Hope for the Future


ANSWERS
AHEAD

5

Hope for the Future

5.1 NMO Clinical Trials – Get Informed

QUICK READ

There is no regulatory-approved therapy for NMO. Clinical trials are designed to determine which medicines or procedures best benefit patients, and which may not. The **first-ever** NMO clinical trials in are in process, which offer hope for the future.

What is clinical research?

Clinical research is research that involves **patients**. Patients and other individuals can **volunteer** to participate in clinical research, carefully designed and conducted to **better understand disease**, and

find ways to prevent, **diagnose**, **treat**, **and eventually cure it**. These advances come with improved understanding of the causes and effects of the disease. **Clinical research** includes two basic types of investigation:

1. **Clinical studies** typically aim to understand disease, its epidemiology or risk factors, and assess proof-of-concept of new ways to prevent or treat it.
2. **Clinical trials** aim to test the safety and effectiveness of therapies to treat a disease with the goal of improving patient health and wellness.

All clinical research is required to adhere to careful protection of subjects and their information, and clinical trials in particular are regulated and monitored by the **U.S. Food and Drug Administration (FDA)** and the **National Institutes of Health (NIH)**.

For more information, please refer to the National Institutes of Health website: www.nih.gov

Why do we need clinical trials?

Clinical trials are designed to determine which medicines or procedures **best benefit patients**, and which may not. These studies often involve expert teams from **academic**, **governmental**, and **pharmaceutical** sectors. In some cases, clinical trials seek to test the **efficacy of a new drug** for a disease which has no

Clinical trials are designed to determine which medicines or procedures best benefit patients, and which may not.

proven effective therapy. In other trials, one treatment is compared with another to examine which may be best in patients of differing disease stage or condition. Clinical trials are usually divided into different **phases**, each of which is designed to address a slightly different question:

- **Phase I:** usually designed to test the **safety** and to learn the best dosing regimen of a new drug to minimize side effects. Subjects are usually healthy volunteers, and the study is often **relatively short** in duration. **Subjects do not usually benefit from a Phase I study.**
- **Phase II:** usually designed to study the drug based on **results from Phase I**. Here, the drug, device, or procedure is evaluated in volunteer subjects who have the disease of interest. Phase II trials further refine safety, minimize adverse events, and begin to **explore** if and how the test agent may benefit the subject. **Some volunteer subjects may benefit from a Phase II study.**

- **Phase III:** usually **compares** the test candidate (drug, device, or procedure) to a commonly-used agent that has been proven to be at least somewhat effective in treating a condition, if one exists. This phase is designed to understand if the test agent is better than existing approaches, and where the agent might best fit in managing a particular disease.

For more information, please refer to the National Institutes of Health website: **www.nih.gov**

Why do people participate in clinical trials?

People participate in clinical trials for **many reasons**. Healthy individuals often say they participate to **help others** and to contribute to new or better ways to prevent or treat disease. **Volunteers who have**

a disease also participate to help others, but **may also receive new or improved experimental treatments**. In addition, subjects who are involved in clinical trials receive **additional care** and attention from the clinical trial staff. Sometimes, blood relatives of the patients with diseases participate in certain trials which evaluate the genetic components that may pose potential disease risks. *Information courtesy of nih.gov*

Who participates in clinical trials?

People from all walks of life participate in clinical trials. Some are healthy, while others may have illnesses. Sometimes, blood or genetic relatives of a person suffering from an illness can participate together in a clinical trial. Usually, each clinical trial or study specifies which subjects may participate. Factors that allow someone to participate in a clinical trial are **inclusion criteria**. Those that exclude or not allow participation are **exclusion criteria**. These criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical

Subjects who are involved in clinical trials receive additional care and attention from the clinical trial staff.

Want to get updates about NMO Clinical Trials?

Get **NMOtion** by visiting our website at:
guthyjacksonfoundation.org/clinical-trials

conditions. Before joining a clinical trial, a participant must qualify for the study. Some research studies seek participants with illnesses or conditions to be studied in the clinical trial, others may need healthy volunteers, whereas some others require both. *Information courtesy of nih.gov*

The Guthy-Jackson Charitable Foundation Clinical Trial Position Statement

The Guthy-Jackson Charitable Foundation (GJCF) supports efforts directed at the prevention, diagnosis, treatment and cure of neuromyelitis optica (NMO) and NMO spectrum disorder (NMOSD). It facilitates scientific and clinical advances directed toward these goals.

