ARIA
Aligning Research to Impact Autism

# Innovative Medicine and Precision Approaches to Clinical Trials (IMPACT) Network
# Request for Applications – Step One

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| KEY DATES | |
|---|---|
| RFA Release Date | May 21, 2025 |
| Grant Portal Opens | Week of June 23, 2025 |
| Pre-Application Submission Deadline | July 14, 2025 |
| Select Applicants Invited to Submit Full Applications | Week of August 18, 2025 |
| Full Application Submission Deadline | October 13, 2025 |
| External Review Period | October 20 - November 24, 2025 |
| Virtual Call with Finalists | December 8-15, 2025 |
| Anticipated Award Notification Date | December 19, 2025 |
| Anticipated Contract Execution Deadline | March 31, 2026 |
| Anticipated Funds Release | Q2 2026 |

## Opportunity

The Aligning Research to Impact Autism (ARIA) initiative envisions the creation of a research and clinical care system working in concert to deliver therapies for people most impacted by autism spectrum disorder (ASD) and related neurodevelopmental disorders (NDDs). Core to this effort is the establishment of the **I**nnovative **M**edicine and **P**recision **A**pproaches to **C**linical **T**rials (IMPACT) Network, a robust and collaborative network of sites that can accelerate clinical trial readiness and implementation in both syndromic and non-syndromic forms of ASD.

ARIA is pleased to announce a Request for Applications (RFA) for institution-based, collaborative, multidisciplinary clinical research teams to join the first wave of participating sites within the IMPACT Network.

# About ARIA

Aligning Research to Impact Autism (ARIA) is a new initiative led and managed by the Coalition for Aligning Science (CAS), with scientific direction from Matthew State, MD, PhD, Oberndorf Family Distinguished Professor at the University of California, San Francisco (UCSF).

ARIA intends to serve as a catalyst to de-silo the ASD and related NDD fields, connecting emerging research, insights, and promising technologies from across scientific fields to advance scientific discovery and to create more therapeutic opportunities for people with profound autism and for people across the neurodevelopmental spectrum who seek additional support. This initiative is made possible by the generous support of the Sergey Brin Family Foundation (SBFF).

## Mission

To accelerate the understanding and treatment of autism and related NDDs through alignment, collaboration, and cutting-edge research.

## Vision

We envision a research and clinical care system working in concert to deliver therapies for people most impacted by autism spectrum disorder and related NDDs.

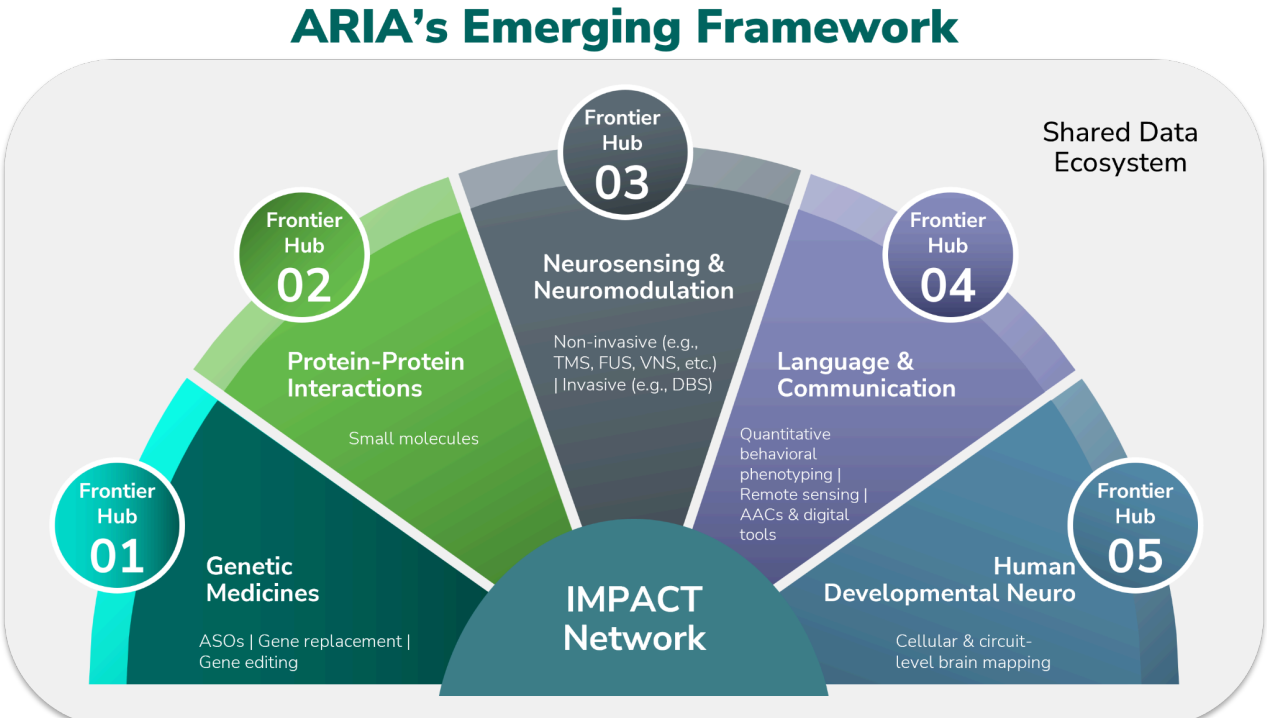
## Approach

ARIA's approach involves three major categories of activity, as illustrated in the figure below:

1. **Establishing the Innovative Medicine and Precision Approaches to Clinical Trials (IMPACT) Network**, a robust and collaborative international network of sites designed to accelerate clinical trial readiness and clinical trial implementation for syndromic and non-syndromic forms of autism spectrum disorder (ASD). **This component is the subject of this RFA.**
2. **Forming Frontier Science Hubs** to support actionable, cutting-edge research opportunities that will directly support ongoing therapeutic programs and drive the development of novel approaches that will eventually integrate into the IMPACT network as the science matures. We are initially launching 5 workstreams to drive research addressing: (1) genetic medicines, (2) protein-protein interactions, (3) invasive/non-invasive neurosensing and neuromodulation strategies, (4) language and communication, and (5) human developmental neuroscience. For more information about the focus of each Frontier Hub, see **Appendix A**.

3. **Creating a Shared Data Infrastructure** to facilitate open science, data harmonization, and data sharing.

With these activities, we envision a network of networks where multi-scale cross-collaboration activities are strongly encouraged across the entire ARIA initiative, from the IMPACT Network to and from the various Frontier Hubs, where possible.




## ARIA's Strategic Priorities

To drive research progress and improve clinical care in ASD and related NDDs, ARIA's strategic priorities are as follows:

- **Achieve near-term impact.** Rapidly expand evidence-based treatment for patients and families seeking care for ASD and related NDDs.
- **Accelerate translation.** Drive biomarker discoveries to speed up the development of personalized therapies through clinical trial infrastructure.
- **Enhance innovation.** Identify game-changing opportunities to bring to the field of ASD and NDD research, including advancements in remote sensing technology, machine learning, and other cutting-edge modalities.
- **Fuel discovery.** Develop a deeper understanding of human brain development and how it is impacted by NDDs.
- **Harness open science.** Bring together diverse biomedical sectors and perspectives and provide transparency and access to our learnings.

# Establishing the ARIA IMPACT Network

## Addressing the Challenge

The overarching goal is to establish an integrated pediatric clinical research network that accelerates clinical trial readiness and implementation in syndromic and non-syndromic ASD and related NDDs by creating a robust network of sites uniquely positioned to foster cross-disciplinary collaboration for innovative therapeutic development.

**Specifically, the IMPACT Network seeks to enable** a) standardized, coordinated quantitative phenotyping and biomarker discovery across participating sites; b) the capacity to deliver cutting-edge clinical research interventions; c) the opportunity to contribute to foundational collaborative human neuroscience research; and d) the ability to run sufficiently powered clinical trials. This will require close collaboration and coordination with existing family organizations and patient cohorts that include profound ASD as well as the establishment of a longitudinal cohort that is deeply phenotyped in a standardized manner across multiple sites – thereby creating a trial-ready population – that can participate in relevant clinical trials as they become available.

Although there have been significant advancements in autism research, effectively translating these discoveries into improved clinical care and better outcomes for autistic people and people with related NDDs remains a significant challenge. This disconnect is driven by several critical roadblocks that hinder the development and implementation of effective therapies, including:

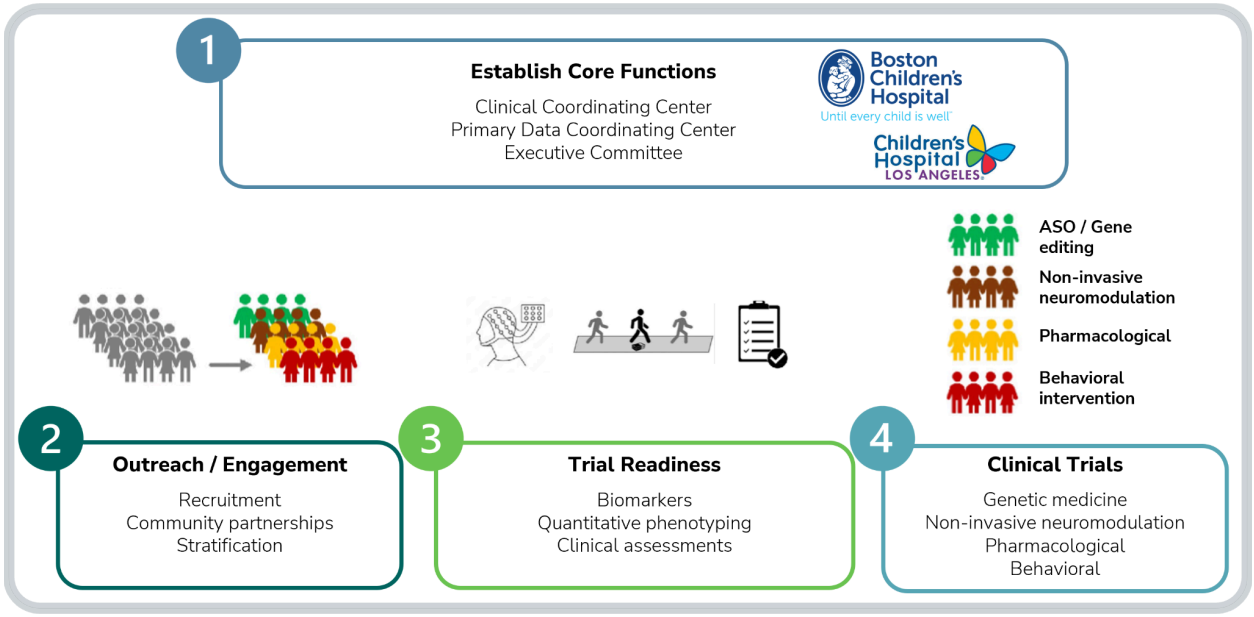
- Lack of clinically meaningful outcome measures.
- Lack of validated biomarkers for patient selection, measurement of drug-target engagement, as well as predicting and monitoring treatment response.
- Lack of standardized approaches to data collection and analysis.
- Fragmented clinical trial infrastructure, funding, and relevant expertise.
- Limited access to clinical trials for diverse populations.
- Difficulties with recruitment and retention in clinical trials.

ARIA intends to create an ecosystem that leverages the experience and lessons learned from existing clinical research consortia and expands upon them to meet the complex needs of a robust, multicenter clinical trial infrastructure and enables rapid and effective therapeutic development. This network will serve as a foundation and catalyst for all types of therapeutics, from targeted treatments for genetically defined cohorts of individuals with syndromic ASD and related NDDs, to large-scale pharmacological and non-invasive

neuromodulatory trials in non-syndromic ASD and related NDDs, to early behavioral intervention and biomarker development studies.

## ARIA IMPACT Network Roll-Out

The ARIA IMPACT Network is rolling out its activities in four phases. See schematic below for an overview of anticipated activities.




- **Phase 1: Establish Core Functions** – Please see the description provided in Appendix B. These core functions will precede site selection for the IMPACT Network.
- **Phase 2: Operational Ramp-Up and Maintenance** – This phase will support master protocol alignment and optimize workflows across sites in preparation for Phases 3 and 4. Additionally, community partnerships will be established to support trial enrollment and retention.
- **Phase 3: Trial Readiness** – This phase supports the establishment of a longitudinal cohort that is deeply phenotyped in a standardized manner across multiple sites. This observational multi-center study will focus on improving biomarker discovery, quantitative human phenotyping, and clinical assessments. This phase is expected to be active in years 2-5; however, if sites are ready to go, this phase could begin in year 1.
- **Phase 4: Trial Implementation** – This phase supports behavioral, pharmacological, and disease-modifying treatment strategies for ASD and related NDDs and is expected to be active in years 3-5. Upon deciding that a trial will be implemented within the network, participating sites will have the opportunity to request the requisite funds at that time. This will allow for maximum flexibility, given that trial implementation costs

can vary widely, and we cannot anticipate which trials will be implemented through the network at this time.

## Site Selection: Funding Available

**This RFA focuses on Phases 2 (Operational Ramp-Up and Maintenance) and 3 (Trial Readiness). If invited to submit a full application,** applicants may submit a total request of up to $15 million USD in direct costs over five years to support participation in the IMPACT Network. The indirect cost rate for all entities is 15%. Maximum available funds vary by phase; however, some overlap is expected in phase initiation and implementation. Payment will be tranched based on phase initiation.

Budgets will be included at the full application stage using a provided template. As a preview, direct costs may include but are not limited to salary support for all required positions (see Appendix C), neuropsychological assessments, behavioral and biomarker equipment (based on requirements that will be established), sample collection, site data storage costs, and patient travel.

### Organizational Eligibility

Applications will be accepted from any public or private-sector organization, including non-profit and for-profit organizations, that provides clinical care for pediatric and adult populations affected by ASD and related NDDs in the United States (including Territories of the United States), Canada, or the United Kingdom.

**Site teams can submit applications from a single organization or a group of up to three organizations.** Applicants that include more than one institution per application will need to justify the structure based on geographical efficiency, expanded research and/or clinical capabilities, and/or specific personnel and leadership requirements. We expect to prioritize individual institutions with a full range of capabilities relevant to the RFA and future Frontier Science Hubs.

