Breakthrough Discoveries for thriving with Bipolar Disorder

Request for Applications (RFA): Integrated Network Sites

July 2024

PERTINENT DATES	
RFA Released	July 18, 2024
Submission Deadline	October 10, 2024
Review Period*	October - November 2024
Projected Award Notification	Mid-December 2024
Project Start	March 2025

*If deemed necessary, applicants may be requested to clarify their proposal through an oral presentation, and/or agree to a site visit by BD² program staff. If either request is to be made, BD² will notify applicants.

Opportunity Snapshot

Breakthrough Discoveries for thriving with Bipolar Disorder (BD²) seeks four clinic sites to join the Integrated Network. The Integrated Network is part of a multidisciplinary initiative to increase understanding of the heterogeneity, progression, and underlying biology of bipolar disorder and, ultimately, to identify novel strategies for improved care and intervention.

BD² plans to award up to $2.3 million USD over five years to each of four clinic sites with the ability to capture in-depth, longitudinal data on people living with bipolar I disorder and a strong willingness to drive improvements in care through collaborative work and learning.

APPLY HERE

About BD²

Bipolar disorder is a highly complex and heterogeneous disorder that is often debilitating. Even though it is prevalent in approximately 3% of individuals worldwide, and is recognized as a leading cause of disability, little is known about its biology. Advancements in our understanding and treatment of bipolar disorder to date remain far from ensuring that everyone living with it can manage their condition and lead independent, fulfilling lives.

BD² is the first organization focused on funding and advancing research and care for bipolar disorder on a global scale. Our collaborative, open-science approach is intentionally designed to transform and shorten the time it takes for scientific breakthroughs to make a meaningful difference in the lives of the tens of millions of people with bipolar disorder. For too long, there have been limited advances in the study and treatment of bipolar disorder due to a lack of collaboration and funding. It's time for a new approach.

About the BD² Integrated Network

The purpose of the Integrated Network is to improve the health and well-being of people living with bipolar disorder by engaging a network of collaborating investigators and clinicians to:

i) build an unprecedented data ecosystem for bipolar disorder comprised of longitudinal clinical and biological data

ii) implement and inform data-driven improvements in care

iii) generate novel insights for interventional approaches

In partnership with people living with bipolar disorder, clinicians, and researchers, BD² established the Integrated Network to accelerate research and dramatically improve systems of care for bipolar disorder. It embraces a two-pronged approach — a traditional Longitudinal Cohort Study designed to generate in-depth phenotypes of bipolar disorder over time, and a Learning Health Network aimed to iteratively improve outcomes.

The Longitudinal Cohort Study (LCS)