The GJCF endorses clinical trials aimed at improving the health of NMO patients. **It neither sponsors nor conducts clinical trials, nor does it advocate for**

any specific therapeutic candidate or endorse any particular clinical trial design. The GJCF **plays no role** in the active enrollment of subjects in clinical trials, **nor does it participate** in interpreting clinical trial outcomes. The GJCF **functions neutrally** and **equitably** in all interactions with clinical trial sponsors, investigators and NMO stakeholders.

The GJCF facilitates access to educational resources in the public domain to provide individuals with the opportunity to learn about the latest scientific and clinical advances in NMO. By increasing awareness of these advances, including information about actively recruiting trials, the GJCF promotes informed decision-making by all members of the NMO community.

5.2 CIRCLES Biorepository for NMO Research

QUICK READ

Because NMO is rare, every blood sample, data point, and patient experience is an **invaluable piece** of the puzzle to solve it. Biospecimens and patient health data are precious resources that contain secrets to curing the disease. **Participating in CIRCLES is one of the most important actions you can take to be part of the cure for NMO.**

Biological samples (i.e. blood and other samples), and clinical health data from NMO patients and controls (qualified donors who do not have NMO) are vital for NMO research. Many developments in NMO treatment come from doctors and researchers studying blood samples, other biological specimens, and clinical health data in a laboratory. Collecting biosamples and health data over years (called a **longitudinal study**) is critical to better understand NMO, including cause, epidemiology, relapse rates, best treatments, and similar factors – all key factors in finding a cure for a disease.

To advance NMO research, **GJCF built a biorepository that collects blood samples, other biospecimens and clinical health data (information)** of volunteer NMO patients and controls. The repository is called:

C ollaborative
I nternational
R esearch in
C linical and
L ongitudinal
E xperience in NMO
S tudies

What is CIRCLES?

CIRCLES is a **research study** that focuses on better understanding and enabling **cures for NMO**. It consists of two complementary programs:

- A network of academic sites and clinical laboratories with special expertise to enroll participants and collect data and biospecimens.
- Data and blood banks that ensure safe storage and ready access of clinical data and biospecimens for breakthrough research in NMO.

What is the CIRCLES Site Network?

The CIRCLES network consists of **multiple centers of excellence** with deep expertise in caring for and studying patients with NMO. CIRCLES sites are located at **leading medical centers** across North America.

The CIRCLES network features:

- CIRCLES sites in regions of the U.S. and Canada (also known as **Home Bases**) where participants can regularly contribute their clinical data and biospecimens.
- Biospecimen draw sites across the U.S. where CIRCLES participants can contribute biospecimens.
- A leading **principal investigator (PI)** in charge of each CIRCLES site.

- A clinical **research coordinator (CRC)** who explains the CIRCLES study, enrolls participants, schedules appointments, answers questions and coordinates clinical data and blood collection.

Regional CIRCLES sites include **leading universities** where neighboring NMO patients and qualified control participants can **donate blood and clinical data**. Regional sites allow participants who are unable to travel far distances to contribute to CIRCLES. These sites are considered **Home Bases** where NMO community members can participate, and join support group meetings, host events, and attend regional **NMO Patient Days**.

The CIRCLES Biorepository for NMO works in association with academic centers, reference laboratories, and commercial research organizations to **ensure best practices in data and biospecimen management**.

The CIRCLES Biorepository is a powerful resource to discover patterns in the course of a disease that are not obvious from any one individual.

What is the CIRCLES Biorepository?

The **CIRCLES** biorepository is a high-tech storage system for data and biospecimens collected through the **CIRCLES** network. The CIRCLES study collects data and biospecimens that need to be carefully prepared for best use in understanding and solving NMO. The CIRCLES biorepository combines a databank and bloodbank to serve this goal. Features of the CIRCLES biorepository include:

- A **centralized system** where samples and data are uniformly stored and secured to protect participant information and **biospecimen integrity**.
- The **largest collection** of clinical data and biospecimens in the world dedicated to **finding a cure for NMO**.
- An **efficient process** by which researchers can access data and biospecimens to accelerate **breakthrough advances** in NMO science and medicine.

How does the CIRCLES Biorepository help NMO research?

