

Milestones Report

2022-2023





BD²

**Breakthrough
Discoveries for thriving
with Bipolar Disorder**

BD² is the first organization focused on funding and advancing research and care for bipolar disorder on a global scale. We are dedicated to transforming bipolar disorder research and shortening 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.



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A MESSAGE FROM EXECUTIVE LEADERSHIP

Today, it is estimated that it takes an average of 17 years to translate a scientific discovery to meaningful interventions for people with bipolar disorder. BD²: Breakthrough Discoveries for thriving with Bipolar Disorder brings an intentional and collaborative approach to science so that we might collapse this timeline and improve understanding and care.

Since publicly launching in the Fall of 2022, BD² has awarded over \$60 million to 24 organizations to implement new scientific research programs for bipolar disorder. These programs are already expanding the bipolar disorder research landscape, working toward our vision that all people with bipolar disorder can thrive. **These initiatives are designed to remove silos, build foundational knowledge, and accelerate the translation of scientific findings to improvements in diagnosis and care.** Over time, this work will shorten the time it takes from diagnosis to effective treatment and change the lives of those with bipolar disorder, their families, and those yet to be diagnosed for the better.

As we look toward the upcoming year, we are excited to see our teams come together for the first full network investigators meeting, watch new collaborations form, and welcome our first participants in the BD² Integrated Network. We expect to celebrate new findings and a greater understanding of current clinical practice. **The wonder of science is that while we can't know where new discovery will come from, we can stack the deck in our favor and aim it towards the greatest impact for people.**

Thank you for following along on the journey to precision care for bipolar disorder.

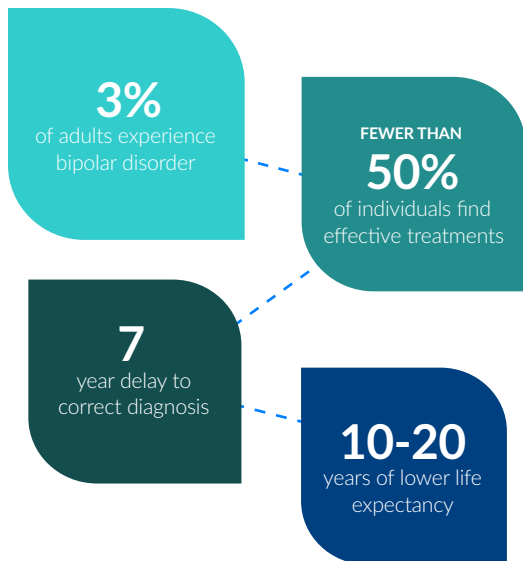
Sincerely,



Cara Altimus, PhD
MANAGING DIRECTOR

Cara Altimus, PhD is managing director of BD² and a senior director at the Milken Institute where she leads the Center's biomedical philanthropy portfolio. A PhD neuroscientist, Altimus developed and leads the Center's work on bipolar disorder. Aligning the interests of multiple philanthropists, the research and clinical field, and people with lived experience, she facilitated the development of BD² from concept to reality.

A LOOK BACK AND LOOK AHEAD



More than 70% of people with bipolar disorder are misdiagnosed at least once¹. It takes seven years on average to diagnose bipolar disorder²—and less than 50% of those who are diagnosed find an effective treatment³. Despite affecting 3% of the global population⁴, and costing an estimated \$200 billion annually in health and economic burden in the United States alone⁵, bipolar disorder is often studied through the lens of other psychiatric conditions like schizophrenia, which receive far greater attention and funding.

Over the past 10 years, due to a lack of focused funding, many researchers have moved away from bipolar disorder research. **BD² was created to provide leadership and commitments that revitalize and expand the field, implement fundamental direction for research, and provide new hope to those living with bipolar disorder and their loved ones.**

OUR VISION is that all people with bipolar disorder thrive.

OUR MISSION is to accelerate scientific understanding of bipolar disorder and advance clinical care through cross-disciplinary collaboration, data sharing, and real-time learning.

Through a process that engaged 100+ scientists and leveraged the responses of 3,000+ individuals living with bipolar, BD² identified outstanding scientific questions. Our 25-member Scientific Advisory Committee, chaired by Dr. Eric J. Nestler, prioritized scientific questions and delineated areas of opportunity. Members of the committee include representatives from NIH, FDA, OneMind, Psychiatric Genomics Consortium, and the Brain and Behavior Research Foundation (BBRF).

