BD²

Breakthrough Discoveries for thriving with Bipolar Disorder

2025 MIDYEAR REPORT

Table of Contents

Moving Bipolar Disorder Research Forward 2

Expanding Voices and Tools 3

BD^2 Integrated Network 4

Discovery Research 6

Genetics Platform 8

Brain Omics Platform 10

Cross-Team Collaborations 11

Supporting Early Career Researchers 12

Looking Toward Success . . . . . *(inside back cover)*

Moving Bipolar Disorder Research Forward

This report highlights the milestones we have achieved so far in 2025, and outlines our ambitions for the rest of the year.

Bipolar disorder affects more than 40 million people worldwide, yet its study has lacked collaboration and has been historically underfunded and under researched. In response to this critical gap, Breakthrough Discoveries for thriving with Bipolar Disorder (BD^2) was launched in 2022 as a collaborative approach to rapidly advance scientific understanding and significantly improve the lives of people with bipolar disorder.

Our vision is clear and ambitious—that all people with bipolar disorder thrive. To realize this, our four interconnected programs—the Integrated Network, Discovery Research, Brain Omics Platform, and Genetics Platform—are designed to generate and share data, methods, and resources. By engaging those with lived experience, whose voices have been included from inception through to today, and committing to open science and community-wide collaboration, we're catalyzing a new era of discovery and progress in bipolar disorder research and care.

Key Objectives Across our Connected Programs

- Generate foundational biomedical data
- Support discovery research
- Drive early therapeutic discovery
- Facilitate rapid learning to improve care

In 2025, we have already made significant strides, making clinical progress and translating innovative ideas into meaningful scientific discoveries. We've strengthened connections across the network—enabling researchers to combine expertise, share resources, and work across disciplines to drive innovation.

Accelerating Bipolar Disorder Science

We are advancing the field of bipolar disorder research—forging new research pathways, removing silos, recruiting participants into a longitudinal cohort study, and expanding our network.

- **$87 Million committed in grants** to close fundamental gaps in scientific understanding of bipolar disorder.
- **300+ scientists and clinicians in our network** who are transforming the bipolar disorder research landscape.
- **750+ participants consented** across over 40 clinics in the longitudinal cohort study.
- **Over 1.5 TB of participant-derived data** amassed in the Central Data Repository.

Expanding Voices and Tools

From the outset, we have made it part of our charter to integrate the insights and feedback from those with bipolar disorder. The contributions of individuals and groups with lived experience help inform research priorities, shape program goals, and provide essential feedback throughout the design and implementation of the two primary components of the BD² Integrated Network, a longitudinal cohort study embedded within a learning health network.

DBSA

Depression and Bipolar Support Alliance

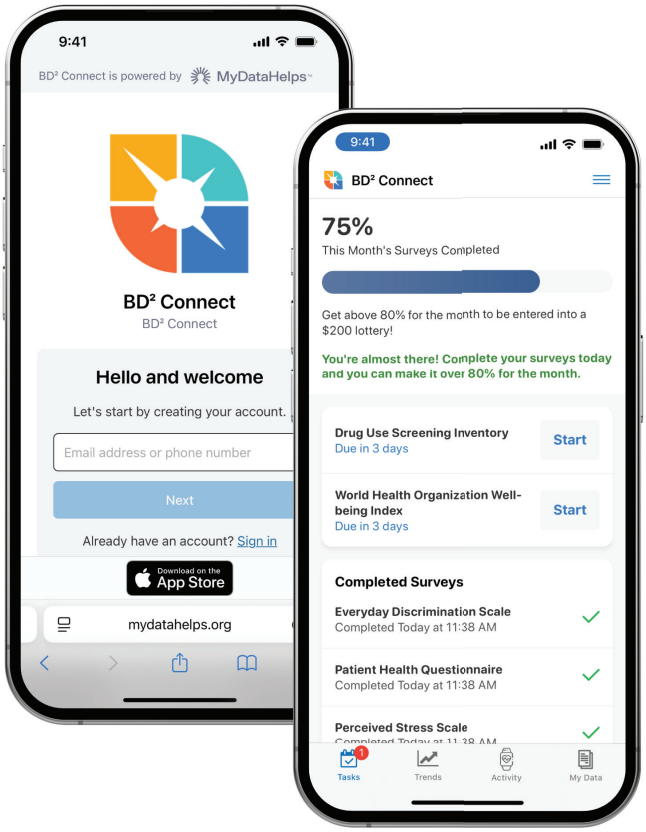
Depression and Bipolar Support Alliance Partnership: BD² Peer Support Portal

In November 2024, we announced a partnership with the Depression and Bipolar Support Alliance (DBSA). The mission of DBSA is to provide hope, help, support, and education to improve the lives of people living with depression and bipolar disorder.