The CIRCLES Biorepository is a **powerful resource** that allows researchers to **discover** common features that many NMO patients share, and aspects of NMO that may be unique to each individual. Special ways in which **CIRCLES advances solutions** to NMO include:

- Enabling careful study of your NMO experience over an extended period of time.
- Understanding the epidemiology of NMO as compared to closely related diseases.
- Expanding the database of clinical features that can help speed best diagnosis and treatment.

Studying NMO in many individuals over a long period of time (called a **longitudinal study**) can reveal discoveries that are not possible otherwise.

Many developments in NMO treatment come from doctors and researchers studying blood samples in the laboratory.

For example, researchers can examine factors that influence disease prognosis and quality of life, describe patient care patterns, assess effectiveness, safety, or toxicity of treatment, and study other outcomes measures. **In these ways the CIRCLES program supports quantum-leap breakthroughs and helps solve unanswered questions including:**

- What causes NMO?
- Is there a difference between AQP4 positive vs. MOG positive NMO?
- Is there a "typical" course of NMO, or does it vary in each individual?

Patients who participate in CIRCLES are critical in the effort to find a cure for NMO.

- How does geography or season relate to the disease course, if at all?
- Does a treatment lead to long-term benefits, such as fewer relapses?
- How is NMO severity or disability affected by new or existing therapies?
- What are the significant predictors of favorable vs. poor outcomes?
- How do NMO clinical practices vary, and what are best practices for managing NMO?
- Are there differences in the delivery and/or outcomes of care for NMO?

CIRCLES may also lead to assisting clinical trials to identify potential improvements in treatment.

NMO patients who participate in CIRCLES are critical in the effort to find a cure for NMO. Biospecimens may ultimately serve to identify the best possible diagnosis and management of each NMO patient, and find new and more effective treatments.

Why is CIRCLES different from other biorepositories?

CIRCLES is the **largest biorepository in the world dedicated to solving NMO**. CIRCLES is uniquely designed to standardize how data and biospecimens are collected, archived and accessed. This allows **apples-to-apples comparison** of NMO in patients from diverse backgrounds and locations. Clinical data and samples are available to study by any qualified researcher. The foundation brings a synergistic team approach to enable this important goal. Its **Medical Advisory Board (MAB)** and **Biorepository Oversight Committee (BOC)** maintain the highest standards of NMO research. Members of the MAB and BOC are leaders in their complementary fields of study, and closely monitor the rapidly-growing medical and scientific

assets the CIRCLES program brings to NMO research. To accelerate breakthroughs that lead to tomorrow's cures, the foundation sponsors CIRCLES but allows institutions and companies to retain intellectual property. This fact incentivizes the process of turning molecules into medicines.

When you participate in CIRCLES, you are participating in the world's leading innovative research for NMO.

5.3 How Can I Become a CIRCLES Participant?

QUICK READ

CIRCLES is an interactive program where **participants help solve NMO** by providing invaluable data and biospecimens for research. In addition, CIRCLES participants are able to **meet one-on-one with leading NMO clinicians** at regular intervals. CIRCLES participants also benefit from opportunities to participate in support groups, meetings, and advocacy events, such as NMO Patient Days and other educational programs. Your regional CIRCLES site is your **Home Base** where you can **make a difference in solving NMO**.

Because NMO is a rare disease there is an urgent need for every patient to participate in the effort to solve this disease.

You Can Help Solve NMO

Thanks to dedicated patients, researchers and industry partners **there has never been a greater chance to solve NMO than there is today**. Because NMO is a rare disease every CIRCLES participant provides an invaluable piece to solving the NMO puzzle. **The more data and samples collected, the sooner answers can be found that will lead to new treatments and cures.** NMO patients and qualified controls can help meet this urgent need by participating in CIRCLES. If you or a family member have been diagnosed with NMO, please help by donating data and blood for NMO research.

NMO patients and blood relatives can HELP!

PARTICIPATE IN THE CIRCLES BIOREPOSITORY

Learn how on page 244

What does it mean to be a CIRCLES participant?

