request.

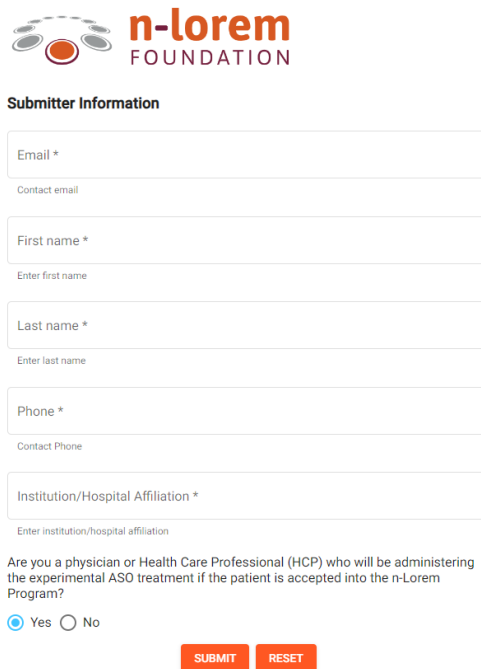
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Request a Submitter Account:

1. Note: Only US research physicians affiliated with a US institution capable of managing a Research IND can submit applications and should request submitter account credentials.
2. Navigate to the n-Lorem Matrix using the following URL: <https://www.nlorem.org/access-treatment/application-for-treatment/#application>
3. Click on “Request a New User Account” and you will be directed to a page where you can submit your access request.



4. Fill out all required fields and click on Submit.



Submitter Information

Email *
Contact email

First name *
Enter first name

Last name *
Enter last name

Phone *
Contact Phone

Institution/Hospital Affiliation *
Enter institution/hospital affiliation

Are you a physician or Health Care Professional (HCP) who will be administering the experimental ASO treatment if the patient is accepted into the n-Lorem Program?
 Yes No

SUBMIT **RESET**

5. You will receive an email with confirmation of your request for submitter account credentials.

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- a. The n-Lorem team will review your request form within three days.
6. Upon approval of your request, you will receive an email with additional details including a login link for you to proceed with submitting an application.
 - a. If you are confirmed to be a research physician from a US institution (tertiary care center) capable of managing a Research IND, your account will be approved.
 - b. If you are not a research physician who meets the required qualifications to submit an application, account access will not be granted.

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Prepare to Submit an Application:

Prior to submitting an application, please ensure you have gathered the following pieces of information and supporting documentation for upload:

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	Description of Documentation
Genetics	<ul style="list-style-type: none"> Genetic diagnostic report with the official name and symbol of the affected gene as defined by Gen Bank Accession Number and NCBI Gene ID. An understanding of the nature of the genetic change (gain of function, loss of function, splicing defect). Evidence of causality and gene function. Number of individuals reported to have this mutation worldwide.
Patient Phenotype	<ul style="list-style-type: none"> A detailed understanding of the patient’s current clinical status including but not limited to: current symptoms, anticipated rate of disease progression in the next 1-5 years, applicable imaging (specifically MRI for pediatric CNS patients), head circumference growth chart, seizure frequency, current scores as measured by standard clinical care assessments for the disease type (i.e., ALSFRS, Vineland, Bayley, etc.), most recent clinic visit notes. Relevant medical history of the patient including but not limited to: age of onset, presenting symptoms, current medications, surgical procedures impacting the proposed route of ASO administration. The clinical outcomes you are seeking for your patient with experimental ASO therapy.
Proposed Treatment Goals and Validated Clinical Measures	<ul style="list-style-type: none"> Proposed clinical goals of treatment for your patient based on collaboration with the patient or family. Primary, secondary and exploratory treatment goals must be defined prior to initiation of treatment. Objective, validated, and quantitative clinical assessments that are suitable to use as outcome measures during an investigational trial for your patient (i.e., laboratory values, EEGs for epilepsy, calculated GFR, proteinuria for renal dysfunction, LFTs for liver dysfunction, etc.). Please note that novel biomarkers for individual patients cannot be validated.
Institution	<ul style="list-style-type: none"> To be considered for n-Lorem’s portfolio, patients must be nominated by an investigator at an institution located in the United States. Current regulatory framework only allows patients to be treated with n-Lorem ASO therapy in the United States. Proposed treating investigators should have experience managing Research INDs. Co-investigators such as medical geneticists, basic scientists, and primary care physicians may also be included during the application process. Please Note: n-Lorem does not provide compensation to investigators. A tertiary care center that is experienced and committed to supporting conduct of Research IND studies without compensation from n-Lorem is required. This includes financial support for drug administration and follow-up visits included in a research protocol that may be considered outside standard of care. The institution where patients will be treated must also have appropriate administrative systems in place such as an institutional review board (IRB) and experience in reporting adverse events and serious adverse events.
Documentation	<p>At a minimum, the following pieces of documentation are <u>required</u>:</p> <ul style="list-style-type: none"> Genetic / diagnostic report with the official name and symbol of the affected gene as defined by Gen Bank Accession Number and NCBI Gene ID Physician’s CV Copy of patient’s Medical Release Form authorizing you to share their protected health information with n-Lorem Clinic notes from your most recent patient visit <p>Publications and information on mouse models and gene functions may also be helpful to submit.</p>
Patient Vitals	Age, weight, height, sex, location