Eric Nestler, MD, PhD

CHAIR, BD² RESEARCH PROGRAMS

Dr. Nestler is the Nash Family Professor of Neuroscience, Director of the Friedman Brain Institute, and Dean for Academic Affairs at the Icahn School of Medicine at Mount Sinai and Chief Scientific Officer of the Mount Sinai Health System. His laboratory studies the molecular mechanisms of drug addiction and depression in animal models.



1 Singh, T., & Rajput, M. (2006). Misdiagnosis of bipolar disorder.

2 Ghaemi, S. N., Sachs, G. S., Chiou, A. M., Pandurangi, A. K., & Goodwin, K. (1999). Is bipolar disorder still underdiagnosed? Are antidepressants overutilized?

3 Geddes, J. R., & Miklowitz, D. J. (2013). Treatment of bipolar disorder.

4 Harvard Medical School, 2007. National Comorbidity Survey (NSC).

5 Cloutier, M., Greene, M., Guerin, A., Touya, M., & Wu, E. (2018). The economic burden of bipolar I disorder in the United States in 2015.

This rigorous planning process resulted in the development of a transformational model—one that’s engineered to rapidly build on new findings and translate cutting-edge science to clinical practice. **BD²’s Theory of Change promises to break the mold in how the brightest scientific and clinical minds collaborate while continuing to engage people living with bipolar disorder at every step.** Our holistic approach features a continuous feedback loop across research programs, brain omics and genetics platforms, and clinical care.

BD² THEORY OF CHANGE

Four foundational questions.
Four interconnected programs.
Zero silos. Closing the research and clinical gap.



What are the biological pathways?

DISCOVERY RESEARCH

Harvard ■ Yale ■
Stanford + Northwestern +
UT Austin ■ NY Genome
Center + Columbia +
NYU + KTH RIT + Rutgers



What are the genetic contributions?

GENETICS PLATFORM

Broad Institute ■
NY Genome Center ■ UCLA



Are there differences in the brain?

BRAIN OMICS PLATFORM

Icahn School of Medicine
at Mount Sinai ■ CalTech ■
University of Pittsburgh



How can we bridge insight with precision psychiatry?

INTEGRATED NETWORK

Brigham McLean Hospital ■
Johns Hopkins ■ Mayo Clinic ■
UCLA ■ University of
Michigan ■ UT Houston ■
Mayo Clinic-Biorepository ■
Feinstein Institutes ■ Indoc ■
Health Rhythms

TIMELINE

Since initiating the journey to precision care for bipolar disorder, BD² has created new ways of doing science, added unprecedented funding into the field of bipolar disorder, and has seen the transformative quality of collaboration in science. 2022-2023 saw the realization of BD² after years of consensus building, which has created a renewed enthusiasm from the research field, the larger mental health community, and people with lived experience.