Through our partnership with DBSA, Integrated Network participants will have access to peer support and other evidenced-based wellness tools. These supportive tools are designed to improve participants' experience and well-being, while also allowing us to study their effects on care and study retention.

CareEvolution Partnership: BD² Connect

As part of the Integrated Network, participants will have access to a digital platform that will allow them to regularly engage with the study, visualize their data, and track their progress. The platform, BD² Connect, will serve as a powerful tool for autonomy of and connection to an individual's health data, while providing unique and vital information about wellness back to participants.



BD² Integrated Network

OBJECTIVE	Accelerate learning to improve care and collect longitudinal, deep-phenotyping data on a large and diverse cohort.
RATIONALE	Over half of people with bipolar disorder report inadequate support from current treatments. We aim to quickly apply insights—large and small—to improve care.
BD² PRINCIPLE	Clinical data is essential to understand the complexity of bipolar disorder. We're committed to turning findings into real-world impact as swiftly as possible.

The BD² Integrated Network combines a longitudinal cohort study with a learning health network to improve care and outcomes for people with bipolar disorder. Through deep, biomedical, clinical, and digital characterization of participants across our first 11 partner institutions, we're generating the most comprehensive bipolar data to date—fueling real-time discovery and continuous care improvement.

2025 HIGHLIGHTS TO DATE

- **Launched five new sites,** University of Cincinnati/Lindner Center of HOPE, University of California San Diego, The University of Texas at Austin, The Feinstein Institutes for Medical Research, and the Ottawa Hospital Research Institute.
- **Announced our first international site,** the Ottawa Hospital Research Institute, and funding partnership with Brain Canada.
- **Reached 750 total participants** consented across the 40+ clinics in the longitudinal cohort study.
- **Published a paper in the Journal of Affective Disorders** that describes the benefits of learning health networks in driving improvements in care for bipolar disorder.