**Sites with clinical capacity for both syndromic and non-syndromic ASD and related NDDs, the ability to integrate translational research into their workstreams, a demonstrated history of successful collaborative research and clinical trials in ASD/related NDDs** will be prioritized in the selection process. Qualified applicants must demonstrate the capacity to:

- Lead a collaborative, multidisciplinary team of scientists and clinicians.

- Collaborate across institutions, family groups, and community organizations to recruit participants with ASD and related NDDs.
- Enroll, evaluate, and retain at least 50 pediatric participants with ASD and related NDDs per year, for five years, for a minimum total of 250 participants.
- Provide clinical care and engage patients in research protocols for five years. This includes serving a range of already ascertained patients with known genetic syndromes and associated medical comorbidities.
- Conduct biomarker discovery, quantitative phenotyping, and clinical assessment for participants with syndromic and non-syndromic ASD.
- Execute phases 2-4 associated with ARIA IMPACT Network activities.
- Conduct investigator-initiated and/or industry-sponsored clinical trials in behavioral and pharmacological interventions.
- Implement, manage, and oversee an IMPACT Network-specific data collection protocol that may include data from electronic health records (EHR), neuroimaging and electrical signal recordings (e.g., MRI, EEG, eye tracking), wearables and/or remote assessments, and other clinical assessments.

# Application Requirements

The application for this funding opportunity has four steps: (1) an open pre-application (2) an invited full application, (3) an external review, and (4) a finalist interview wherein the applying institution's lead investigator and core team will present key aspects of their application and address any questions based on submitted external reviews.

**All applications will be submitted online through a grants portal. The portal will be open to all applicants during the week of June 23, 2025. The portal will close to all submissions by 11:59pm ET on Monday, July 14, 2025. All application questions are included below to allow all interested candidates to prepare their teams and responses in advance of the portal's open date.**

## Step 1: Pre-Application

This pre-application is open to interested eligible institutions. It consists of short-answer questions and prompts designed to assess the capabilities of the applying team and their institutional support.

### *Organizational & Team Profile*

#### ORGANIZATIONAL PROFILE

Applications can be submitted by a site team represented by at least one organization, up to a maximum of three organizations. We expect to prioritize individual institutions or closely affiliated institutions that have chosen to establish a productive collaborative relationship.

1. **Background information** – All organizations represented in the application will provide the following basic information:

| | Name of Organization | Type of Organization | Location |
|---|---|---|---|
| Site #1 | [dropdown list] | [dropdown list: e.g., Academic Medical Center, Hospital, Research Nonprofit, etc.] | [USA, Canada, UK] |
| Site #2 | [if applicable] | | |
| Site #3 | [if applicable] | | |

2. **Lay summary** – Provide a lay-level summary describing how your team will help the IMPACT Network achieve the desired level of coordination and care to execute multicenter longitudinal cohort studies and clinical trials successfully. Again, note that if your application includes more than one institution, kindly provide a justification for our proposed structure and how it can be leveraged by the IMPACT Network successfully (300-word maximum).

## LEADERSHIP AND TEAM PROFILE

Any site team selected to be part of the IMPACT Network must fill up to fifteen (15) positions. See **Appendix C** for a full description of all required roles and the minimum percent effort required for each position.

3. **PI Information** – At the pre-application stage, candidate site teams will be asked to provide the names and corresponding information for the first three proposed principal investigator positions indicated below:
    - **Coordinating Lead PI (25%)** must devote a minimum of 25% effort to this role, provide overall site oversight, and collaborate with PIs across IMPACT sites and with ARIA leadership teams. Consider adding expertise in basic/translational neuroscience and genomic medicine.
    - **Clinical Research Lead (Co-PI) (25%)** must devote a minimum of 25% effort to this role and will oversee the site clinical assessment team, recruitment, enrollment, and community outreach.
    - **Biomarker Research Lead (Co-PI) (25%)** must devote a minimum of 25% effort to this role and will oversee the site biomarkers team and activities (imaging, EEG, eye tracking, quantitative assessments).

**Applicants will complete this table in the grants portal:**

| Name | Degree(s) | Institution | Position/ Title | Email | Role on Team | Biosketch or CV Upload |
|---|---|---|---|---|---|---|
| [fill-in field] | [fill-in field] | [dropdown list] | [fill-in field] | [fill-in field] | *[dropdown list: 1 - Coordinating Lead PI 2 - Clinical Research Lead (Co-PI) 3 - Biomarker Research* | [pdf upload field] |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | *Lead (Co-PI)]* | |
| | | | | | | |
| | | | | | | |

4. **Leadership model** – As ARIA evolves, our vision is for the sites to have the capacity to integrate research and clinical ecosystems to enable real-time exchange of findings and rapid translation of research to the bedside. Therefore, we are interested in sites that can espouse a collaborative, distributed leadership model. Describe your proposed leadership structure and management strategy for your proposed IMPACT Network site team, as well as your ability to integrate basic and translational science at your clinical site related to any of our Frontier Hub priorities (see **Appendix A**). For applications with multiple sites, please describe how the leadership team will coordinate and communicate (500-word maximum).