Becoming a CIRCLES participant is one of the most important actions you can take to be part of the cure to NMO. By participating, you are providing an invaluable contribution to solving NMO by:

- **Enrolling** in the CIRCLES study to establish baseline clinical data and biospecimen sets
- **Attending** regular follow-up visits at your regional CIRCLES Home Base to update your clinical data and biospecimens
- **Reporting** relapses or other clinical events to your CIRCLES site clinician principal investigator (PI) and clinical research coordinator (CRC)

How to Become a CIRCLES Participant

You can volunteer to become a CIRCLES participant by following these 4 simple steps:

1. **Locate** your regional CIRCLES site via:
   - **GJCF website**
   - **Smartphone App**
   - Page 247 of this book
2. **Contact** the CRC at that site to schedule an appointment
3. **Prepare** to receive an enrollment package in the mail and complete it prior to your first visit. Your CRC can help you complete this information.
4. **Schedule** follow-up appointments with your CRC throughout the year, every year

Why is it important that I participate at my Regional CIRCLES site?

An important goal of the CIRCLES project is to collect data and biospecimens from participants consistently and at regular intervals. Each participant enrolls in CIRCLES through their regional CIRCLES site. **This site is your designated Home Base** for collection of clinical data and biospecimens. Collecting these materials at the same time as your clinical exam maximizes the quality of information you provide and enhances convenience for you. By actively participating in CIRCLES and related events at your regional Home Base CIRCLES site, you stay up to date in contributing to the cure through the CIRCLES program, **Regional NMO Patient Days**, and educational events.

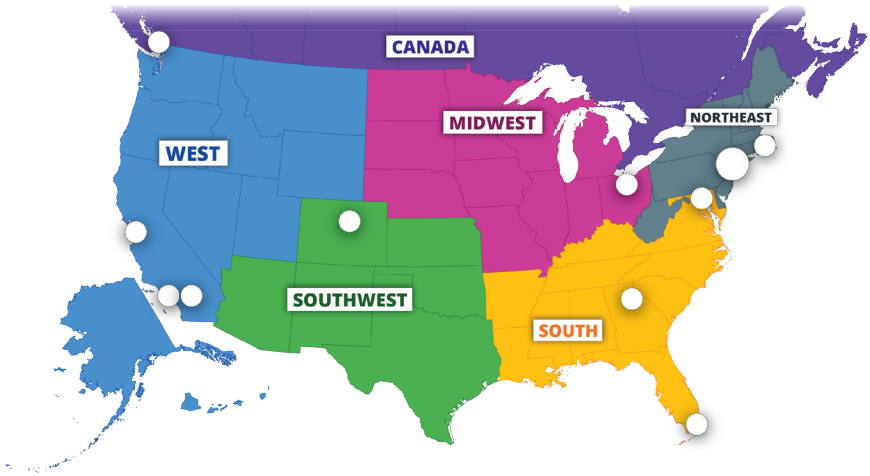
What happens to my specimens and data?

Blood samples are stored at the CIRCLES Biorepository, which is carefully controlled to ensure high-quality samples for NMO research. Qualified research staff enter data in a manner that protects participant information and coordinates data with biospecimens. Researchers

Blood samples are stored at a carefully controlled repository to ensure high sample quality.

request samples from the CIRCLES biorepository by submitting a written proposal describing their intended research. Proposals are reviewed by the BOC and GJCF to **ensure all samples distributed are used for cutting-edge research** that has the best chance for **quantum-leap advances** in understanding NMO, its causes, treatment, and cure.

Researchers who apply for and receive samples from the biorepository agree to **rapidly share results** from their research for inclusion in a database to **help other researchers make breakthroughs of their own**. This **success-drives-success model** accelerates turning discoveries in the test tube into treatments in the clinic.



Find your regional CIRCLES site home base to participate:

Western Region

Los Angeles, CA
Cedars-Sinai Medical Center
P.I. Nancy Sicotte, M.D.

University of Southern California
P.I. Lilyana Amezcua, M.D.

Stanford, CA
Stanford University
P.I. May Han, M.D.

Seattle, WA
Swedish Medical Center
P.I. Pavle Repovic, M.D.

Midwest Region

Cleveland, OH

Cleveland Clinic

P.I. Sarah Plachon Pope, Ph.D.

Northeast Region

Boston, MA

Harvard Medical School, Brigham & Women's Hospital, Partners MS Center

P.I. Tanuja Chitnis, M.D.

Massachusetts General Hospital, Multiple Sclerosis Clinic, Wang Ambulatory Care Center

P.I. Eric Klawiter, M.D.

New York, NY

Columbia University Medical Center

P.I. Claire Riley, M.D.

Judith Jaffe MS Center, Weill Cornell Medical College

P.I. Nancy Nealon, M.D.