BD² Integrated-Network Sites

Discovery Research

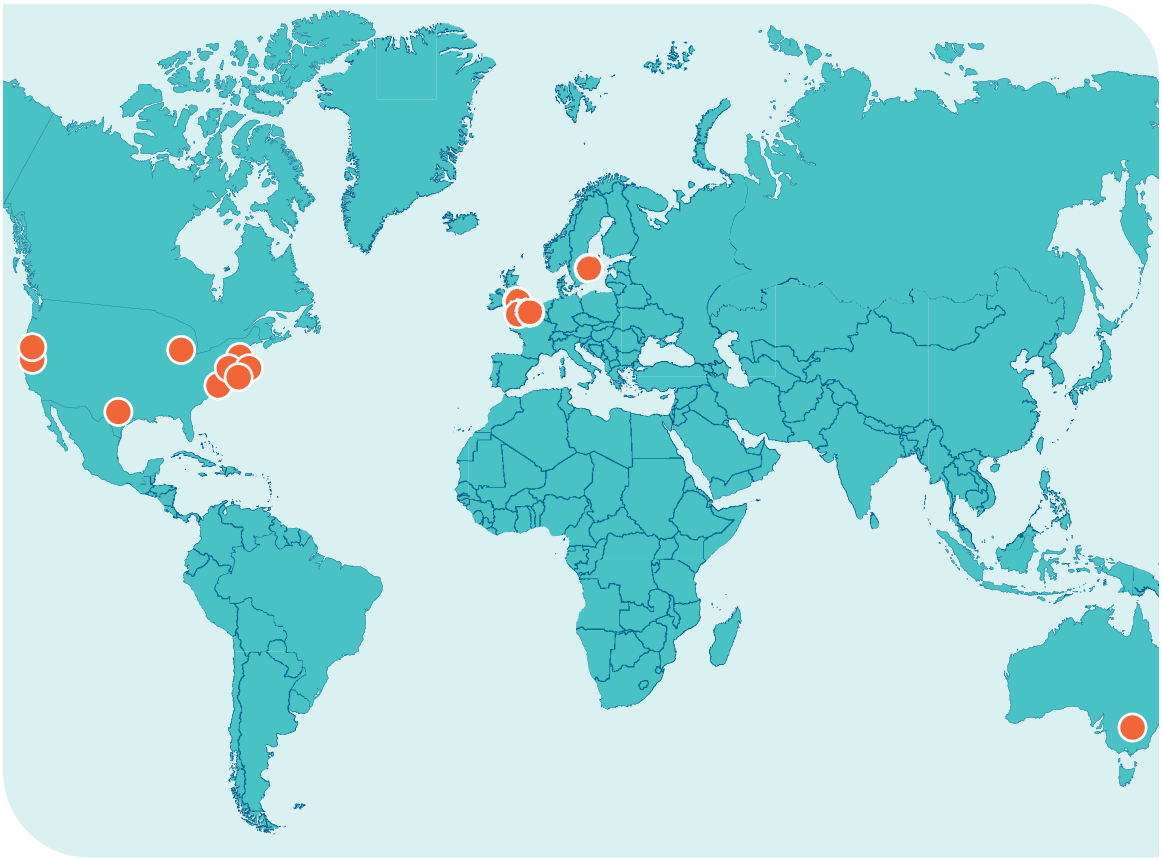
OBJECTIVE	Advance the biological understanding of bipolar disorder to funnel new ideas into the clinical research and development pipeline.
RATIONALE	Bipolar disorder-specific funding has continued to decline, limiting reproducibility and progress, and the biological mechanisms underlying bipolar are poorly understood.
BD² PRINCIPLE	Open access research, shared via an online hub and public repositories, and the support of collaborative efforts encourages cross-network partnerships and accelerates the pace of discovery.

BD² Discovery Research grants support multi-faceted teams investigating the biological mechanisms of bipolar disorder. Through data sharing and open access, these hypothesis-driven, multidisciplinary projects aim to accelerate discovery and treatment. Focus areas represented across the eight multi-investigator teams include genetics, molecular biology, cellular function, neural circuits, and behavior.

2025 HIGHLIGHTS TO DATE

- **Received proposals for Cycle 3 grants.** Applicants' projects will delineate the etiology and biological mechanisms of bipolar disorder, allowing the development of effective interventions. Cycle 3 had a spotlight call for applications leveraging novel neuromodulatory techniques and proposals are undergoing review.
- **The first publications from the Discovery Research teams** were seen this year, including preprints from Team Tam and Team Blumberg.
- **The Discovery Grant teams** are continuing to build a comprehensive picture of bipolar biology by addressing multiple domains of neurobiology. While each team is focused on a particular set of bipolar disorder-focused questions in fields such as sleep and circadian biology, neuroimmunology, cellular signaling, metabolism, molecular targets, and genetics, numerous collaborations have begun to push these boundaries together. Several publications are expected this year, as teams are uncovering new findings that may soon lead to new therapeutic targets, biomarkers, and biological mechanisms of bipolar disorder.

Discovery Team Institutions



Brigham and Women's Hospital
Columbia University
Harvard University
KTH Royal Institute of Technology
Lieber Institute for Brain Development
Mass General Brigham
Massachusetts General Hospital
New York Genome Center
New York University
Northwestern University
Princeton University
Rutgers University
Stanford University
Swinburne University
The Broad Institute of MIT and Harvard
University College London
University of California Berkeley
University of Oxford
University of Reading
University of Texas at Austin
Wyss Institute at Harvard University
Yale University