5. **History of intra-team collaboration** – To what extent have the three PIs listed above collaborated? Include relevant examples of leadership of team-based research and/or care delivery, including cross-disciplinary and cross-departmental initiatives within the home institution, as well as any multi-institutional and/or consortia-based experience (500-word maximum).

6. **Partnership profile** – Describe your leadership team's participation in, contributions to, or partnerships with the following (300-word maximum per sub-question):
    a. Collaborative efforts in pediatric ASD and related NDDs (e.g., ABC-CT, RDCRN, IBIS, SPARK, ACE, Brain Gene Registry-IDDRC, BSRC, POND Network, ABCD, HBCD, etc.)
    b. Rare disease organizations, patient advocacy groups, and/or regional academic/community partners that your organization may leverage as a Participating Center.
    c. Biotech and/or industry companies that your organization may leverage as a Participating Center.

## *Clinical Profile*

### CLINICAL CARE

7. **ASD/NDD capacity** – Do any of the organizations represented by your site team have a dedicated ASD or NDD clinic? *[YES, NO]*

a. If yes, on average, how many pediatric patients with ASD/related NDDs have been evaluated and/or managed per year, over the last five years? What percentage of these pediatric patients have a diagnosed genetic variant associated with their ASD/related NDD diagnosis (please provide an estimate)?
b. If no, please provide an estimate of how many children with an ASD/related NDD diagnosis are evaluated and/or managed in your institution per year, over the last five years. What percentage of these pediatric patients have a diagnosed genetic variant associated with their ASD or NDD diagnosis (please provide an estimate)?

8. **Profound ASD capacity** – Do any members of your site team have experience evaluating and treating patients with the following conditions (check all that apply):
   - ☐ non-verbal / minimally verbal
   - ☐ severe intellectual disability
   - ☐ epilepsy
   - ☐ full-time assistance with activities of daily living

## CLINICAL TRIALS

9. **Relevant pediatric trial history** – To understand the pediatric clinical trial experience represented by the leadership of your site team, **please list up to 10 pediatric clinical trials** (i.e., defined as a clinical study with an intervention, including gene therapy, pharmacological, or behavioral) that any one of your three site team leads has been a part of in the past ten years.

| | **Pediatric Condition** | **Trial Stage** | **Trial Status** | **Clinicaltrials.gov Link** | **Number of patients enrolled at your site** |
|---|---|---|---|---|---|
| 1 | [write in field] | [1, 2, or 3] | [dropdown: active, ongoing, terminated, ended] | *[URL]* | *[# write in]* |
| 2 | | | | | |
| 3 | | | | | |
| 4 | | | | | |
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| 6 | | | | | |
| 7 | | | | | |
| 8 | | | | | |
| 9 | | | | | |
| 10 | | | | | |

10. **Genetic medicine capacity** – From the studies listed in the table above, describe your team's experience and capacity in coordinating industry or investigator-initiated genetic medicine interventions in trials involving participants with syndromic or non-syndromic ASD and related NDDs. Also, describe any experience coordinating IND-enabling studies and/or regulatory submissions pertaining to investigator-initiated genetic medicine (300-word maximum).

### CLINICAL BIOMARKERS

11. **Quantitative human phenotyping** – Describe your site team/organization's clinical research capabilities with quantitative human phenotyping participants across the four different developmental stages indicated in the table below. Check all that apply:

| **Biomarker Modality** | **Infancy:** 0-1 years | **Early Childhood:** 1-5 years | **Middle Childhood:** 6-12 years | **Adolescence:** 13-18 years |
|---|---|---|---|---|
| EEG | ☐ | ☐ | ☐ | ☐ |
| MRI | ☐ | ☐ | ☐ | ☐ |
| Eye tracking | ☐ | ☐ | ☐ | ☐ |

## Step 2: Invited Full Application

Successful applicants will be notified if they are invited to submit a full proposal during the week of August 18, 2025. The full application guidelines will be shared at that time. We expect to invite up to 30 applicants to submit the full application with a final selection of up to 10 sites.

## Confidentiality

The review process will be confidential among all parties involved in the application evaluation. Application materials will not be returned to applicants.

## Contact Information

Receipt of application materials will be confirmed within 24 hours of submission. If you do not receive confirmation within 24 hours of submitting your application, please check your spam filters and contact grants@aligningscience.com.

For inquiries about scientific priorities, eligibility requirements, and application submission, please contact grants@aligningscience.com. For all other questions, including general and media inquiries related to ARIA, please contact info@aligningscience.com.