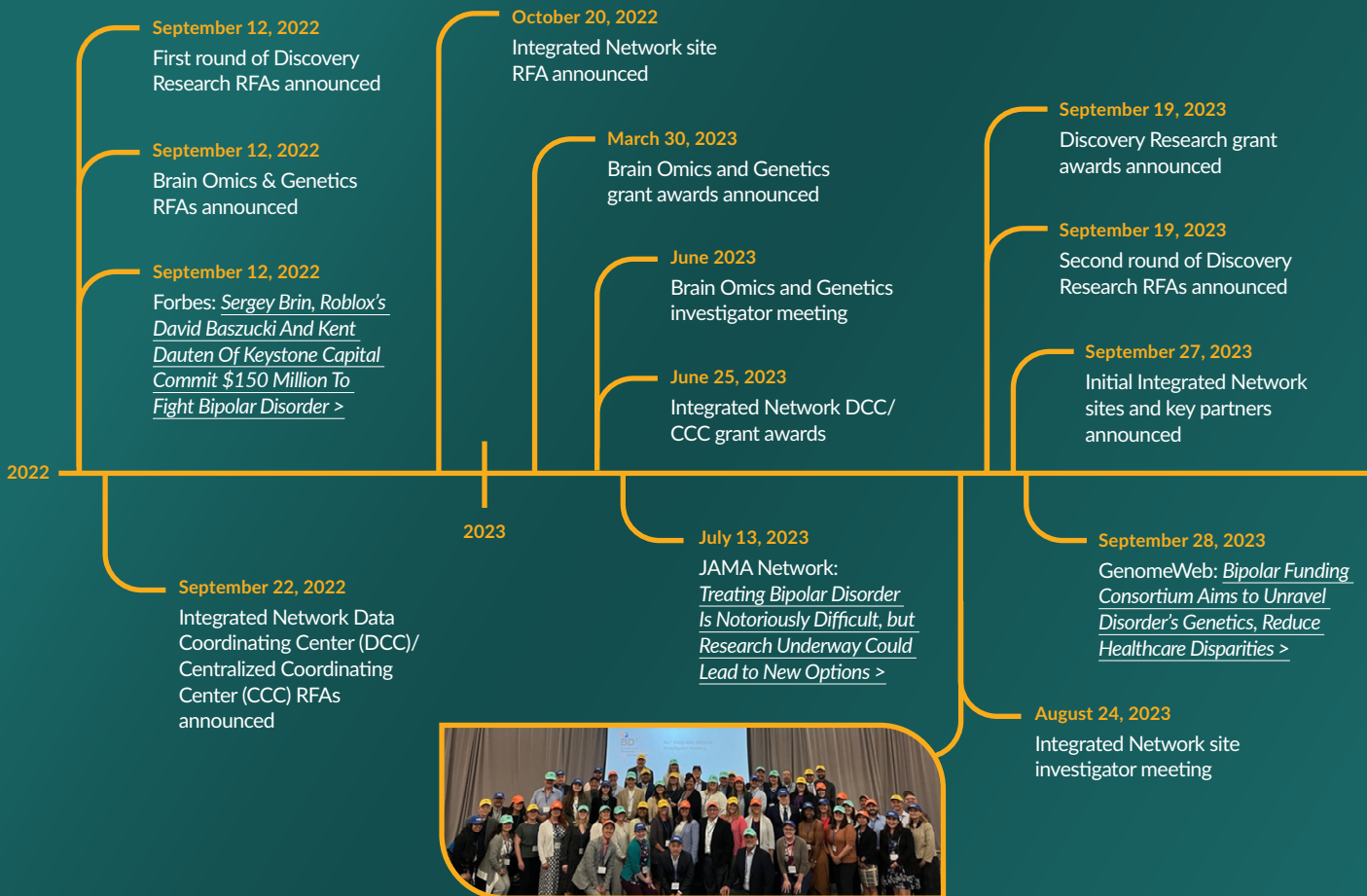
Looking into the next year and beyond, the groundwork accomplished will propel exciting scientific opportunities, further collaboration, and breakthroughs.