Genetics Platform

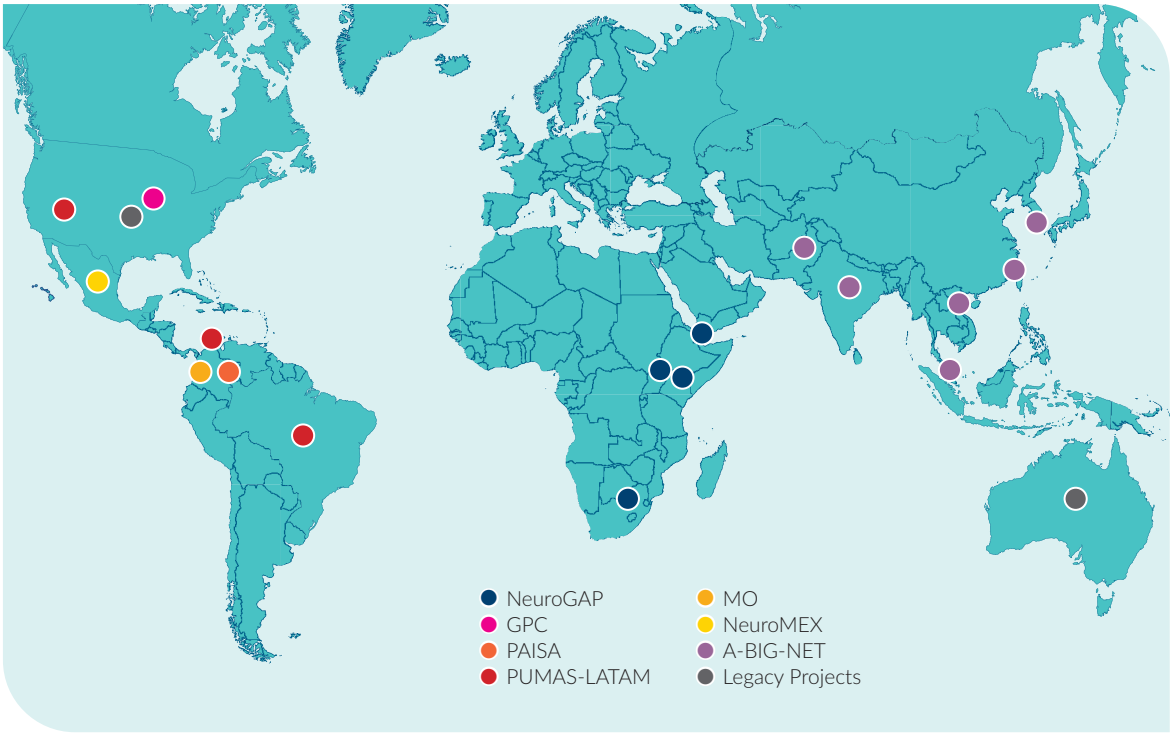
OBJECTIVE	Build foundational datasets and tools to guide our scientific roadmap.
RATIONALE	Bipolar disorder is underrepresented in core neuroscience and psychiatry datasets, limiting early discovery and cross-disease insights, and large-scale datasets often lack diversity beyond European ancestry.
BD² PRINCIPLE	Conduct large-scale sequencing in diverse populations, repurpose existing samples, and ensure open data access.

The BD² Genetics Platform is sequencing over 30,000 samples from one of the largest and most diverse bipolar disorder populations, including individuals from Africa, Central and South America, and Asia. The team will also sequence samples from individuals enrolled in the BD² Integrated Network.

2025 HIGHLIGHTS TO DATE

- **Identified 29 new potential bipolar significant genes,** expected to be published in 2025.
- **Assembled a cohort of ~100,000 bipolar samples** with matched controls from 10 sites across four continents.
- **Harmonized phenotype data** and aligned across the mental illness field.
- **Facilitated data sharing through BipEx:** a Bipolar Exomes browser, a collaboration between multiple institutions across the globe.

Sample Collection Sites



Sequence Complete

Colombia, Ethiopia,
S. Africa, Uganda

23,300
Bipolar

18,000
Controls

Active Recruitment

Brazil, Mexico, Pakistan,
Taiwan, S. Korea, Singapore

6,150
Bipolar

4,250
Controls

Brain Omics Platform

OBJECTIVE	Build foundational datasets and tools to guide our scientific roadmap.
RATIONALE	Bipolar disorder is underrepresented in core neuroscience and psychiatry datasets studying brain tissue of people with bipolar, limiting early discovery and cross-disease insights.
BD² PRINCIPLE	Generate and share critical datasets, repurpose existing samples, and ensure broad data accessibility.