# Appendix A: Frontier Hubs

## Genetic Medicines

### *Purpose*

The Genetic Medicines Frontier Hub seeks to streamline gene-specific learnings across the 200+ ASD-linked genes and help advance the science into accessible medicine. This Hub has three primary goals: to (a) develop therapies, (b) optimize methods development and generate foundational datasets, and (c) harness the capabilities of community partners.

### *Focus Areas*

- **Seeding Patient-centric Partnerships** – The Genetic Medicines Frontier Hub will develop fit-for-purpose partnerships that reflect both the unmet research needs and scientific accomplishments to date of the many monogenic, disorder-focused foundations that constitute the syndromic ASD and NDD space.
- **Launching an Integrated & Scalable Pre-competitive Ecosystem** – The Genetic Medicines Frontier Hub will establish a unified and collaborative ecosystem focused on gene-specific research and development (R&D). This includes clinical trials, scalable methods for developing ASO, CRISPR-based editing, and delivery platforms, as well as gene replacement therapy, along with novel technologies and foundational resources such as datasets and tools to support the broader ARIA ecosystem. This framework will balance open innovation with mechanisms to enable downstream development.

## Protein-Protein Interactions

### *Purpose*

The Protein-Protein Interaction (PPI) Frontier Hub aims to uncover and target actionable protein interaction networks associated with high-confidence ASD genes. By harnessing advances in proteomics, structural biology, and computational modeling, the Hub seeks to identify novel, druggable PPIs and accelerate their translation into innovative therapeutic strategies.

### *Focus Areas*

- **Building a Discovery-to-Therapy Pipeline** – The PPI Frontier Hub will implement a two-stage effort to (1) identify and characterize high-value PPIs using scalable screening and modeling platforms, and (2) translate these targets into therapeutic

leads through screening of compound libraries and high-throughput small molecule screening approaches.

- **Facilitating Access to Critical Biosamples for PPI Studies** – This Hub will collaborate with other Frontier Hubs (e.g., Genetic Medicine) to facilitate access to essential biosamples. This access will enable the generation of foundational datasets and ensure integration across discovery science, validation, and translational efforts with the ARIA ecosystem.

## Neurosensing and Neuromodulation (NS/NM)

### *Purpose*

The NS/NM Frontier Hub aims to develop therapeutic strategies for sensing and modulating circuit-level activity in humans to address core ASD symptoms and co-morbid, impairing phenotypes. For this effort, we are developing a unique collaborative research environment, leveraging patient cohorts requiring neurosurgery to capture high-density multimodal data, from neurophysiology to autonomic responses, in real-time.

### *Focus Areas*

- **Understanding the Underlying Circuits and Neural Dynamics Enabling Functional Communication** – This Hub seeks to understand the circuits underlying sensory processing that govern how people perceive their environment and generate behavioral outputs for environmental interaction. Investigators will explore whether those circuits can be targeted and modulated for therapeutic benefit.

- **Developing and Building Models** – Following data capture, we plan to develop and build computational models to help us investigate important questions and generate a deeper understanding of brain activity patterns underlying human behaviors for functional communication. We will integrate existing open datasets with our newly generated data to produce more comprehensive and robust models.

## Language & Communication (L&C)

### *Purpose*

The goal of this Frontier Hub is to design a fit-for-purpose, cutting-edge research and/or incubator program that advances our understanding of L&C processes in ASD and related

NDDs. Currently in the scoping phase, we are implementing a collaborative working group (WG) process to identify key research priorities that will drive **quantitative human phenotyping** and **biomarker development**.

### *Focus Areas*

This workstream is structured around 3 working groups (WGs), each led by experts in the field, to ensure a comprehensive and multidisciplinary approach:

- **Neurobiology of Language –** This WG is focused on the core principles of language processes – acquisition, development, production, comprehension, and impairment.
- **Technology Development** – This WG is focused on developing and improving digital health and other technological tools for assessment and intervention.
- **Data Analysis** – This WG is focused on developing methods to collect and analyze comprehensive datasets to generate insights.

## Human Developmental Neuroscience

### *Purpose*

The Developing Brain Frontier Hub aims to decode how dynamic, age-dependent neurobiological processes contribute to ASD onset, symptom expression, and treatment response. By anchoring research across critical stages—from mid-fetal life through adolescence—and integrating insights from genetic, cellular, and circuit-level investigations, this Hub will generate foundational knowledge to inform when, where, and how to intervene. This developmental lens will guide the timing and design of next-generation therapeutic strategies and enable model systems that reflect key windows of vulnerability and plasticity.

### *Focus Areas*

- **Building Developmental Brain Maps** – Create cellular atlases and spatial reference maps of the human brain during critical developmental stages, expanding efforts that have focused primarily on adult brains and addressing gaps in early neurodevelopmental knowledge.
- **Harnessing Model Systems Across Scales** – Leverage a range of experimental systems, including animal models, organoids, differentiated cell types, and postmortem tissue, to explore how genetic and molecular changes unfold across developmental windows and brain regions implicated in ASD.