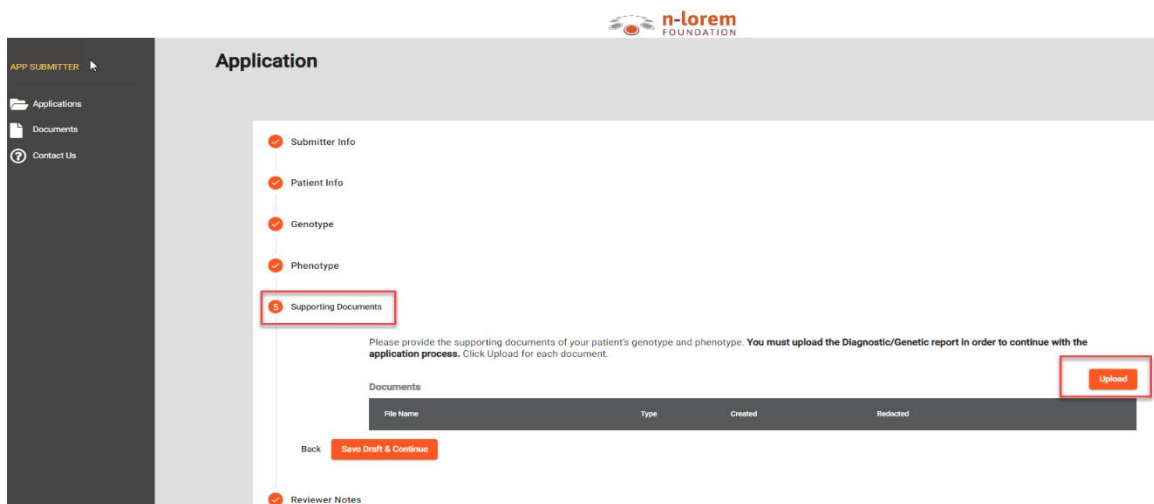
Complete / Submit an Application:

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1. Once your account has been established and you have gathered the required documentation, you may login to submit an application on behalf of your patient(s).
2. Navigate to the n-Lorem Application Portal <https://nlorem.acrossmatrix.com/> and follow the prompts to login.
3. Click on the “Applications” menu item on the left navigation panel.
4. Click on “New Application”, which will open a new application page.

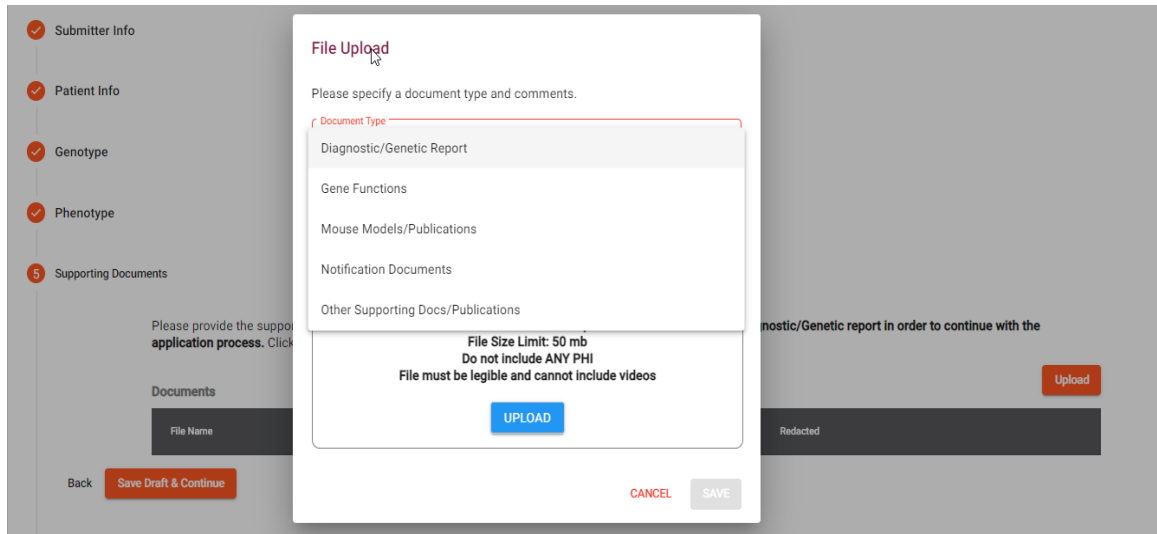


5. Enter all required fields on the Application. Required fields are noted with a “*”.
6. Save application as a draft by clicking, “Save Draft” on each section. This will save the application as “In Progress” on your Applications List.
7. Upload Documents:
 - a. Under the “Supporting Documents” section, click on upload.