Research catalyzed by the foundation has dramatically changed the landscape of NMO science and medicine.

Mount Sinai - Icahn School of Medicine
P.I. Ilana Katz Sand, M.D.

New York University Langone Medical Center
P.I. Ilya Kister, M.D.

Southern Region

Atlanta, GA
Shepherd Center
P.I. Ben Thrower, M.D.

Baltimore, MD
Johns Hopkins
P.I. Michael Levy, M.D., Ph.D

Miami, FL
University of Miami Miller School of Medicine
P.I. Leticia Tornes, M.D.

Canada

Vancouver, BC
University of British Columbia
P.I. Robert Carruthers, M.D.

Do You Know...

More and more CIRCLES sites are being created. Visit the foundation's website and/or smartphone app to find your regional CIRCLES site at:
guthyjacksonfoundation.org/draw-sites

5.4 What exciting discoveries have come from NMO research?

QUICK READ

The Guthy-Jackson Charitable Foundation is dedicated to advancing prevention, treatment, and an ultimate cure for NMO. Its research focus aims to better understand the causes and effects of NMO and NMOSD from the level of molecules and cells to the clinical impact of disease in patients.

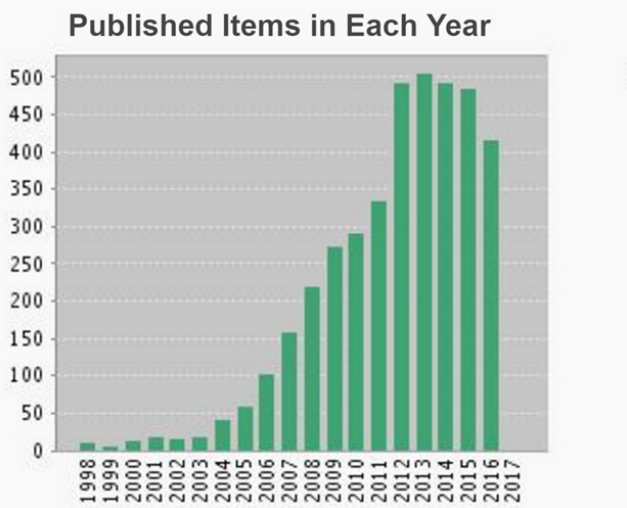
Research catalyzed by the foundation has dramatically changed the landscape of NMO science and medicine. There are many ways through which these advances are evident, including:

- NMO is now known to be more common than previously estimated or reported.
- Gender, race, geography and other factors are now known to contribute to NMO epidemiology.
- NMO pathogenesis involves a coordinated interaction among immune cells and molecules.
- Genes that potentially influence NMO risk have been analyzed and are being investigated.
- NMO diagnosis has been modernized for improved accuracy, specificity, and therapy.
- Biomarkers are emerging as signals of pathogenesis, relapse, and treatment effects.

The Guthy-Jackson Charitable Foundation is dedicated to advancing prevention, treatment, and an ultimate cure for NMO.

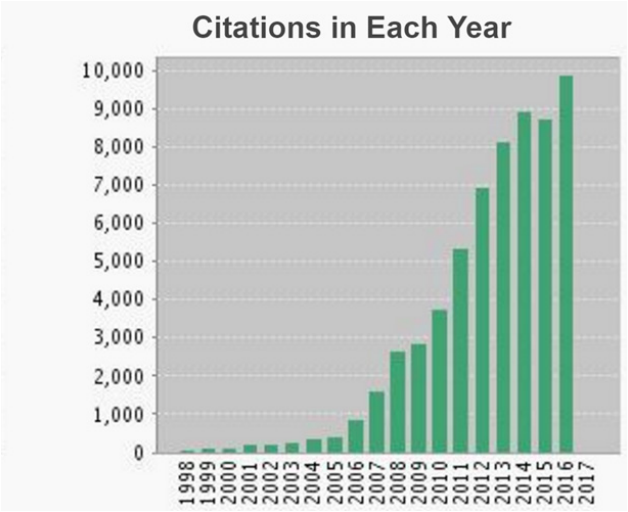
- NMO has been discovered to affect the brain and brainstem as well as the optic nerves and spinal cord.
- NMO is now clearly differentiated from MS in pathogenesis, diagnosis, and treatment.
- Existing treatments for NMO have been refined to best address each unique NMO case.
- Multiple clinical trials are now underway based on these exciting advances in NMO science.