Built and connected
a network of
100+
scientists and
clinicians

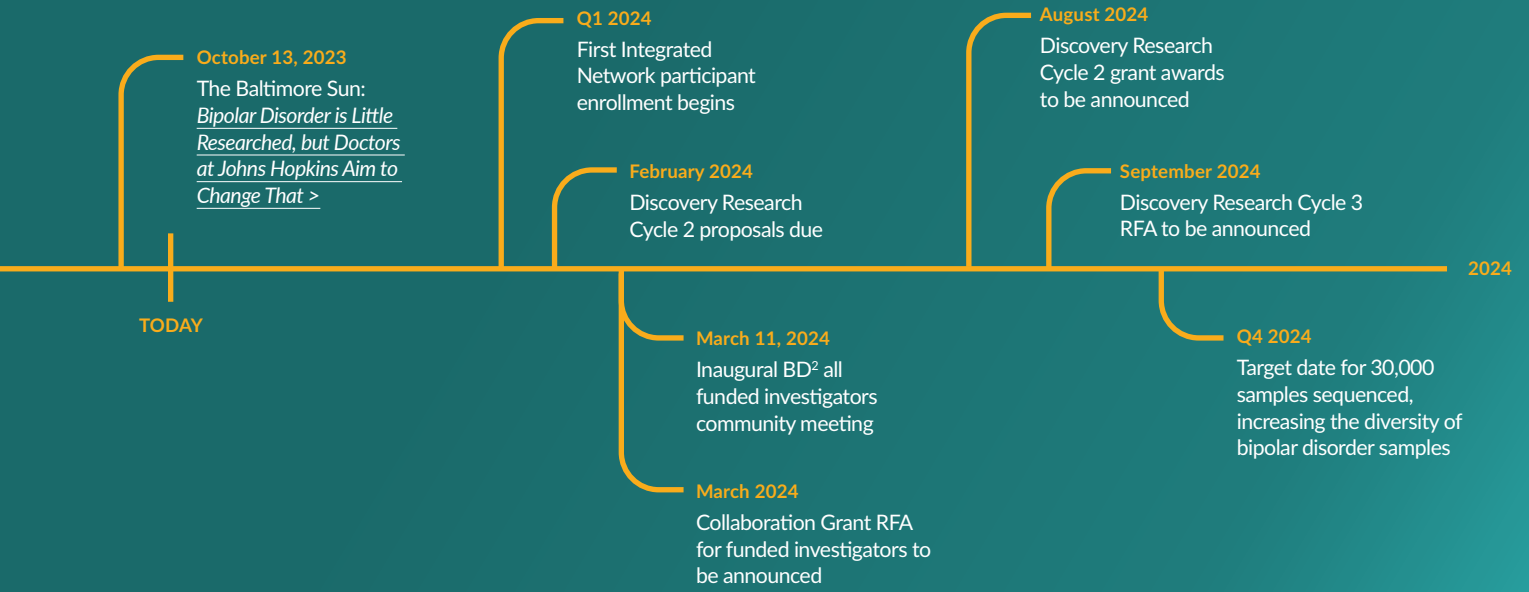
Committed
\$60 million
in grants that will close
fundamental gaps in
science's understanding of
bipolar disorder

Featured at
10 conferences
among leaders in the field of
mental health, psychiatry, and
bipolar disorder research