- **Linking Development to Therapeutic Timing** – Investigate how changes in neurobiology interact with learning, attention, and affective regulation to identify time-sensitive intervention strategies. This includes exploring neuromodulatory approaches that may enhance receptivity to behavioral therapies at key developmental stages.

## Engaging the Patient Community

An effort of this scale and magnitude requires deep engagement and partnership with the rare disease and the NDD community writ large. Recognizing this need, we are:

- **Building relationships:** During the design, scoping and now launch of the ARIA initiative, our staff have been building relationships with several patient groups to learn about their research priorities, understand their pain points, and glean feedback regarding their appetite for engagement with the initiative. As the IMPACT Network infrastructure is being built, we will identify the relevant groups with which to partner to inform decision-making and ideal next steps.

- **Building capacity:** We have launched the ARIA Capacity Grants Framework, which aims to establish strategic organizational partnerships to support cross-effort collaborations that align with our strategic priorities and workstreams. These collaborations are expected to foster synergy, avoid redundancy, and accelerate progress towards shared goals.

# Appendix B: Establishing Core Functions

## Centralized Services

The ARIA IMPACT Network will utilize centralized services to ensure standardization of clinical and data processes and efficient workflows for future clinical trials. By centralizing certain core activities, we expect to reduce the administrative and cost burden on the site teams, allowing them to focus on recruitment and engagement.

### *Clinical Coordinating Center:*

The ARIA Clinical Coordinating Center (CCC) serves as the nucleus of the ARIA Network and provides clinical research operations, administrative leadership, and oversight. The CCC's overarching goal is to create an environment where clinical research relevant to ARIA's goals can be effectively and efficiently designed, conducted, and disseminated.

The CCC is jointly led by Shafali Jeste, MD, at Children's Hospital Los Angeles, and Mustafa Sahin, MD, PhD, at Boston Children's Hospital. They will collaborate with ARIA leadership to manage participating sites and facilitate collaboration and communication amongst site teams in the IMPACT Network.

### *Data Coordinating Center:*

The Data Coordinating Center (DCC) will manage all data collected at the Participating Sites, ensuring that data collection is standardized and integrated from multiple sites. The DCC team will also create pipelines for rapid data quality control and feedback, and oversee all data cleaning, signal processing, and analyses. The DCC will also provide a user-friendly platform for the sites and participants to view summary data. The DCC will coordinate with the CCC, working closely with the CCC Data Coordination Director, and both entities will collectively report to CAS.

## Appendix C: Required Roles

Given the ambition, scale, and scope of these projects, the sheer amount of data that will be generated, and the required coordination between funded teams and ARIA staff, each applicant must budget for the following positions, which this award will fully fund.

The site team will focus on the initial longitudinal natural history study, which will serve as the framework for future clinical trials. This funding will provide ongoing fixed costs for essential personnel at IMPACT sites, with the understanding that additional funding and per-patient reimbursement may come with future individual clinical trials.

The roles described below reflect the key areas of expertise required to support the IMPACT Network's clinical research mission. This list is intended to articulate functions, not prescribe the number or structure of positions. In some cases, a single individual may fulfill multiple roles—for example, a neurologist may serve as the Coordinating Lead PI—as long as the requirements for minimum percent effort are met or exceeded. Applicants should demonstrate that their team collectively brings the necessary capabilities, regardless of how responsibilities are distributed across personnel.

The minimum percent effort requirements for each role are as follows:

1. **Coordinating Lead PI (25%)** must devote a minimum of 25% effort to this role, provide overall site oversight, and collaborate with PIs across IMPACT sites and with ARIA leadership teams. This person will be the primary point of contact for ARIA staff.
2. **Clinical Research Lead (Co-PI) (25%)** must devote a minimum of 25% effort to this role and will oversee the site clinical assessment team, recruitment, enrollment, and community outreach.
3. **Biomarker Research Lead (Co-PI) (25%)** must devote a minimum of 25% effort to this role and will oversee the site biomarkers team and activities (e.g., imaging, eye tracking, quantitative assessments).
4. **Neurologist (20%)** will provide pediatric neurology expertise for IMPACT clinical and translational research. They will assist in developing and implementing protocols to maximize the quality of neurological data acquisition in participants. They will perform participant neurological exams as part of the longitudinal natural history studies.

5. **Medical Geneticist (20%)** will provide medical genetics and genomics expertise for IMPACT clinical and translational research. They will assist in developing and implementing protocols to maximize the quality of genetic data acquisition in participants. They will review genetic testing reports, oversee results disclosure, and conduct participant dysmorphology exams as part of the longitudinal natural history studies.

6. **Genetic Counselor (100%)** will serve as the bridge between clinical and research programs for ASD and NDDs, facilitating participant entry to clinical research projects. The genetic counselor will provide support and resources to families participating in projects within the ARIA network, provide guidance as to the genetic testing process and return genetic results to participants and families.