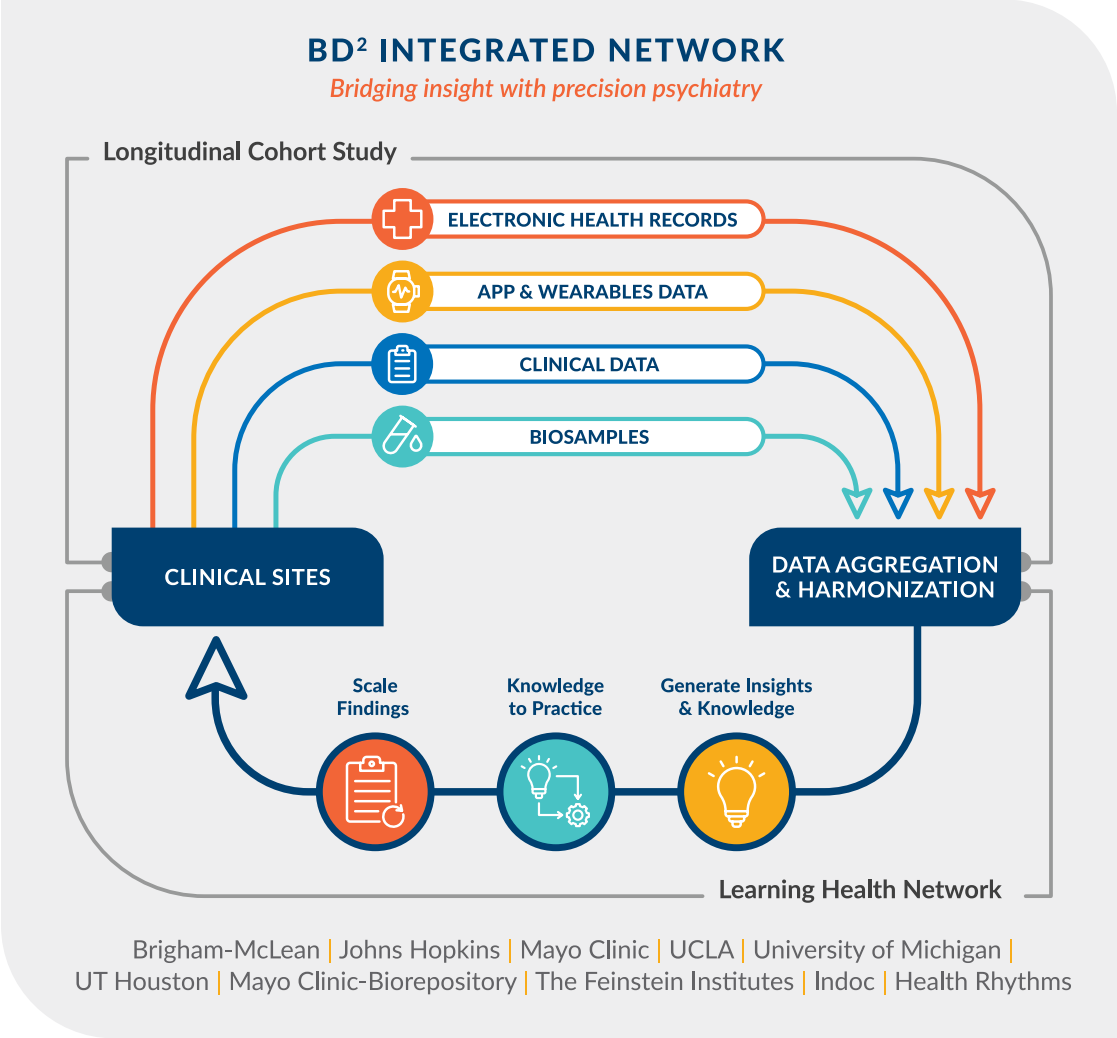
The Integrated Network is conducting deep phenotyping of a diverse group of people with bipolar I disorder to accurately capture the trajectory of disease and to clarify its underlying biology. This will enable the identification of key clinical (e.g., recurrence rate, comorbid diagnoses, early life adversity, sleep disruption, cardiovascular risk), neural (e.g., structural changes in gray matter, white matter disease, cognitive deficits), and biological (e.g., inflammation, elevated stress hormones, genomics) processes that drive outcomes in bipolar disorder.

The Learning Health Network (LHN)

At each site, a core team of clinicians will carry out best clinical practices with their patients and learn from other teams within the network to augment their care through evidence-based approaches. These clinicians, with local IT support, will be champions of the LHN within their institution, and will work to implement on-the-ground, near-real-time improvements in clinical care based on emerging insights generated from network data.

Coupling an LCS with an LHN links discovery research with improvement of clinical care, so insights from basic science research and clinical practice inform improvement targets and health outcomes goals — ultimately increasing the health of people with bipolar disorder (Figure 1).

Figure 1. Overview of the BD² Integrated Network. The BD² Integrated Network brings together research and care in a unique way that sets the stage for personalized care. The ultimate model of change will come from combining these data streams and processes in novel ways. Through the learning health network, we will intentionally facilitate the application of findings from the longitudinal cohort study data to care settings.



We are seeking the participation of team-orientated investigators committed to realizing BD²'s vision to build adaptive, networked approaches to mental health care and research. Investigators and their associated health systems are expected to bring their leadership, capabilities, and resources to the effort. They must demonstrate a long-term commitment to building and participating in a community dedicated to developing new solutions to the challenge of providing the best care for those living with bipolar disorder.