LOOK BACK

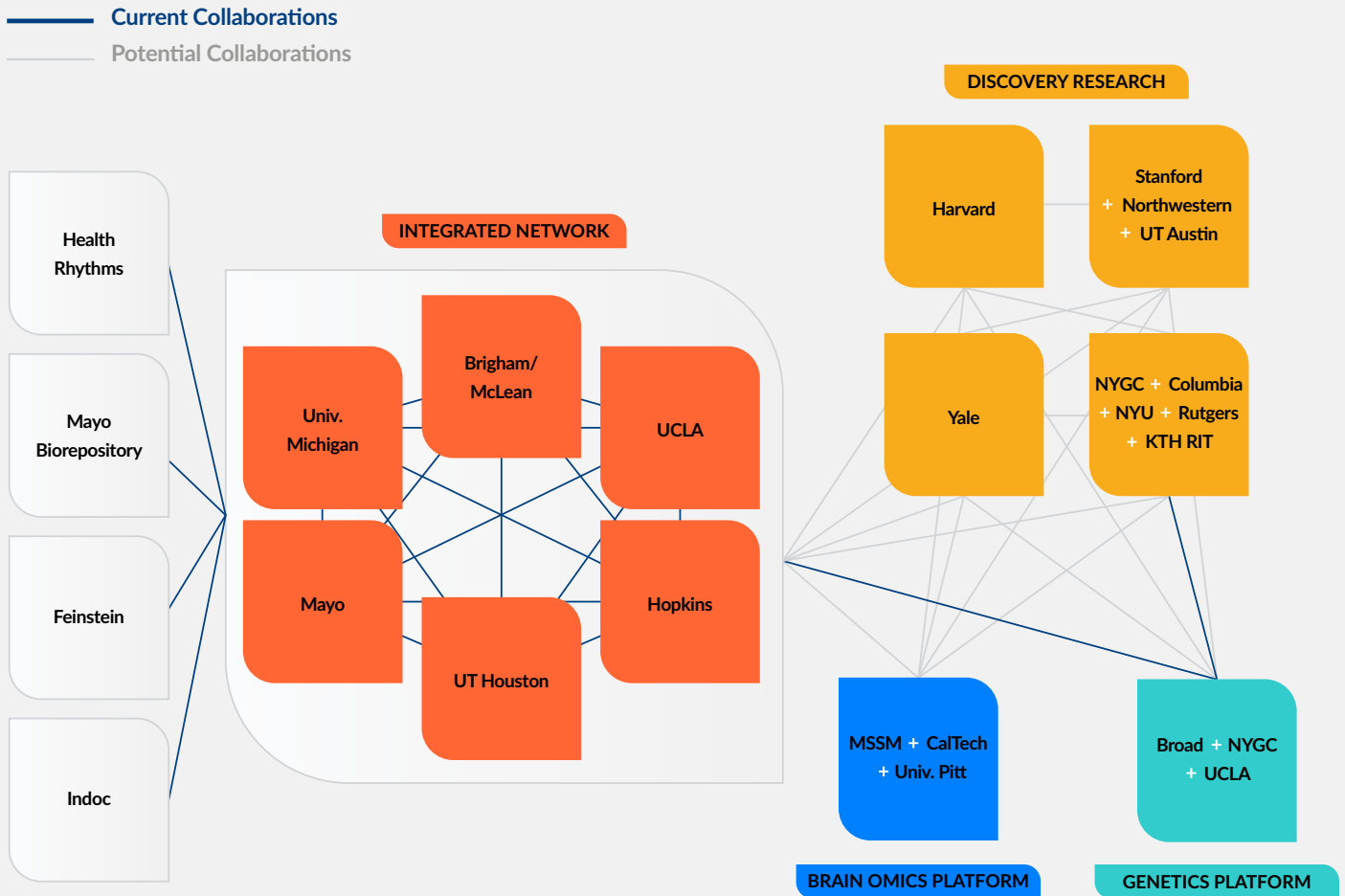


LOOK AHEAD



PROGRAM OVERVIEW & MILESTONES

BD² is focused on bringing excellent science out of silos and connecting the dots between teams. To that end, team development and collaboration are fostered across the network. The graphic below highlights the initial network map following just one cycle of funding. As BD² continues to build the community this map will grow and connections will strengthen, accelerating research progress to impact the care and outcomes for bipolar disorder.



BD² INTEGRATED NETWORK

“Using some of the most sophisticated scientific and research tools that are available today, the network is designed to build in-depth clinical and biological profiles of each participant so that we can better understand the variability of bipolar disorder and drive continuous improvements in care.”

—Emily Baxi, PhD, BD² Integrated Network Program Director

The BD² Integrated Network brings together researchers and clinicians from leading medical institutions to expand knowledge of bipolar disorder while accelerating the translation of that knowledge into clinical care.

Over the next five years, the program will engage 4,000 people living with bipolar disorder as part of a longitudinal cohort study. To maximize the impact and speed with which insights can be leveraged to improve care, BD² will also develop a Learning Health Network — a community of clinicians, researchers, and patients that is designed to rapidly identify and endorse effective care practices. Clinical and biological data collected across sites will be shared through a centralized data system so researchers can collaborate on research and improve understanding of bipolar disorder, which could lead to more personalized treatments.

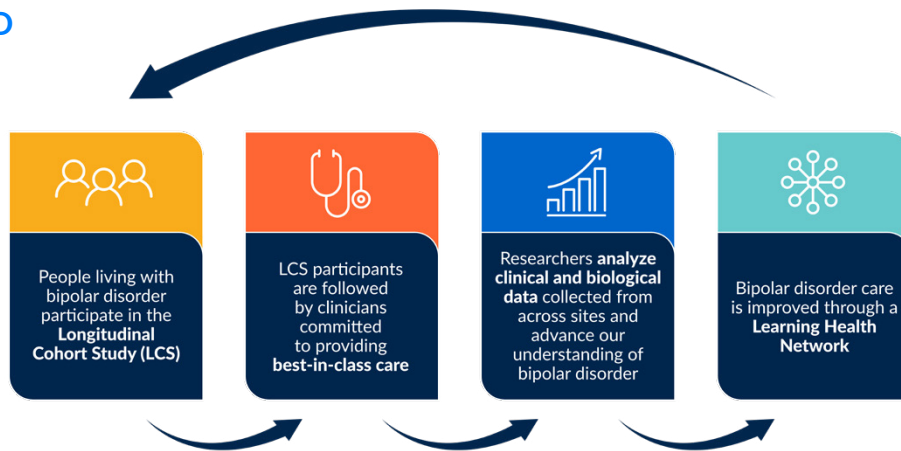
Emily Baxi, PhD

INTEGRATED NETWORK PROGRAM DIRECTOR

Emily Baxi, PhD is the program director of the BD² Integrated Network for Bipolar Disorder program and a director at the Milken Institute. She joined the team in January 2022 to lead and operationalize the Integrated Network program. Before joining the BD² team, Baxi was an assistant professor at Johns Hopkins University where she served as the executive director of the Packard Center for ALS Research and program director for Answer ALS, a multi-institutional ALS research program.