7. **Psychologist/Psychometrist (100%)** will serve as the site lead for staff training on all measures, fidelity checks, and administration of testing. They will oversee and conduct reviews of relevant videotaped administrations, participant research reports, and results disclosure/feedback sessions for participants. They will directly administer and score behavioral/psychological assessments as per standard operating procedures. They will collaborate with other IMPACT site psychologists to ensure cross-site consistency of battery administration and adherence to best practices.

8. **Biomarker Assessment Coordinator (100%)** will directly oversee and administer imaging and quantitative data procedures as per standard operating procedures. They will also lead the coordination of wearables and home assessments. The coordinator will facilitate communication with the site study team, including visit scheduling, study data provision, results return, and coordinate activities across IMPACT sites.

9. **Clinical Research Coordinator (100%)** will coordinate daily activities of research studies in accordance with standardized procedures and good clinical practice. They will plan and conduct study visit procedures and collect, manage, and store study data.

10. **Behavioral Specialist (100%)** will have expertise in behavior management of children with NDDs, such as experience with ABA and other interventions. They will assist in developing and implementing protocols to maximize the quality of data acquisition in participants.

11. **Regulatory Specialist (50%)** will serve as the site's regulatory expert, providing guidance and assistance on the preparation and maintenance of IRB applications and associated submissions, including site reliance agreements. They will also oversee E-regulatory binder submissions and management, conduct/assist with site regulatory

audits, and ensure the provision of appropriate regulatory training to relevant study staff personnel.

12. **Program Manager (100%)** will manage the day-to-day coordination of all site team member efforts to consistently maintain a high level of functionality and communication to meet all stated deliverables.

13. **Data Manager (100%)** will be responsible for site oversight of data processing, curation, and analysis activities. The Data Manager, as envisioned by this award, is responsible for:

    - Developing and maintaining the Data Management Plan in coordination with the CCC.
    - Developing documentation required to ensure transparency and accessibility, with the end goal of ensuring that other researchers can effectively analyze data from all projects undertaken at this site.
    - Sharing data to the Bridge Analytics architecture and ensuring that documentation is complete.
    - Sitting on the ARIA Data Advisory Board, which will, in turn, have representation on the Bridge Analytics Data Operating Committee to establish alignment with other members of the ARIA Data Advisory Board on the approach to data curation, ensuring that the initiative's data requirements will be met.
    - Meeting regularly with the CCC Data Coordination Director, the Primary DCC, and other IMPACT site Data Managers to coordinate efforts across the Network.

Of note, these positions must be named within three months of the award. If hiring is required for any position, a job announcement must be posted within two months of the award, and hiring must be completed within six months of the award. Successfully filling these required positions is required for the release of a portion of funds. Full-time positions stated above may be split up for a total effort of 100% per position.

# Appendix D: Organizations and Governing Bodies Powering ARIA

## Organizations

### *About SBFF*

The Sergey Brin Family Foundation supports efforts to understand and treat central nervous system (CNS) conditions through research and translation through an effort known as the CNS Quest. ARIA will be the third large-scale CNS Quest initiative to launch on behalf of the foundation and is built on the model developed through Aligning Science Across Parkinson's (ASAP) and Breakthrough Discoveries for Thriving with Bipolar Disorder (BD2).

### *About CAS*

The Coalition for Aligning Science (CAS) is a program development and management firm that designs and implements large-scale research programs to accelerate discoveries in biomedical research by guiding strategic philanthropic funding to fuel breakthroughs and catalyze impact. Sergey Brin Family Foundation (SBFF) has retained CAS to develop and manage various aspects of its science philanthropy portfolio, including the CNS Quest. CAS staff will be assigned to execute programmatic components of the ARIA initiative.

### *About Bridge Analytics*

Bridge Analytics is a data services organization that ensures that data generated within the CNS Quest is accessible, harmonized across initiatives, and ready for advanced analytics. Bridge works across CNS Quest initiatives to ensure that funded programs are generating evidence that is useful for therapy developers and can be used to drive decision-making by regulators and payers.

## Governing Bodies

### *ARIA Executive Leadership Team*

The ARIA Executive Leadership team comprises leaders from the University of California, San Francisco, and CAS. Drs. Matthew State (UCSF), Ekemini Riley (CAS), and Sonya Dumanis (CAS) serve as Scientific, Managing, and Deputy Directors, respectively. View bios on the ARIA website here.

### *ARIA Scientific Advisory Board (SAB)*

The SAB will guide ARIA's long-range scientific strategy. Chaired by the Scientific Director, the board consists of multidisciplinary scientists, including physician-scientists, clinical trialists, basic researchers, pediatric psychiatrists, and neurologists. View members and bios on the ARIA website here.

### *ARIA Data Advisory Board (DAB)*

The DAB will advise on all aspects of data curation and analysis. The board will consist of the Data Managers from each team and a few individuals who have data science expertise and/or experience working with various data types that each project team will generate.