MAYO CLINIC

Name and Clinic Number

Approval Date: **September 11, 2026**
Not to be used after: **September 10, 2027**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: PIONEER: **P**OLR2 **I**nvestigation **O**f **N**atural History, Outcom**E**s, and **E**valuation for **R**esearch

IRB#: 26-008313

Principal Investigator: Dr. Radhika Dhamija, M.B.B.S. and colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits, or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to study the natural history of patients with POLR2A or POLR2B variants to enable better understanding of the disorder, with the long-term goal of helping researchers plan future treatment studies. You (or someone you care for) have been asked to take part in this research because there is a confirmed, suspected, or pending diagnosis of a POLR2 (A or B) genetic variant.
What's Involved	Study participation involves a one-time study visit, questionnaires, one blood draw, and research assessment that help us understand development, movement, walking, thinking, daily function, and quality of life. These research assessments may be done at the beginning of the study and about once each year for up to 3 years. There is also an optional skin biopsy that you may choose to skip.

Key Information	There are few risks to you, including the potential that some of your private health information or biological data might be leaked or made public despite our best efforts to keep it private and confidential. There is a risk of discomfort and bleeding with blood draws or procedures. A skin biopsy, if you choose to undergo, contains risks of discomfort, bleeding, infection, and a small permanent scar.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

If you are signing this consent form for someone else, "you" in the consent form refers to the participant.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Radhika Dhamija, M.B.B.S. **Phone:** 507-266-2967 **Study Team Contact:** POLR2 Research Team (Rochester, MN) **Email:** RSTPOLR2Study@mayo.edu **Institution Name and Address:** Mayo Clinic 200 1st Ave SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Why are you being asked to take part in this research study?

You are being asked to participate in this study because you (or someone you care for) have a confirmed, suspected, or pending diagnosis of a POLR2A or POLR2B gene variant.. These variants are extremely rare and you have been identified either by a Mayo Clinic physician or referred to Mayo Clinic by another provider.

Approximately 50 people will participate in this research study.

Why is this research study being done?

Researchers at Mayo Clinic are hoping to study patients with POLR2 (A or B) variants to provide a better understanding of the disease progression, disease characteristics, and better improve the care for patients impacted by this disease. We are also interested in reviewing how past treatments have been successful or unsuccessful for patients. This information may help us develop future plans and studies.

Information you should know

Who is Funding the Study?

Mayo Clinic is funding this research study using donor funds exclusively for this disease.

How long will you be in this research study?

Your active participation in study visits and assessments may last up to 3 years. You may be asked to complete research assessments at the start of the study and about once each year for up to 3 years. The study team may continue to review your medical records after that to learn about your health and disease course over time, unless you ask us to stop or the study ends.

What will happen to you while you are in this research study?

If you take part in this study, the study team may review your past, current, and future medical records. We may also ask you to complete research assessments at enrollment and about once each year for up to 3 years. These assessments are done for research only. They are not meant to diagnose or treat you, and they are not meant to replace your regular medical care.

Baseline Visit:
At the baseline visit, you may complete all research assessments, questionnaires, blood draw, and optional skin biopsy. The blood draw and skin biopsy will only be performed during the baseline visit. Other research assessments, noted in the **Baseline and annual visits** section will be performed at baseline and each year for up to three years.

During this research study, you will undergo a single blood draw. This may be paired with a clinical draw that is already scheduled for you. For this research you will be providing 29 mL (less than two tablespoons) of blood for long-term storage. We may collect less blood on young subjects or those with low weight. This blood draw may be completed at Mayo Clinic in Rochester, Minnesota or at your home using our third-party service, MediPro, who bring qualified staff directly to your location within the continental U.S.

If you have tissue, cerebrospinal fluid, or other samples collected for your regular medical care, the study team may use leftover samples for research if they are available. These samples would only be used after all clinical testing is complete. No extra procedure will be done only to collect these leftover samples.

Up to 10 participants in this study may choose to have an optional skin biopsy. A skin biopsy is where a physician will use a small punch tool, much like a small cookie cutter, to remove a 3-millimeter piece of skin (smaller than the eraser on a pencil). Researchers will use this piece of skin to create cells called fibroblasts so that we can replicate and study the genetic condition in greater detail.

Optional Procedure Permission: Skin Biopsy
The skin biopsy is optional. You may take part in the rest of this research study even if you do not agree to the skin biopsy. If you agree, a study doctor will remove one small piece of skin, about 3 millimeters wide, using a small punch tool. The sample will be used to grow skin cells called fibroblasts so researchers can study POLR2 (A or B) conditions.

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Please mark your choice:

I agree to the optional skin biopsy.

☐ Yes ☐ No Please initial here: _____Date: _____

Baseline and annual visits (up to three years):

- **Movement and hand function assessments (~70-130 minutes):** These may include simple activities such as moving small blocks or pegs, checking hand strength, checking arm and hand movement, or doing age-appropriate motor tasks.
- **Walking or mobility assessments (~10-15 minutes):** If you are able to walk, you may be asked to walk for a short period of time while study staff measure walking distance, walking pattern, balance, or use of braces or assistive devices. You may stop or rest at any time.
- **Developmental or cognitive assessments (~60-100 minutes):** You may be asked to complete age-appropriate activities that look at thinking, problem solving, memory, language, attention, or development. For younger children or participants with developmental delays, these may include play-based activities.
- **Daily function and behavior questionnaires (~50-90 minutes):** You, a parent, or caregiver may be asked questions about communication, daily living skills, social skills, behavior, emotions, school function, or everyday activities. You may skip any question you do not want to answer.
- **Quality-of-life questionnaires (~10-20 minutes):** You or your caregiver may be asked questions about physical, emotional, social, school, family, or caregiver impact. You may skip any question you do not want to answer.