INTEGRATED NETWORK MODEL



GOAL

Activate a collaborative infrastructure between clinical settings and a longitudinal research study to effectively translate real-time findings into improvements in care.

FUNDING

\$2,300,000 over five years per site

MILESTONES



“The BD² Integrated Network is the first initiative in the field of psychiatry that embeds a longitudinal cohort study within a learning health network.”



Katherine Burdick, PhD
Vice Chair for Research, Department of Psychiatry Brigham and Women’s Hospital, Professor of Psychology in Psychiatry at Harvard Medical School, and BD² Integrated Network Scientific Director

“Our goal is to achieve a paradigm shift in our overall understanding of the condition, accelerating the diagnosis and treatment of bipolar disorder worldwide.”



Mark Frye, MD
Consultant in the Department of Psychiatry & Psychology at Mayo Clinic and BD² Integrated Network Scientific Director

BD² INTEGRATED NETWORK SITES

The network consolidates the expertise of bipolar disorder clinicians and researchers into a collaborative initiative that will advance clinical care and lead to better outcomes for those living with bipolar disorder.

The inaugural six sites each have the capacity for significant participant enrollment in the longitudinal study. They demonstrate a commitment to BD²'s mission of equitable healthcare and meaningful ethnic and racial representation in clinical trials and research studies.



Mayo Clinic
Location: Minnesota
Lead PI: Balwinder Singh, MD



University of Michigan
Location: Michigan
Lead PI: Kelly Ryan, PhD



Brigham and Women's Hospital-McLean Hospital
Location: Massachusetts
Lead PI: Kathryn Eve Lewandowski, PhD



Johns Hopkins University
Location: Maryland
Lead PI: Fernando Goes, MD



University of California, Los Angeles
Location: California
Lead PI: Jennifer Kruse, MD



UTHealth Houston
Location: Texas
Lead PI: Jair Soares, MD, PhD

KEY PARTNERS

Each site works with partners that centralize data, samples, processes, and analysis for the Integrated Network. These tools and expertise are essential to the functional model.

Clinical Coordinating Center - The Feinstein Institutes for Medical Research

The Clinical Coordinating Center will help to improve bipolar disorder care protocols across the field.



Anil Malhotra, MD

Data Coordinating Center - Indoc Research

The Data Coordinating Center will provide environments, tools, and processes necessary to maximize the utility of standardized data collected by the sites, enabling data aggregation, curation, sharing, and analysis.



Mojib Javadi, PhD

App-Based Monitoring – Health Rhythms

Monitoring behavioral data will provide the intelligence to enable personalized precision care for people in the longitudinal study.



Ellen Frank, PhD

Centralized Biosample Repository - Mayo Clinic Biobank

The repository will provide the infrastructure for standardized sample collection, handling, additional testing, and data dissemination.



Mine Cicek, PhD

DISCOVERY RESEARCH

“The overall goal of the Discovery Research grants is to create a pathway to building foundational knowledge that lets the data do the exploring.”

—Daniel Pham, PhD, BD² Research Program Director

The Discovery Research program is the cornerstone of our hypothesis-driven, cross-disciplinary approach. Each project will proactively share findings to facilitate progressive collaboration and the improvement of clinical care more quickly. Modeled after Aligning Science Across Parkinson's (ASAP), multidisciplinary research teams are examining the genetic, molecular, cellular, circuit, or behavioral mechanisms of bipolar disorder.

GOAL

To improve scientific understanding of the biological mechanisms of bipolar disorder.

FUNDING

Awards of up to \$4,500,000 support teams for three-year research projects.

Additionally, with collaboration being a fundamental pillar of BD²'s approach, funded teams can also apply for \$150,000 annual grants to form new collaborations across the BD² network.

Daniel Pham, PhD RESEARCH PROGRAM DIRECTOR

Daniel Pham, PhD is the program director of the BD² Research Programs and a director at the Milken Institute. He has played a lead role in building the foundation for BD², cultivating productive collaborations and co-authoring multiple publications on bipolar disorder. Pham also researched and wrote the Institute's Giving Smarter Guide, "Giving Smarter: Philanthropic Opportunities to Advance Bipolar Disorder Research."