These promising advances are just the first steps on the path to solving NMO once and for all.



The Guthy-Jackson Charitable Foundation Funded Scientific and Clinical Research Sites

- Brigham and Women's Hospital, Harvard Medical School
- Charité Berlin
- Cleveland Clinic
- Duke University
- Johns Hopkins University
- Massachusetts General Hospital
- Mayo Clinic
- Mt. Sinai
- New York University
- Oxford University Medical Centre



- St. George's, University of London
- Stanford University
- The Scripps Research Institute
- The University of British Columbia
- University of California, Los Angeles
- University of California, San Francisco
- University of Colorado, Denver
- University of Texas Southwestern Medical Center
- University of Utah

For detailed descriptions of current and completed research projects, visit the GJCF website at:

guthyjacksonfoundation.org/research

Make a Financial Donation to NMO Research

You or someone you know can make an impact in the world of NMO by funding NMO science projects. **100 percent of all donations go directly to scientific research.** All financial donations are directed to **The Guthy-Jackson Research Foundation, Inc**. This includes donations from public, private and government organizations, as well as donations from fundraising events, families, friends, and individuals like you.

If you or someone you know is interested in donating to NMO research, please visit: **guthyjacksonfoundation.org/donate** to start the process, or contact us by phone at: 858-638-7638.

Want to learn more about donating to NMO research? Join the **NMO Advocacy Network**. Refer to chapter 6 to learn more.

5.5 NMO International Clinical Consortium (ICC)

The number of patients followed at any one site is generally too small to study all aspects of the disease. To meet this challenge, GJCF formed an **International Clinical Consortium (ICC)** comprised of clinicians and researchers from international centers. These worldwide centers work together in collaboration to apply uniform disease definitions, clinical assessment tools, and research advances. The goal of the ICC is to **create a multi-center collaboration for sharing clinical and biological data from NMO patients**. Members of the ICC have authored, co-authored and/or contributed to numerous NMO international collaborative consensus review articles. **These critical-**

path publications helped to advance NMO research and treatment. The ICC continues to be part of the cure for NMO. Visit the foundation's website for more information and access to review articles.

ICC SCIENTIFIC SNAPSHOT

NMO international collaborative consensus review articles published in collaboration with the GJCF ICC.

- **Treatment of NMO: Review and Recommendations**
  Mult Scler Relat Disord.
  2012 Oct;1 (4):180-187
  PMID: 24555176

- **Challenges and Opportunities in Designing Clinical Trials for NMO**
  Neurology.
  2015 Apr 3. Epub
  PMID: 25841026

- **Update on Biomarkers on NMO**
  Neurol Neuroimmunol. Neuroinflamm.
  2015 July 23;2(4). eCollection 2015.
  PMID: 26236760

Find more ICC articles on the NMO Resources smartphone app and Spectrum, our digital NMO Library: guthyjacksonfoundation.org/spectrum

5.6 International Panel for NMO Diagnosis (IPND)

Formed in 2011 and funded by The Guthy-Jackson Charitable Foundation, the International Panel for Neuromyelitis Optica Diagnosis (IPND) updated the 2006 diagnostic criteria for NMO. In its landmark paper published in 2015, this body of experts modernized the way NMO is diagnosed and differentiated from other diseases. This significant advancement also provided a global standard for NMOSD diagnosis. As a result, NMO patients — as well as patients who do not have NMO — receive more rapid and accurate diagnoses to speed the best therapy for their condition. The IPND 2015 criteria have already helped countless patients receive the best diagnosis and medical care.

The goal of the ICC is to create a multi-center collaboration for sharing clinical and biological data from NMO patients.

The IPND 2015 Diagnostic Criteria for NMOSD address the following key issues:

- Updated definitions and diagnostic criteria for NMO and NMOSD
- How related diseases such as MS may be differentiated from NMO
- NMO in relation to other autoimmune diseases
- Role of serological testing in diagnosis
- Role of radiology in diagnosis

Refer to section 2.5 for details about the IPND and the IPND 2015 NMO/NMOSD diagnostic criteria.

Do you know?

IT'S EASY TO FIND AN
NMO CLINICIAN ON

CONNECT THE DOCS

Visit guthyjacksonfoundation.org/doctors
to find your nearest NMO clinician.