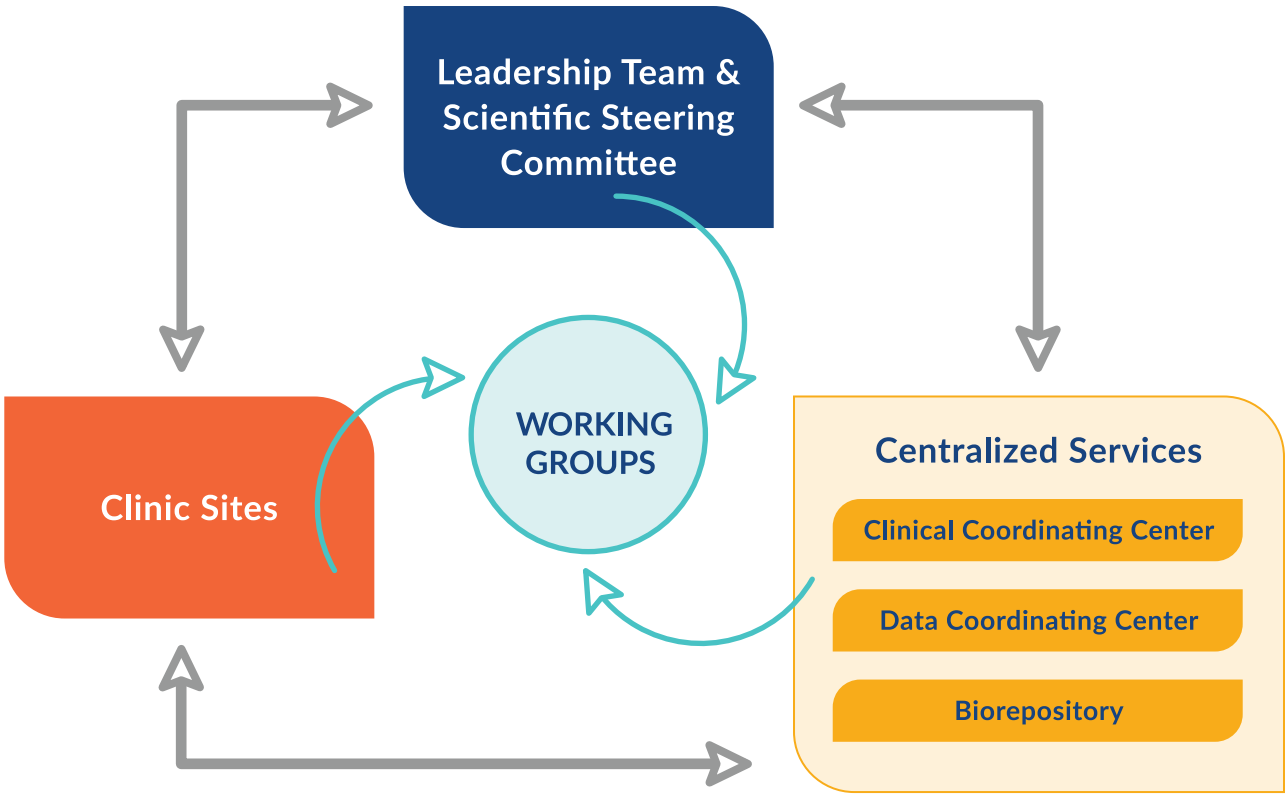
BD² Integrated Network Organizational Structure

The Integrated Network's operations are directed and managed by Integrated Network program team staff and the Scientific Directors, collectively known as the Integrated Network "Leadership Team." The Leadership Team regularly receives strategic input and advice from the Scientific Steering Committee (SSC), which is comprised of leading experts in psychiatry, clinical psychology, neuropsychology, lived experience, neuroimaging, genomics, translational neuroscience, community outreach, and mental health informatics.

A key goal of the program is to aggregate consistent and complete data from clinic sites. To this end, the Leadership Team has selected centralized service providers to standardize clinical and data processes across the Integrated Network study, including a Clinical Coordinating Center (CCC), a Data Coordination Center (DCC), and centralized biosample processing, analysis, and storage facilities ("biorepository"). These Integrated Network centralized service providers report to the Leadership Team. For more information on these partners, please see the "Centralized Service" section on page 7.

Members of the Leadership Team and representatives from the centralized service providers meet regularly with each of the clinic sites to discuss program design, implementation, data collection and transfer, progress, and results. The program also consistently relies on expertise embedded within the sites. In line with their subject matter expertise, site team personnel are expected to attend regular "Working Group" meetings with members of other site teams, centralized service providers, SSC, and the Leadership Team to provide feedback and recommendations on specific portions of program strategy, execution, and assessment. Current Working Groups include those focusing on neuroimaging, applications & wearables, bioassays & biorepository, clinical assessments, data, and various components of the LHN.

Figure 2. BD² Integrated Network Governance Structure. The BD² Integrated Network Leadership Team, SSC, awardee clinic sites, and centralized service providers consistently work together to improve and implement LCS data collection, extraction, and analysis procedures. This crosstalk occurs through regular 1:1 check-ins between these partners as well as consistent Working Group meetings, which involve members of all centralized service providers, clinic teams, and external partners sharing expertise around a specific goal.



Funding

BD² intends to fund up to four clinic sites during the current recruitment round, bringing the total number of Integrated Network clinic sites to ten. The anticipated award date for the next four sites is approximately mid-December 2024.

Each applicant site may request up to $2,300,000 (USD) for use over five years to administer the LCS protocol and LHN as outlined in this RFA. This includes costs to recruit a goal of **100 bipolar I disorder participants within the first year (cohort 1), collecting longitudinal data for an additional four years, and the necessary clinical and administrative process changes to support the study within their institution**. All grant totals are inclusive of indirect costs up to a maximum of 15% of the site budget.