- b. In the pop-up window, click on “Document Type” and select the appropriate document type for each document you will upload. **Note: A “Diagnostic/Genetic report”, “Physician CV”, “Medical Release Form,” and at least one “Clinical Assessment” are required to proceed with the application.**

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8. Submit application:
 - a. When ready to submit the application, click on “Submit Application”. The application will change status to “Submitted” and will then be sent to n-Lorem for review.

Addressing Scientific Reviewer Questions:

1. Should the n-Lorem scientific review team have questions for you, they will return your application to your queue which will trigger an email notification to you.
2. Login to the Application Portal and select the application from your Applications list.
3. Scroll to the bottom of the application and review the content of the “Notes for Submitter” field. These notes will specify which additional information is required to continue processing your application.
4. Upload any additional documentation by following the Upload Documents steps above.
5. Should you wish to provide additional detail to the reviewers, please enter it using the “Submitter Notes” field.
6. Once all documentation has been uploaded and information provided, click on “Submit Application”.
7. Please Note: Response times to provide requested information directly impact turnaround time to process your application.

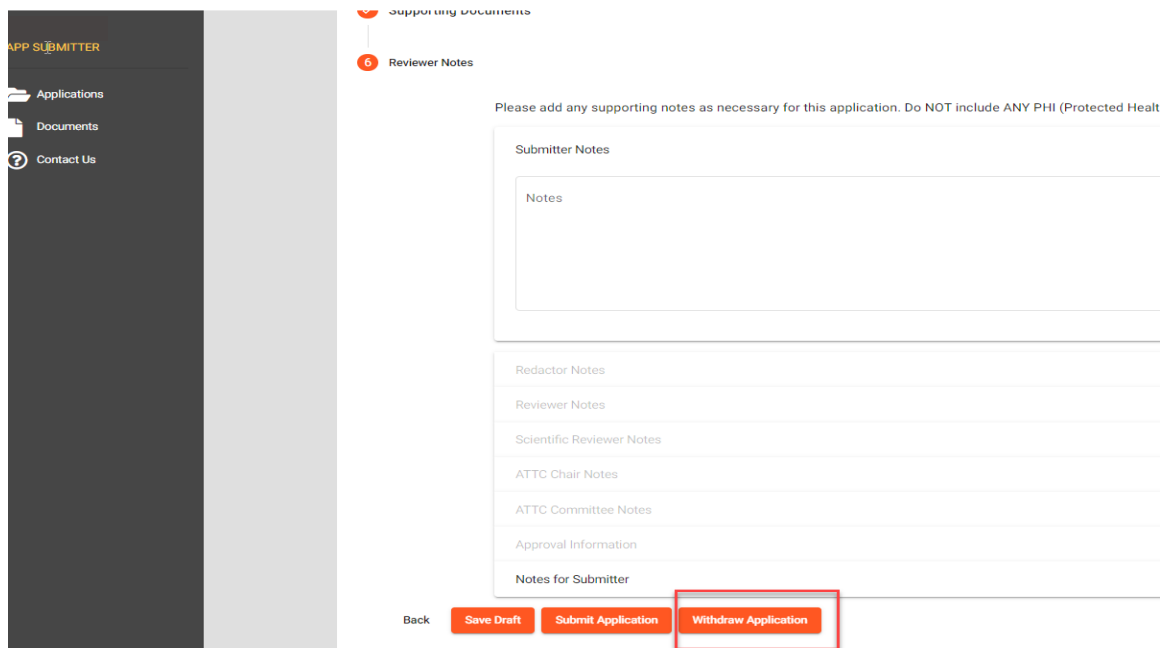
Application Decision Notification Process:

1. Details regarding the application review process can be found here: [Committees – nlorem](#)
2. Once a final decision has been reached for your application, you will be notified via email.

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How to Withdraw an Application:

1. At any point during the review process, you have the ability to withdraw an application.
2. To do this, select the application you wish to withdraw from your Applications list.
3. Within the application, at the bottom, click on “Withdraw Application”. Doing so will prompt a message box to confirm this action.



The screenshot shows the application submission interface. On the left is a dark sidebar with the title 'APP SUBMITTER' and navigation links for 'Applications', 'Documents', and 'Contact Us'. The main content area is titled 'Supporting Documents' and includes a '6 Reviewer Notes' section. Below this is a text area for 'Submitter Notes' with a placeholder 'Notes'. Further down are sections for 'Redactor Notes', 'Reviewer Notes', 'Scientific Reviewer Notes', 'ATTC Chair Notes', 'ATTC Committee Notes', 'Approval Information', and 'Notes for Submitter'. At the bottom, there are three buttons: 'Back', 'Save Draft', and 'Submit Application'. The 'Withdraw Application' button is highlighted with a red box.

4. Applications that have been withdrawn cannot be reinstated. Should you wish to proceed with an application for a withdrawn patient in the future, please submit a new application.

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