“The work done by these teams will increase our understanding of effective interventions for the millions of people who live with this complex, debilitating disorder.”



Eric J. Nestler, MD, PhD
Icahn School of Medicine at Mount Sinai,
and Chair, BD² Research Programs

“Through our shared principle of open science, ASAP and BD² are helping create collaborative, effective strategies that can be applied across scientific disciplines to accelerate discoveries that lead to breakthroughs.”



Ekemini A.U. Riley, PhD
Founder of the Coalition for Science and
Managing Director of Aligning Science Across
Parkinson's (ASAP)

MILESTONES



GRANTS

Mechanisms of Mitochondrial Dysfunction

Integrate molecular, cellular, circuit, and imaging approaches to understand a pathway associated with mitochondrial dysfunction in bipolar disorder using mice, stem cell lines, and humans with bipolar disorder.



LEAD PI:
Hilary Blumberg, MD
Yale University

Mechanisms of Sleep and Circadian Rhythms

Manipulate sleep genes using CRISPR to study its effects on the circuit function and behavioral outcomes in mouse models associated with bipolar disorder.



LEAD PI:
Julie Kauer, PhD
Stanford University

GRANTS [CONT.]

Genetics of Bipolar Using Stem Cells

Uncover the genetic underpinnings of bipolar disorder using stem cells from people with African ancestry. Examine how rare and common genetic variants might converge onto common biological pathways.



LEAD PI:

Thomas Lehner, PhD, MD
New York Genome Center

Mechanisms of Current Treatments

Examine the mechanisms of current FDA-approved drugs to identify better alternatives for bipolar disorder. Promising drug candidates will be further studied in stem cells, mouse models, and individuals with bipolar disorder.



LEAD PI:

Jenny Tam, PhD
Harvard University

BRAIN OMICS & GENETICS PLATFORMS

“The Brain Omics and Genetics Platforms are designed to fill specific scientific knowledge gaps with dedicated funding and emphasis on bipolar disorder.”

—Daniel Pham, PhD, BD² Research Program Director

The Brain Omics and Genetics Platforms aim to close fundamental gaps in scientific understanding of the biological and genetic foundations of bipolar disorder and generate data that can be used by all. The research and findings produced by the teams provide basic research for continued scientific exploration while also building the brain atlas and identifying the genetic architecture of bipolar disorder.

“BD² is the driving force bringing together foundational and hypothesis-driven research in bipolar disorder. The discoveries from this research will over time enable long-sought advances in clinical care.”



Eric J. Nestler, MD, PhD
Icahn School of Medicine at Mount Sinai, and
Chair, BD² Research Programs



Cara Altimus, PhD
BD² Managing Director

“This work will lead the way in a diversity-first approach to building out the genetic architecture and understanding of bipolar disorder.”

MILESTONES



GRANTS

Brain Omics Platform

GOAL: Assess the transcriptomic, epigenetic, and proteomic characteristics of brain tissue derived from people with bipolar disorder.

DETAILS: Assess genomic, epigenomic, transcriptomic, and proteomics of the subgenual anterior cingulate cortex and basolateral amygdala on 100 brains from people with bipolar disorder and 100 brains of people without bipolar disorder. Provide results in the form of a brain atlas.

FUNDING: \$5,000,000 over three years



LEAD PI:

Panos Roussos, MD, MS, PhD
Icahn School of Medicine at Mount Sinai

Genetics Platform

GOAL: Perform genetic sequencing on a large, diverse population of people with bipolar disorder to contribute to the genetic database.

DETAILS: Perform blended genome exome sequencing on more than 30,000 samples collected from across Africa, Central America, South America, and Asia to identify risk genes for bipolar disorder. Generate deep whole genome sequencing on a 2,000-sample subset. Provide whole genome sequencing for all participants in the Integrated Network.

FUNDING: \$10,000,000 over two years



LEAD PI:

Benjamin Neale, PhD
Broad Institute

BD² IN THE MEDIA

BD²'s vision requires expanding the field of scientists, clinicians, and people with lived experience engaged in improving research and clinical care. To that end, BD² works to publicize its work to engage greater numbers of partners. Scientific and mainstream media outlets have covered, and are continuing to show increasing interest in BD²'s groundbreaking research and model.

TOP STORIES

- 1 | The Baltimore Sun**
[Bipolar Disorder is Little Researched, but Doctors at Johns Hopkins Aim to Change That >](#)
- 2 | Forbes**
[Sergey Brin, Roblox's David Baszucki, And Kent Dauten Of Keystone Capital Commit \\$150 Million To Fight Bipolar Disorder >](#)
- 3 | Philanthropy News Daily**
[Platform for Bipolar Disorder Research Launched With \\$150 Million >](#)
- 4 | Forbes**
[Imagine If There Was Someone Like Patagonia Billionaire Chouinard— But Focused On Mental Health >](#)
- 5 | Inside Philanthropy**
[Why Three Deep-Pocketed Funders Joined Forces to Take on Bipolar Disorder >](#)
- 6 | JAMA Network**
[Treating Bipolar Disorder Is Notoriously Difficult, but Research Underway Could Lead to New Options >](#)
- 7 | Philanthropy News Digest**
[BD² Awards \\$18 Million for Bipolar Disorder Research >](#)
- 8 | GenomeWeb**
[Bipolar Funding Consortium Aims to Unravel Disorder's Genetics, Reduce Healthcare Disparities >](#)
- 9 | GenomeWeb**
[UPDATE: Bipolar Disorder Research Funding Organization Awards \\$18M in Grants to NYGC, Others >](#)
- 10 | Alliance Magazine**
[Why Widespread Philanthropic Coordination is so Elusive: Lessons from the Sector >](#)
- 11 | Research America**
[Mary Woolley's Weekly Letter >](#)

GRANTEE FEATURES

- 1 Business Wire**
[Feinstein Institutes Awarded \\$6.1M to Fund Bipolar Disorder Patient and Research Hub >](#)
- 2 Yale Daily News**
[Yale Awarded \\$4.5M Grant to Investigate Bipolar Disorder >](#)
- 3 Wyss Institute**
[Wyss Institute's CircaVent Team Awarded Grant From BD² to Advance Research into Bipolar Disorder and Development of More Effective Drugs >](#)
- 4 UTHealth Houston**
[UTHealth Houston Receives \\$2.5 Million to Transform Knowledge and Treatment of Bipolar Disorder >](#)
- 5 University College of London**
[UCL Researchers Contribute to a Multidisciplinary Study to Better Understand Bipolar Disorder >](#)
- 6 New York Genome Center**
[New York Genome Center Awarded Grant from BD² to Help Uncover Biological Causes of Bipolar Disorder >](#)
- 7 Yale**
[Yale Researchers Launch Study Aimed at Accelerating Understanding of Bipolar Disorder >](#)
- 8 Brigham Clinical Research News**
[Transforming Bipolar Disorder Research and Care >](#)

BD² AT PROMINENT CONFERENCES

BD² has taken part in conferences, panels, and other appearances across the world to bring awareness of the Theory of Change and programs to a wider audience.

1. Health Research Alliance

2. National Network of Depression Centers (NNDC)

3. Global Partnerships in Brain Research at the 78th United Nations General Assembly

4. Society for Neuroscience's Neuroscience Scholars Program Conference

5. National Academy of Science, Engineering, and Medicine

6. International Society for Bipolar Disorders (ISBD)

7. American Psychiatric Association (APA)

8. Milken Institute Global Conference panel: Seeding Science for Impactful Discoveries: Philanthropy's Role in Driving Research Forward

9. Living well with Bipolar Disorder webinar discussion

10. American College of Neuropsychopharmacology

11. Depression and Bipolar Alliance (DBSA) Gerald L. Klerman Awards

12. Milken Institute's Catalyzing New Research in Bipolar Disorder meeting

13. Research!America Alliance Discussion



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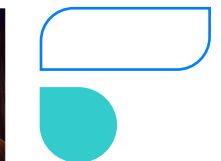
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INAUGURAL INVESTORS

BD² is an initiative housed within the Milken Institute and seeks additional support to realize its vision. Inaugural investors include the **Sergey Brin Family Foundation**, the **Dauten Family Foundation**, and the **Baszucki Family Foundation**.

To learn more, visit bipolardiscoveries.org.



BD²

Breakthrough
Discoveries **for thriving**
with Bipolar Disorder