In year 1, selected sites will receive $500,000 in the form of two milestone-based payments: $150,000 will be awarded once the BD² contract is finalized, and the remaining $350,000 will be awarded once (1) all institutional and BD² criteria for study data collection & transfer to the DCC are met, (2) all study staff have completed the necessary training conducted by the centralized service providers, and (3) the site has consented its first participant.

In years 2-5, upon successful completion of milestones, up to $450,000 per year will be awarded.

Table 1. Milestone-based payment schedule for cohort 1 (100 bipolar I disorder participants).

Cohort 1 (100 participants)	Milestone Payment
Year 1 - Milestone 1	$ 150,000
Year 1 - Milestone 2	$ 350,000
Year 2	$ 450,000
Year 3	$ 450,000
Year 4	$ 450,000
Year 5	$ 450,000
Total	$ 2,300,000

In addition, in years 2 and 3, new rounds of milestone-based funding will become available as follows:

Once the initial 100 participants are enrolled, each individual site will be eligible to apply for an additional $1,300,000 to enroll and follow a new cohort of 100 participants for five years (cohort 2). A third milestone-based grant valued at $1,300,000 to enroll and follow another 100 participants for five years (cohort 3) will be made available once the site has recruited a total of 200 participants. Thus, each awarded site will be eligible for funding of up to $4,900,000 to support the enrollment of a total of 300 participants – each of whom will be followed for a total of five years.

Organizational Eligibility

Proposals will be accepted from any United States (including Territories of the United States) or Canada-based public or private-sector organization, including non-profit and for-profit organizations, that provides clinical care for people with bipolar disorder.

Qualified applicants must demonstrate the capacity to:

- Recruit 100 individuals with a diagnosis of bipolar I disorder into the initiative per year for three years, for a total of 300 participants.
- Provide clinical care and treatment to those participants for five years.
- Implement, manage, and oversee the data collection protocol for the longitudinal study protocol, which includes data from electronic health records (EHR), neuroimaging, wearables, ecological momentary assessments, and other clinical assessments.
- Participate in the planning and community building of the LHN by reporting EHR data, contributing to reviewing site and network-level interim analyses, and developing interventions to improve care that draw on data generated using the LHN.

Organizations with prior experience in longitudinal studies (particularly in the field of psychiatry), learning health system development, clinical coordination, quality improvement, outcomes research, and the development of large, multi-center programs relevant to bipolar disorder are encouraged to apply.

Scope of Work

BD^2 seeks four additional institutional partners who are dedicated not only to improving the standards of care for people with bipolar disorder but also to challenge the status quo to advance our scientific understanding. Investigators at these institutions, in collaboration with the current Integrated Network community, will help to both lead the LCS as well as participate and guide the LHN to achieve improvements in care delivery and patient outcomes. The overall goal is to recruit and retain 4,000 participants with bipolar I disorder within the Integrated Network.

The Longitudinal Cohort Study

Each participating site will recruit 100 individuals living with bipolar I disorder into the LCS. The goal is to enroll 100 individuals during year 1 and monitor outcomes for an additional four years. The opportunity to enroll up to 200 additional participants will be milestone-driven and based on a review of the efficiency and retention rates at each site.

Data generated by the longitudinal study will be deposited within a centralized data repository (the BD^2 Data Platform), which will aggregate, harmonize, and share data across the Integrated Network. A research team at the site will be responsible for these data collection efforts and ensuring that the site carries out the longitudinal protocol with rigor. The range and cadence of data captured through the longitudinal study reflect the complexity of the illness and its dynamic nature. The LCS will provide investigators and clinicians with an opportunity to integrate clinical, behavioral, and biological data from participants to gain new insights into pathophysiology, illness trajectory, and treatment response. Our ultimate study goal is for a more complete understanding of the disease and to charter a path toward precision care optimized at the individual level. To view the IRB-approved protocol, please see Appendix A: “LCS Protocol”.

The Learning Health Network

Given a shared goal to improve care delivery and outcomes, the Integrated Network's LHN will capture input and generate consensus across multiple stakeholders. Since the program's launch, the inaugural six clinical sites of the Integrated Network have worked in concert with the Integrated Network's Leadership Team, SSC, partners, and people with lived experience to design the LHN's structure. Clinicians at each participating site are engaging care teams (e.g., physician leader, RN, coordinator or staff, patient/family member) and organizational leaders to drive transformation efforts. Further, sites are collaborating with one another to establish measurement systems that can be used to identify and learn from variations in care. This framework will allow the Integrated Network to test and deploy best practices and innovations aimed at improving care. For more information, please see Appendix B: "LHN Overview".

Centralized Service

A foundational characteristic of this initiative is the use of centralized service providers. This includes a CCC, a DCC, and a biorepository. These partners standardize clinical and data processes, including administration of psychological assessments as well as data capture and distribution. Additionally, centralizing these services reduces site administrative and cost burden allowing them to focus on recruitment and engagement. Personnel from the centralized service teams work closely with the participating investigators to assist with any issues, provide clinical and data support, and ensure that sites are standardized across the network. Investigators can also access data from the CDR to directly improve care and learn from efforts within the network, as well as analyze data for research.

The Clinical Coordinating Center

The CCC, led by the Feinstein Institutes for Medical Research, is managed by a team of bipolar disorder clinicians and care providers. The CCC team coordinates the central IRB approval and works with each site to obtain local IRB ceding approval. Members of the CCC team perform a variety of clinical assessments, including structured interview-based validation of the bipolar I diagnosis and comorbid psychiatric diagnoses, mood symptom ratings, sleep surveys, and more. Centralizing these services allows for improved standardization of the assessments. The data are summarized and sent back to the sites so that clinicians can track their patients more rigorously over time and apply insights to treatment planning to inform care. The CCC team also works with each site's research members to ensure that the clinical assessments performed on-site, including cognitive and functioning assessments, are standardized and rigorous. Note that the CCC provides services distinct from clinical management/treatment of bipolar disorder, which will remain the responsibility of the participating site clinical team.

The Data Coordination Center

The DCC and CDR are both managed by Indoc. The DCC is responsible for supporting program data standardization and harmonization efforts, as well as aggregating and integrating data that are collected across sites and modalities. The DCC-operated BD² Pilot Data Platform (Indoc Pilot Platform) will house clinical data (including data derived from EHRs), biosample data, neuroimaging data, and mobile health data collected from study participants. Sites will send EHR extracts, processed wearable data, and neuroimaging data directly to the BD² Data Platform. Data scientists will work with site data teams to ensure that incoming data are correctly standardized, packaged, and meet the initiative's criteria. The DCC team will also help troubleshoot and provide any support required by the site on data-related matters.

Biosample Processing Facility and Biorepository

The Integrated Network has partnered with the Mayo Clinic (BioPharma Diagnostics and Bioservices teams) to manage biosample collection, processing, analysis, and storage. Biosamples are minimally processed at sites before shipment to Mayo.

Application Requirements

The application for this funding opportunity has two stages: i) a written proposal and ii) a finalist site interview (including, if necessary, a site visit).

Stage 1: Written Proposal Submission

Interested applicants should complete the application through the online grant portal: HERE. The application assesses the applicant's suitability to join the Integrated Network and consists of a series of short answer questions and prompts, as outlined below. Please keep all answers to **250 words or fewer** unless otherwise indicated.

Organization and Clinic Profile

1. In what country is your organization based?
   - ❏ United States (including Territories of the United States)
   - ❏ Canada
2. What is your organization's name and core mission statement?
3. What diversity, equity, and inclusion strategies are in practice within your organization?
4. Within your organization's clinical practice, how many adult patients have a confirmed bipolar I disorder diagnosis at time of application?
5. What percentage of the current bipolar I patients receive care from a specialty clinic? What percentage receive care from a primary care provider?
6. How many new bipolar I disorder patients were added to your organization's clinical practice in the past year?
7. How many providers are in your organization's clinical practice?

Leadership

8. How do you envision the future of bipolar disorder clinical care and research? What is your organization's role in the future? How does this vision align with the BD^2 Integrated Network?
9. Describe your proposed leadership structure and management strategy for your proposed Integrated Network site team. Please identify the overall site lead PI, clinical lead, research lead, and relevant structures and organizations. **(500-word maximum)**
   a) Please upload biosketches of the lead investigator and each co-investigator (clinical lead & research lead). Biosketches utilizing the NIH template are preferred, but a CV is acceptable.
10. What is the collaboration history of each investigator? Include references to past multi-team experience where relevant. **(500-word maximum)**
11. Integrated Network lead investigators are expected to actively contribute to topic-based "Working Groups," which currently include those focused on neuroimaging, applications & wearables,

biospecimens, clinical assessments, data, and the Learning Health Network. Please identify which Working Groups the members of your site team would be interested in joining — and specify people if already identified.

12. Discuss institutional buy-in and relationships between bipolar disorder clinical and research programs with relevant institutional bureaucracies that will ensure efficient implementation and management of the Integrated Network program.

13. Describe any experience your organization has with Learning Health Systems work.

14. Are there early-career team members as part of the proposed leadership/site team? If so, how will they be mentored?

Bipolar Disorder Expertise

15. Describe your clinical infrastructure that serves the bipolar disorder community. Please incorporate the demographic information of clinicians providing care for bipolar disorder, including percent breakdown of gender, race, ethnicity, and relevant specialties.

    a) Please upload any figures or tables that support your answer to question 15.

16. Provide general demographic descriptions of the bipolar disorder population you serve. This should include percent breakdown of gender, race and ethnicity, diagnoses of bipolar I disorder and bipolar II disorder.

    a) Please upload any figures or tables that support your answer to question 16.

17. Describe your Integrated Network participant recruitment strategy, including ways to enhance recruitment (e.g., from patient registries, or inviting patients who have already given permission to be contacted for research studies). What explicit policies and strategies will you implement to ensure that you recruit a diverse population with regard to race, gender, age, and socioeconomic status of participants? **(500-word maximum)**

18. Describe your organization's and/or team's experience in implementing longitudinal bipolar disorder studies. What types of data are/were collected? **(500-word maximum)**

Data Collection, Transfer, and Analysis

The BD² Integrated Network's LCS protocol requires the collection of numerous data modalities as well as the transfer of these data to an external data repository. The LHN leverages clinical data for shared analysis and learning across the Integrated Network. The Data Coordinating Center (DCC) is responsible for supporting Integrated Network program data standardization and harmonization efforts, as well as aggregating and integrating data that are collected across sites and modalities.

The following questions will establish if your site is currently positioned to meet the necessary requirements to fulfill the data-related goals of the Integrated Network. To aid in answering these questions, please refer to the RFA Appendix materials that provide additional information about the Integrated Network's data infrastructure: "EHR Data Dictionaries" (Appendix C), "EHR Data Manual" (Appendix D), "Neuroimaging Protocol" (Appendix E), and "Neuroimaging Data Manual." (Appendix F).

I. General

19. Describe your organization's research data management and support processes and resources. This includes data management expertise in processing, harmonization, and curation of various research data modalities outlined in the protocol. Please include details on resources, personnel, and processes your proposed team or institution provides for research teams conducting the data processing and curation prior to transfer to central repositories. **(750-word maximum)**

20. Sites will need institutional computing infrastructure for storage and processing of data collected at the site, prior to transfer to the DCC. These include neuroimaging scans, EHR extracts, and processed Fitbit data. Please describe the institutional research computing infrastructure available to your team to support required program data activities, including the data processing and curation activities required for transfer to the DCC, and retention of study data at the institution for the required retention period of five years. Details should include the capability to support storage needs, analytic environments required for data processing and curation, and intra-institutional capabilities to transfer data between departments/functions (i.e., from imaging core to the research team responsible for uploads, etc.). **(750-word maximum)**

21. To ensure highly effective workflows between the Integrated Network sites and the DCC, sites are required to assign a "Data Lead" who will be a primary point of contact for all data-related activities. Please identify your proposed site data lead. Have they had prior experience working with a multi-institutional research program? If so, please provide details.

22. Please describe the support your team will receive from institutional IT and security personnel for initial configuration and ongoing operational requirements.

23. The DCC-operated BD² Data Platform (Pilot) offers two methods of data transfer to the platform: a web-accessible portal and the Indoc Pilot command-line interface (CLI), allowing programmatic access. The Indoc Pilot CLI requires installation in a local Linux environment with access to the data to be transferred and access to the internet. Please confirm if your site can use one of these options.

    ❏ Yes

    ❏ No

    a) If you answered "Yes" to Question 23 please state which option your site will use.

24. Please describe any standard institutional vendor screening/assessment processes or requirements (including IT/information security screening, privacy screening, etc.) that would be required of the DCC — and/or any of the other BD² centralized service providers (see Page 7: "Centralized Service") before they are able to support your team and/or your team is able to receive IRB approval.

    a) Please upload institutional instructions and documentation related to these assessment processes, if possible.

II. EHR Data

25. Does your organization use an electronic health record (EHR) system?

    ❑ Yes

    ❑ No

    a) If you answered "Yes" to Question 25, please state which EHR your organization will use.

26. Please describe any major changes to the EHR system anticipated in the next five years. This may include shifts in EHR vendor, or general institutional reorganization that may impact EHR access.

27. What types of data are currently being collected in your EHR?

28. Does your organization routinely collect patient-reported outcomes? If so, which ones? What clinical purposes do they serve? (e.g., screening, monitoring, or measurement-based care)? Are any of these integrated into the EHR? **(500-word maximum)**

29. The submission of EHR data to the DCC requires Integrated Network site personnel to extract, pseudonymize, and process key data elements. How does your organization make EHR system extracts available for research use? Does your organization have prior experience with EHR data extraction and harmonization processes? Please provide relevant examples. **(500-word maximum)**

III. Neuroimaging Data

30. Does your organization currently have access to at least one of the following 3T MRI scanner(s): SIEMENS Prisma or SIEMENS CIMA-X or a GE variety?

    ❑ Yes

    ❑ No

    a) Please list the model and current software of all MRI scanners available to for your team to use in this study.

    b) Please list any information about the timing of future upgrades to your scanner(s) software.

31. How long will your site team have access to this scanner(s)?

32. Does your organization have a research agreement with Siemens/GE that allows you to run these Consumer-to-Producer (C2P) software packages: multi-band accelerated EPI pulse sequences C2P from CMRR, morphometry C2P from MGH and vNavs/PROMO for real-time motion correction (used in the ABCD study scanning protocol)?

    ❑ Yes

    ❑ No

    a) If you answered "No" to Question 32, can your organization acquire these materials prior to the expected study start (March 2025)? Do you have on-site support for sequence installation?

33. Does your scanner(s) have a projection system?

34. What is the distance between the clinic where participants will be seen and the scanner(s)?

35. Is your site currently part of any multi-site imaging study (e.g., ABCD, PPMI, ADNI, HCP)? Please list notable examples.

36. Please identify a proposed "Neuroimaging Lead" from your site to assist in BD² protocol implementation procedures and attend regular troubleshooting meetings with the DCC and BD² Neuroimaging Working Group.

IV. Wearables and Ecological Momentary Assessment (EMA) Data

37. Does your organization have experience extracting Fitbit data from a research Fitabase subscription?

    ❑ Yes

    ❑ No

    a) If you answered "Yes" to Question 37, please provide details.

38. Does your organization have experience with EMA data collection?

    ❑ Yes

    ❑ No

    a) If you answered "Yes" to Question 38, please provide details.

V. Data Analysis

39. As part of a Learning Health Network, Integrated Network sites participate in both the generation and analysis of participant-derived datasets to (1) support site and network learning and to plan and (2) measure improvements in care. Does your site's leadership include expertise in any of the data modalities included in the Integrated Network (EHR, clinical, neuroimaging, wearables, app, etc.)? **(500-word maximum)**

Institutional Framework to Support Multi-Center Research and Open Science

40. Does your proposed site team's Lead PI have a track record of participating in programs that require data sharing and open science? Please share any relevant examples. **(500-word maximum)**

41. What are your institutional policies for sharing data with a cloud-hosted central data repository in the United States?

    a) Please upload any relevant data-sharing policies implemented by your institution.

42. Does your organization have experience in the inclusion of EHR data as part of a research program and — therefore — are there processes currently in place to allow sharing of EHR data for research purposes? Please provide relevant examples.

43. Has your organization participated in a multi-center, central IRB-approved study? What is your organization's process for ceding to a central IRB? Please include details on the length of time and process to receive ceding approval.

44. Can your organization enter clinical participant data into a centralized, HIPAA-compliant REDCap system?

    ❑ Yes

    ❑ No

    a) Please provide any additional details regarding your response to question 44.

45. Can your organization support the transfer of consented, partially pseudonymized participant data (i.e., non-defaced images, dates of health care service provisioning, DOB) to a cloud-hosted central data repository in the United States?

    ❑ Yes

    ❑ No

    a) If you answered "Yes" to Question 45, please upload any relevant policies and procedures implemented by your institution.

Budget & Supplemental Information

Each applicant organization may request up to $2,300,000 (USD) for use over five years to administer the Longitudinal Cohort Study (LCS) protocol and Learning Health Network (LHN) initiatives outlined in this RFA. This award supports the costs to (1) recruit a goal of 100 bipolar I disorder participants within the first year, (2) collect longitudinal data for an additional four years, and (3) cover the necessary personnel and process changes. *Funding to support the recruitment of additional participant cohorts will be awarded on a milestone basis and should not be reflected in the current application or budget*.

Award funding must cover:

- Staff time, including one full-time study coordinator and another half-time study coordinator to administer and/or oversee the following study responsibilities:
  - Clinical screening
  - Cognitive and functional assessments
  - Biosample collection, pre-processing, storage, and shipment
  - Neuroimaging protocol implementation and imaging data pre-processing
  - Data extraction, transformation, packaging, and transfer
- Protected time for the site leads to participate in LHN activities, which include engagement in learning and teaching activities with clinicians, researchers, participants with lived experience, and hospital administrators (recommend 0.1 FTE each)
- Protected time for the site leads to participate in and contribute to Working Groups structured around their expertise (see "BD^2 Integrated Network Organizational Structure" on Pages 3-4)
- Local IRB and other required regulatory committee review costs
- Study participant reimbursement:

- Participants will be paid $275 for completing the baseline visit and $150 for each completed annual visit. Additionally, participants will be paid $100 for each completed MRI over the course of the study. If a participant does not complete any full visit, they will be paid for the number of hours that they have completed at a rate of $25 per hour.
- Participants who complete 80% of the remote assessments each month will also be entered into a monthly, site-specific $200 gift card lottery.

- Equipment use costs:
  - Sites will need to reserve time on their organization's MRI scanner. Each neuroimaging session is scheduled for completion in 1 hour (including set-up time)
- Equipment purchase costs:
  - Sites will need to purchase Fitbit for any participants who opt into this portion of the study. Estimates suggest up to 75% of participants will opt into Fitbit use. (See Appendix G: "Site Budget Template" for details)
  - Site will need to purchase a voice recorder for the qualitative interview portion of the study. (See Appendix G: "Site Budget Template" for details)
- Costs associated with neurocognitive assessments (see Appendix G: "Site Budget Template" for details)

Travel associated with the Integrated Network activities will be covered by BD² and should not be included in the budget.

Using the "Site Budget Template" (Appendix G), please address the following prompts:

46. Please fill out and upload the "Site Budget Template".
    a) Describe how the funding will be used to ensure that there is expeditious and efficient use of funds to carry out the LCS and LHN components of the program.
    b) Justify any proposed use of funds that were not outlined in the budget template or any major discrepancies or differences from the template.

Letters of Support & Commitment

Please generate and upload a letter of commitment signed by the **lead investigator** and each co-investigator **(clinical lead & research lead)**.

Please upload a letter of support from institutional leadership (department chair and/or other relevant leadership), using this template form.

Stage 2: Initial Review & Finalist Site Interviews

Written proposals will be reviewed by the BD² Leadership Team, SSC, members of the centralized service provider teams, as well as additional experts and stakeholders within the field of bipolar disorder. Proposals will be evaluated based on the responses to all requirements in this RFA. Following an initial review of the written proposals, a subset of applicants will proceed to the final review stage, consisting of an interview with the applicant team. Members of the BD² Leadership Team and additional reviewers will meet virtually with the applicant site's lead investigator, clinical lead, and research lead to further assess the site's ability to contribute to the Integrated Network and its goals. If deemed necessary, site visits may also be requested.

Final Selection

Following proposal review and finalist interviews, the BD² Leadership Team and SSC will convene to select the successful applicants. The evaluation of an organization's ability to contribute to the Integrated Network will be based on the written material submitted, interviews, and, if requested, presentations. Following approval by the BD² Program Broad, successful applicants will be notified, and the BD² Leadership Team and members of the centralized service provider teams will work with the selected organizations to begin onboarding.

Evaluation and Monitoring

Once investigators are funded and the initiative is implemented, progress reporting and assessments will be required. Site leadership teams will meet regularly with members of the BD² Leadership Team. Regular monitoring by the centralized service providers will ensure continuous rigor of data collection. Members of the BD² Leadership Team will perform a formal review as often as every six months.

Funding Awarded at BD²'s Discretion

Responding to this RFA and/or submitting an application does not entitle any individual or organization to receive funding from BD². Funding, if any, would be provided in BD²'s sole discretion pursuant to the terms of a written agreement executed by BD² and the selected organization, the terms of which BD² may require to be acknowledged by the awardee.

Contact Information

An automated email confirmation is generated upon application submission. If you do not receive confirmation within 24 hours of submitting your application, please check your spam filters and then contact integratednetwork@bipolardiscoveries.org.

For inquiries about scientific priorities, eligibility requirements, and application submission, please contact integratednetwork@bipolardiscoveries.org. For all other questions, including general and media inquiries related to BD², please contact: info@bipolardiscoveries.org

Please use these additional Integrated Network-specific materials to view the current requirements and infrastructure of the Integrated Network and assess organizational fit:

Appendix A
Longitudinal Cohort Protocol for Deep Phenotyping

Appendix B
Learning Health Network Overview

Appendix C
EHR Data Dictionaries

Appendix D
Longitudinal Cohort Study Electronic Health Record Data Manual

Appendix E
Longitudinal Cohort Study Neuroimaging Protocol

Appendix F
Longitudinal Cohort Study Neuroimaging Data Manual

Appendix G
Site Budget Template