We are funding groundbreaking research using post-mortem brain tissue from people with and without bipolar disorder, defining cellular and molecular changes using state-of-the-art multi-omic analyses. By leveraging and expanding existing biobank samples, this program will create a molecular brain atlas to uncover biological signatures of bipolar and accelerate scientific progress.

2025 HIGHLIGHTS TO DATE

Continued efforts toward processing and analyzing tissue samples from 160 bipolar and 304 control individuals. An initial publication from this work is expected in 2025.

Cross-Team Collaborations

OBJECTIVE	Synergize expertise across the network to enrich experimental pipelines.
RATIONALE	Through promoting collaborative efforts, the network can optimize the collection and analysis of data and add additional research perspectives to funded projects.
BD² PRINCIPLE	Foster collaboration through grants, shared data via the virtual hub, resource exchange, workgroups, and partnerships.

The BD² network promotes deep collaboration across clinical and discovery science teams to accelerate understanding of bipolar disorder's complexity. Through Collaboration Projects and workgroups, we empower multidisciplinary teams to share insights, share methodologies, and develop shared resources—working together to advance science at an accelerated pace, ultimately leading to improved outcomes so that all individuals with bipolar disorder can thrive.

2025 HIGHLIGHTS TO DATE

- **Developed an outline and proposal for a Cell Repository** that would help standardize the development and quality control of human-derived iPSCs to optimize the data collected from those cell lines. This effort also promotes sharing of knowledge, resources, and expertise, and is led by the iPSC and Organoid Workgroup.
- **Launched additional workgroups** focused on Sleep & Circadian Science, Women's Health, and Qualitative Analytics to bring together experts across teams, share data, and generate new ideas. Additional workgroups are coming soon to accelerate new discoveries and collaborations.
- **The first round of Collaborative Projects,** funded proposals between Discovery Research teams, reached their halfway point in April and are expected to conclude in October. The forthcoming findings represent an exciting and novel endeavour in promoting cross-institutional scientific progress.

Supporting Early Career Researchers

OBJECTIVE	Develop mechanisms to support early career scientists and clinicians with childcare needs to stay in the bipolar field.
RATIONALE	The bipolar disorder research and clinical field need new perspective, personnel, and resources to ensure a long-lasting and robust ecosystem. Childcare is often a barrier that prevents many young minds from staying in the field.
BD² PRINCIPLE	Provide financial support to funded investigators who have childcare needs, allowing them to focus on the science and clinical care for bipolar disorder.

We are dedicated to ensuring that our network of researchers includes perspectives from all levels of experience—from trainees to early career investigators to recognized experts in the field. All Discovery Research teams have at least one early career researcher within their core leadership team, and multiple groups across both the Discovery Research programs and Integrated Network are led by an early career researcher.

We have made further efforts to support the needs of researchers in our network by launching the Care and Career Program in 2024. In its inaugural year, this program provided financial support for 13 researchers and clinicians in our network who have childcare needs. Notably, most of the awardees are in an early phase of their careers, including graduate students and postdoctoral fellows.

2025 HIGHLIGHTS TO DATE

- **Launched second round of enrollment** to continue supporting working parents within the BD² network.

Looking Toward Success

Building on accomplishments so far in 2025, programs across the BD² network are working to publish new insights, continue expanding research teams, and accelerate clinical progress in the next year.

IN 2025

The Integrated Network will:

- Publish insights for bipolar disorder care improvement
- Launch an educational series for clinicians focused on improving physical wellness in individuals living with bipolar disorder
- Share aggregate findings from cohort participants' baseline data
- Publish use of a new survey tool used to collect qualitative wellbeing in bipolar patients

The Discovery Research program will:

- Fund four new teams with greater emphasis on the neural circuits underlying bipolar disorder
- Identify and champion additional workgroups to standardize methodology of common protocols
- Share additional preprints and publications of experimental results

The Genetics Platform will:

- Share preprint from the blended genome exome sequencing effort

The Brain Omics Platform will:

- Approach completion of omics assays on 100 brains from people with bipolar disorder and 100 controls across two key brain regions

BD² will:

- Expand across the network to drive translational research efforts between the Integrated Network and Discovery Research teams
- Define a strategy for a partnership with Psychiatric Biomarkers Network and FNIH

BD²

Breakthrough
Discoveries for thriving
with Bipolar Disorder