What are your responsibilities?
If you take part in this research, you will be expected to:

- Come to the study visits and follow the instructions you are given by the study doctor or other study staff. If you are unable to attend visits in person, please contact the study team. Some parts of the study may be completed virtually or remotely when possible. Virtual procedures may collect less detailed information than in-person assessments.
- Tell your study doctor or study staff if you think you are experiencing a harmful effect from the study participation.
- Tell the study doctor or study staff if you want to stop being in this research study.

If you are part of the POLR2 Registry at the University of Pittsburgh, and you provide the necessary consent below, we will share information gathered in this research study directly with their researchers. This will include information that would directly identify you (such as your name and medical record number) so that we may learn more about your disease.

You may choose to not share your information in a later section titled, "Will your information or samples be used for future research?"

If you choose to have your blood drawn by our remote phlebotomy team (at-home blood draws) then we will share information that would directly identify you (such as your name, address, email address, and date of birth) with the third-party service, MediPro. You do not have to use this service to be a part of the research study.

What are the possible risks or discomforts from being in this research study?

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

The risks of a skin biopsy include pain or discomfort, redness, bleeding, infection, and a small permanent scar.

Other assessments, including movement, walking, development, cognitive assessments, or questionnaires may cause emotional or behavioral distress. However, trained professionals will be conducting these assessments and they may be stopped at any time if they are stressful or uncomfortable. Your participation in this study or your regular healthcare will not be affected if you stop an assessment for any reason.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator, or study team, if you decide to stop. In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest.
- If you don't follow the study procedures.
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used. We will tell you about any new information that may affect your willingness to stay in the research study. Upon your request, we may also dispose of your samples to prevent future research or use.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

What are the possible benefits from being in this research study?

You won't benefit from taking part in this research study. It is for the benefit of research.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Blood draw
- Collection of archived tissue samples (previously collected)
- Skin biopsy, if applicable
- Movement and hand function assessments
- Walking or mobility assessments
- Developmental or cognitive assessments
- Daily function and behavior questionnaires
- Quality-of-life questionnaires

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will not be paid for taking part in this study. However, travel reimbursement up to $3,000 per visit is provided. This can cover hotel stays, if required, meals and mileage. Itemized receipts are required. You may be reimbursed for travel to and from the study site for any study visit that you attend. Your reimbursement for travel is calculated based on the round-trip number of miles you travel from your home address to the site address and back as determined by a web-based mileage calculator (e.g., MapQuest). This distance (miles) will be documented in your study file. You will receive reimbursement per mile at the current IRS mileage rate.

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Will your information or samples be used for future research?

Unless you give your permission below, your information or samples collected for this study will not be used or shared for future research, even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

We would like to keep your information and samples for future research. You can still take part in this current study even if you don't want your information or samples used for future research.

Researchers at Mayo Clinic who aren't involved with this study may ask to use your information and/or samples for future research. Researchers at other academic or medical institutions or companies may also ask for a part of your information and/or samples for future studies. Unless you indicate otherwise, the future research may be on any topic. No direct benefits to you are expected from the future research. Your information and/or samples will only be shared consistent with your consent, and with all applicable laws and regulations.

If you approve release of your information and/or samples by checking 'yes' below, Mayo Clinic may send the information and/or samples to researchers who request them, but Mayo Clinic will not send your name, address, phone number, social security number, or any other identifying information with the information and/or samples. Your information and/or samples may be sent with a code, and only the researchers for this study at Mayo Clinic would be able to link the code to you.

Some future studies may examine your DNA, the genetic information you inherited from your parents (genetic testing). This testing may include whole genome sequencing (mapping your entire genetic code). If there are findings which may be useful for your health care, the researchers may contact Mayo Clinic, so Mayo Clinic can give you the option of learning the results. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

To support future research, de-identified genetic information may be placed in databases accessible by the internet. Some of the information may be available to anyone using the internet, and some will be released only to approved researchers. Combined study information (including genomic summary results) may be published, but the information will not identify you.

Even though information traditionally used to identify you will not be shared, people may develop ways in the future to allow someone to link your genetic information back to you. For this reason, confidentiality cannot be guaranteed. It is also possible that reidentified information could be used in discriminating ways, and there could be additional unknown risks. We will limit access to information that can identify you and follow data security standards to protect your confidentiality.

Please read the following statements and mark your choices:

1. I permit my information and samples to be stored and used in future research RELATED TO POLR2 (A or B) genetic conditions at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my information and samples to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my information and samples to researchers at other institutions and companies:

☐ Yes ☐ No Please initial here: _____Date: _____

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved.

How will your privacy and the confidentiality of your records be protected?

General Protections

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Our team will code your samples and information with a

number, use password-protected data systems, store samples in locked storage, and retain any paper documents within locked cabinets only accessible to the study team. If the results of the research are made public, information that identifies you will not be used.

Authorization to Use and Disclose Protected Health Information (HIPAA)
During this research, information about your health will be collected. Under Federal law called the Privacy Rule (also referred to as Health Insurance Portability and Accountability Act [HIPAA]), health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other healthcare providers involved in your clinical care.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private, and it may no longer be protected by the Privacy Rule.

Genetic Information Nondiscrimination Act (GINA)

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law.
Be aware that this Federal law doesn't protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

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If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 First St. SW
Plummer Building PL 3-02
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Signature of Legally Authorized Representative for Adult Participant

- I give permission for the participant to take part in this research study and agree to allow his/her health information to be used and shared as described above.

Signature Printed Name Relationship to Participant Date \ Time

Signature of Parent(s)/Guardian for Child:

I give permission for my child to take part in this research study and agree to allow his/her health information to be used and shared as described above.

Printed Name of Child

Printed Name of Parent or Guardian Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature of Parent or Guardian

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Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature