

Discovery Grants Request for Applications (RFA)

September 2022

Executive Summary

We invite you to apply for a [BD²: Breakthrough Discoveries for thriving with Bipolar Disorder](#) Discovery Grant. This new grant program will support an innovative and collaborative group of researchers who will work together to improve our understanding of the biological mechanisms that underlie bipolar disorder. BD² will fund teams of multidisciplinary scientists to develop targeted and groundbreaking research applications that will examine the genetic, molecular, cellular, circuit, and/or behavioral mechanisms of bipolar disorder. BD² plans to award up to \$1.5 million per year for three years (up to a total of \$4.5M USD) to identified teams of three to five scientists, with an intended opportunity for continued funding up to an additional two years based on strong commitment, productivity, and promise. Additional \$100,000 – \$250,000 annual collaborative grants may be available to funded teams during the award phase to act upon new discoveries and insights. BD² intends to fund up to five Discovery Grant awards.

Background

Bipolar disorder is a highly complex and heterogeneous disorder that is often debilitating. Even though it is prevalent in about 3% of individuals worldwide, little is known about its underlying 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 a collective force to transform what we know about and how we treat bipolar disorder. It is a commitment to the 40 million people living with bipolar disorder, those not yet diagnosed, and their loved ones.

The Baszucki, Brin, and Dauten families united with the Milken Institute to create BD² to advance discoveries for families like theirs. For too long, there have been limited advances in the study and treatment of bipolar disorder due to lack of collaboration and funding. It's time for a new approach.

The Discovery Grants program, a BD² initiative, aims to delineate the etiology and biological mechanisms of bipolar disorder, allowing the development of effective interventions for all individuals with bipolar disorder.

We plan to make this a reality by funding and developing a network of interdisciplinary researchers with the complementary knowledge and tools to strategically advance our understanding of bipolar disorder and accelerate the development of effective interventions.

The Opportunity

Throughout the decades of bipolar disorder research, it has become clear that research strategies must shift drastically to ensure faster and more significant discoveries. Philanthropic support has presented a once-in-a-generation opportunity to develop a unique mechanism to bring the most capable and innovative minds together to explore one of the most complex mental disorders.

Teams of three to five scientists may apply to receive up to \$1.5 million per year for three years, totaling \$4.5 million per award. Selected grantees will work with the BD² program staff and the Scientific Steering Committee (SSC) to develop a scientific scope that is impactful and will significantly contribute to our understanding of the causal mechanisms of bipolar disorder. Funded teams will be expected to share resources, data, and progress with other teams in the network throughout the funding period. Teams will also have the opportunity to develop new partnerships with other teams within the network and potential to access additional collaborative grants, ranging from \$100,000 to \$250,000 per year. We intend to continue funding for an additional two years beyond the original three-year grant period for teams exhibiting strong productivity and promise.

A Focus on Mechanisms of BD

We are seeking multidisciplinary teams of researchers from across the world to pool ideas and work together across expertise to explore fundamental mechanisms of bipolar disorder. Funded teams should be champions of team science, open science, and innovative thinking. We seek to build a vibrant community of funded investigators who will use ambitious strategies to test causal mechanisms and hypotheses to better understand the etiology, temporal dynamics, and heterogeneity of bipolar disorder. Applications with animal models, cell models including human iPSCs and brain organoids, or human subjects that are focused on causal mechanisms will be considered. Applications that seek to collect data or samples from existing patient cohorts will be accepted. **Applications focused on clinical efficacy of a treatment or intervention, especially recruitment of participants into new or existing trials, or administrative or infrastructure support for clinical trials, are not within the scope of this program.** All applications should outline specific aims as well as milestones for those aims so that the scientific leadership and BD² program staff can identify where potential synergies or alignment across applications is advantageous.

Co-Developing the Scientific Scope

Researchers will apply with a team of three to five interdisciplinary experts representing different disciplines or experimental approaches, all of whom should be interested in addressing underlying mechanisms of bipolar disorder. These teams shall submit a 5-page scientific scope outlining their ideas and aims. These applications will be peer-reviewed. The most promising applications may be encouraged to modify their aims to ensure that all grants funded throughout the portfolio are coordinated and provide the highest likelihood of scientific breakthroughs in our understanding of bipolar disorder mechanisms.

Grant applications will be evaluated on an aim-by-aim basis. Applications may be selected for partial funding based on the promise of an application's individual aims.

Funds for Integration and Additional Collaboration

During the application review process, the SSC and BD² program staff may suggest the formation of new collaborations between principal investigators (PIs) on different grants. This may be done if there is significant scientific alignment, expertise considerations, or resource management across multiple applications. In these cases, if applicants agree to participate in these new collaborations, they will be eligible to access one-time collaboration grants of \$100,000 – \$250,000 to facilitate these novel collaborations.

Once funded, investigators will continue to have access to apply for additional collaboration grants, which will be available on an annual basis. These \$100,000 – \$250,000 annual grants will be awarded to promote new collaborations between funded PIs within the network.

Commitment to Open Science

Open science is a key governing philosophy of BD², as it will allow for rapid and efficient sharing of new knowledge, catalyzing novel hypotheses to test. Funded investigators will be expected to adhere to BD²'s open science policies, including pre-print submissions, and sharing protocols and datasets to pre-approved repositories. Teams must also publish results in open access publications, of which all publication fees will be covered by BD² and do not need to be budgeted in the grant proposal. Teams and their affiliated institutions should review our Open Science Policy prior to submission.

Important Dates

- September 12, 2022: RFA released
- December 12, 2022: Applications due
- December 2022 – March 2023: Scientific and strategic evaluation
- April 2023: Awardees notified
- May 2023: Grants awarded

Eligibility

Application will only be considered from teams who meet all eligibility criteria below:

Institutional Eligibility

- Each applicant organization must be a non-profit academic or research institution, including domestic and non-U.S. non-profit organizations, domestic and non-U.S. public/private academic universities, or institutions of higher learning (including colleges, universities, medical schools, and other related academic research organizations). Certain governmental agencies with active biomedical research programs may also apply.
- The Lead PI must be affiliated with the institution submitting the application. If the Lead PI's institution is selected for funding, grant funds will be awarded to that institution, which will take responsibility for distributing funds as subawards to any institutions with which other members of the collaboration are affiliated.

Leadership Eligibility

- Each team must consist of three (3) to five (5) PIs. Each PI must hold a doctorate (e.g., Ph.D., M.D.) or related research doctorate degree. Each PI must be affiliated with an institution eligible to hold funds.

Each PI will lead a component or subproject of the team project. PIs can be recruited from existing or previous collaborations, or from new collaborations. PIs from groups that are under-represented in science, as defined by the [National Institutes of Health](#), are encouraged.

- A Lead PI must be identified within each team of three to five PIs. The Lead PI is responsible for the scientific and technical direction of the proposed research project, contractual and financial obligations, and other organizational assurances and certifications. The Lead PI will submit the application and be the primary point of contact between the research team and the BD² team during the application and evaluation process, as well as during post-award progress reporting and other matters throughout the entirety of the grant period, if applicable.
- There is no minimum number of institutions required to be represented within each team. All PIs can be from the same institution. However, interdisciplinarity of the PIs will be strongly considered as a priority.
- Regardless of the size of the team, there must be at least one PI who is considered an early career researcher. An early career researcher is considered as a PI who has completed their terminal research degree or post-graduate clinical training in the last 10 calendar years (i.e., since 2012), and currently holds a fully independent faculty position or equivalent.
- All PIs must allocate a minimum of 25% of their time and effort to the project.
- Regardless of the size of the team, there must be at least two different scientific disciplines (i.e., experimental approaches) or expertise represented on the team.
- Individual PIs may be on multiple grant applications but may only serve as the Lead PI on a single application, while being cognizant about the minimum effort required for each grant.

Personnel Eligibility and Requirements

- Key personnel, collaborators, and consultants must be named in the application.
- Each funded team must identify a project manager (PM) to manage all administrative responsibilities, as well as to optimize scientific interactions, across the component labs. The PM must be from the same institution as the Lead PI, and overseen by the Lead PI. The PM must dedicate a minimum of 50% of their time to this effort. The remaining effort of the PM could be as an active member of the research team. This PM must be appointed within six months of award and can be a new hire or someone recruited to the project from within the Lead PI's institution. BD² program staff will reach out to the Lead PI at the six-month deadline to ascertain the name and contact information of the PM. We strongly recommend that the PM is a doctoral level scientist or clinician and is principally managed by the Lead PI. The PM would be supported by BD² Discovery Grants and their salary will be determined by the applicant, to be listed on the Budget Sheet. PMs will:
 - Liaise between the labs within their team, program staff, and other funded teams via monthly meetings;
 - Manage data processing and upload requirements for all labs on their team;
 - Lead and organize monthly affinity group meetings, described in the "Evaluation and Monitoring" section;
 - Communicate challenges and feedback to program staff; and
 - Manage progress reporting requirements.

Ineligibility

- Longitudinal cohort studies will not be funded by this grant.
- Applications that primarily seek to develop new interventional strategies will not be prioritized in this initiative.
- Applications that focus on clinical trials, especially recruitment of participants into new or existing trials, or administrative or infrastructure support for new or existing clinical trials, are not within the scope of this grant.

The Application

One application is required per team of three to five PIs. All applications will be submitted via the [Submittable online grant portal](#). All Lead PIs must create an account to access the portal and submit applications. The application is due **December 12, 2022**.

An application shall be submitted by the Lead PI on behalf of their team. The application should convey the scientific concepts and hypotheses that will be tested and outline the strategies to do so. See below for specific application content and formatting requirements.

Scientific Rationale (maximum 5 pages)

- **Project title**
- **Lay project summary:** Describe your project to a public, non-scientific audience.
- **Scientific goals:** Describe the central question the application seeks to address, as well as the proposed platforms (e.g., animal models, cell lines, datasets, and existing patient registries) and methods (e.g., specific assays such as genetic methods, circuitry approaches, pharmacological strategies, or clinical paradigms) that will support examination of the hypotheses. As the goal of this initiative is to make true progress in understanding bipolar disorder, successful applications will have convincing, actionable, and consequential ideas to advance the field beyond what has already been achieved.
 - **Outline specific aims:** Describe the various aims of the study. As aims will be considered for funding on an individual basis, it is strongly recommended that a given aim's success is not fully dependent on a previous aim's results.
 - **Cost estimates per aim:** Provide a rough, total estimate of cost to fund the execution of each aim. This estimate should include equipment, personnel, storage, reagents, and overhead. See the budget section below for further detail around items eligible for budget inclusion.
 - **Milestones:** Outline the various milestones that each aim will encompass. Milestones must be in six-month increments and be specific, attainable, and measurable. Milestones will be used to assess progress during the award phase.
- Figures are included in the five-page limit.

References (maximum 2 pages)

References cited: Provide citations supporting the scientific rationale of your proposed project. Include a DOI link for each citation. There is no specific formatting requirement.

Team Description (maximum 2 pages)

- **Roster of PIs:** Provide the name, institution, and expertise of the Lead PI and all other PIs on the team. Note which of the PIs is an early career researcher (ECR). More than one PI may be an ECR.
- **Resources:** Provide the catalogue of resources available from each PI. Resources include expertise, reagents, equipment, clinical and research cores, existing datasets, and access to biobanks.
- **Collaboration potential:** Provide details of how proposed team members have collaborated in the past, and/or why the proposed team is uniquely poised for a successful collaborative relationship.
- **Collaboration plan:** Outline the strategies that the team will adopt to ensure adequate collaboration among the PIs. This may include frequency of meetings, modes of communication, and data sharing strategies.
- **Open science practices:** Describe the activities and efforts that have been undertaken by each PI to adhere to open science practices. Describe how all team members plan to demonstrate commitment to open science practices in the proposed research.

Letters of Commitment (maximum 2 pages each)

- **Institutional commitment:** Each application must include letters of commitment that demonstrate each institution's commitment to administering the grant according to a written grant agreement to be entered into between the selected organization and BD². The letter shall be signed by a department chair or a relevant authorized organizational representative, such as the Dean of Sponsored Research. Applications that have multiple institutions can either have separate letters of commitment from each institution or have one letter of commitment signed by all relevant authorized institutional representatives from each institution.
- **PI commitment:** Each PI represented in the application shall also provide a letter stating that they are willing and able to commit at least 25% of their time to overseeing this grant. The letter must also state that each PI is willing and able to commit to executing this project, to communicate regularly with program staff and the SSC as needed, and to adhere to open science principles. Applicants can submit separate letters of commitment by each PI or have one letter of commitment signed by all PIs.

PI Biosketches (maximum 5 pages per PI)

A biosketch of the Lead PI and co-PIs, utilizing the [NIH template](#), is required and shall not exceed five (5) pages per PI. If the Lead PI or co-PI does not have a biosketch in an NIH template, a CV is sufficient.

Detailed Budget (use template)

A detailed budget in USD, using the provided template: Acceptable expenditures shall include salary, fringe benefits, equipment, software, storage, reagents, project-related travel, and up to 15% indirect costs to support institutional infrastructure. Note that publication costs to open access journals will be covered by BD² and do not need to be budgeted in your proposal. The Lead PI's institution shall be proposed as the applicant organization and the other institution(s) shall be included as sub-grantees, managed by the applicant institution. Each collaborating site must outline their subaward budget to clarify needs for all parties.

- The maximum allowable budget is inclusive of 15% indirect expenses. For applications including a sub-grantee(s), the maximum allowable indirect rate across both grantee and sub-grantee institutions remains 15% of the total award budget.
- For international applicants: Please note grants will be made in USD, and BD² is not responsible for changes in conversion rates.

- Grants selected for funding will be made payable to the Lead PI's institution. Under no circumstances will funding be paid to an individual. Please note that funds will be disbursed on an annual basis to the Lead PI's organization.

Selection Criteria

The BD² selection criteria is based on the following characteristics. Applications displaying strength and creativity across the following domains will have a higher likelihood of success.

- **Scientific and technical merit:** The quality of the scientific rationale and aims, and the uses of resources, equipment, and experimental designs to adequately address a causal mechanism of bipolar disorder. This includes innovative use of current resources or unique perspectives of examining current dogma. Experimental design is adequately rigorous, and the study is appropriately statistically powered to produce significant findings even in the absence of results that support the study hypothesis.
- **Commitment to team science:** Proposed team of three to five PIs has been thoughtfully developed; unique advantages of proposed collaboration are clearly communicated in the application; proposed team reflects a diverse collection of expertise, thinking, affiliation, and demographics.
- **Commitment to open science:** Proposed data sharing plan has been thoughtfully constructed and aligns with tenets of open science according to the terms outlined below; application exceeds standard methods and approach of sharing data and results with the research community.
- **Potential impact:** The success of this proposed scope of work would be significant in understanding the biology and mechanisms of bipolar disorder, bringing meaningful change to the lives of individuals living with bipolar disorder. This includes an application's innovation, or ability to bring new ideas to the field and develop unique avenues to investigate bipolar disorder.
- **Team capabilities:** The team's demonstrated collaborative potential and leadership capacity of the Lead PI. This includes each institution's demonstrated ability to adequately support the proposed research.
- **Cost realism:** A realistic budget that adequately supports personnel, equipment, overhead, and other needs to carry out the project.

Review Process

There will be a multi-step review process carried out by the scientific leadership and program managers of the BD² Discovery Grants program. Application review comprises the following:

- **Eligibility review:** Prior to content review, all applications will be assessed to ensure that all eligibility criteria listed in this RFA are met. Applications are subject to rejection if one or more of these criteria are not met.
- **Scientific scope review:** Members of the SSC and BD² program staff, scientific leadership, and administrative teams will review each application to ensure that the scientific scope is aligned with this RFA. Applications that are out of scope may be rejected.
- **Peer review:** Applications will be peer reviewed against the selection criteria listed above. Applications will be ranked according to peer review, and a select number of highly prioritized applications will move forward to the next round.
- **Scientific leadership review and integration:** The scientific leadership of BD² will examine the highly prioritized peer-reviewed applications. Teams may be asked by the leadership to participate in new

collaborations with other teams. These teams may be eligible for additional grants to facilitate these collaborations.

- **Scope modification:** Finalists may be asked to meet with the SSC and/or program staff of BD² to discuss potential changes to their application prior to funding. The teams will work together to develop an application that may be better aligned with the overall scientific scope of the portfolio of projects. A short amendment document may be asked of teams, subject to approval from the SSC, prior to funding.
- **Program Board approval:** The scientific leadership of BD² will provide a final prioritized list of applications for approval by the Program Board, which consists of the funders of the initiative. Applications that are approved by the Program Board will be funded subject to a written grant agreement as further discussed below.

Evaluation and Monitoring

Once the grants are awarded, grantee progress will be monitored by the PM with input from the SSC. These actions will ensure that grantees are able to work together among the newly formed teams and partnerships, share data, and conduct their research using best practices and standardized approaches implemented across all funded projects. Funded teams will use a shared virtual platform to streamline communication and sharing to improve collaboration potential within the network.

Bi-Annual Updates

Each team will provide short bi-annual updates on their milestone progress and any challenges they have faced along the way. Milestones will be determined by the scientists in their applications and disclosing progress against these milestones on a bi-annual basis will provide clarity on scientific advancements or setbacks made by the teams.

Affinity Group Meetings

Funded teams will join affinity group meetings with other teams within the network. Affinity groups will be created by the funded teams and will comprise of PIs who share similar hypotheses (immunology, energy and metabolism, circadian rhythms, etc.), or experimental procedures (genetics, neuroimaging, actigraphy, etc.). These group meetings will allow teams to share progress, successes, and challenges with PIs outside of their teams. These meetings, which will be recorded and shared with the network, serve as an opportunity for informal progress updates.

Annual Investigator Meetings

On an annual basis, investigators will be convened to share progress on work funded by BD² and to further facilitate collaboration across teams. Expenses for attending these meetings will be covered under a separate budget provided by BD².

Grant Terms and Policies

Each funded organization will be required to co-sign and agree in writing to BD²'s grant terms within thirty (30) days from receipt of notice of the award and prior to funds being released. BD²'s grant terms include, but are not limited to, the following items.

Use of Funds

Each team will be applying for a grant that would provide up to \$1.5 million per year, for up to three years. Because applications may be partially funded, teams will receive the amount that is sufficient to carry out the aims that are selected for funding.

- **Use of funds:** Funds may be used for scientific and technical personnel, supplies, and standard equipment needs directly related to the successful execution of the proposed scope or work. This also includes travel to relevant conferences and events. However, funds may not be used for laboratory or facility renovation.
- **Carryover funding:** Unused research funds may be carried over to the following year, with approval, and requests for no-cost extensions will be considered.
- **Indirect costs:** Indirect costs are included in the \$1.5 million per year award. Up to 15% of the entire grant budget may be slated for indirect costs. Note that awards may be lower than the maximum \$1.5 million per year. In such a case, only up to 15% of that specified grant budget may be allocated to indirect costs.
- **Unexpended funds:** Any funds not expended or committed for the purposes of the grant by the conclusion of the grant term must be returned to BD² unless otherwise agreed to by BD² in writing.
- **No cost extensions:** No cost extensions can be requested by teams within the last year of the award period.
- **Supplemental funding:** If a funded organization proposes to supplement any funds provided by BD² with funds provided by a third party, the organization must first provide notice to BD² and must ensure that the funding terms associated with any such third-party funds do not preclude sharing of data or publication or project results as outlined in this RFA.

Data Sharing

Open and responsible data sharing is a key tenet to preventing roadblocks and delays in research findings. Therefore, data sharing and open science are foundational pillars of BD² Discovery Grants. Teams and their affiliated institutions should review and confirm that they can comply with our Open Science Policy prior to submission.

- **Open access:** All data resulting from the Team's work will be available to the scientific community at large at the earliest opportunity on preprint servers, online protocol platforms, and in an open access journal format.
 - **Publications:** All publications related to this funded work must be submitted to a preprint server, such as bioRxiv, before or concurrent to the first submission to a journal. An open access journal format is a requirement of this funding opportunity. Experimental protocols should be made publicly available through a protocol sharing service, such as bio-protocol or protocols.io. In addition, early sharing of null and incremental results, within the network and publicly, is encouraged. Scientific publications, preprints, and presentations that result from this award be acknowledged as being supported by this funding.
 - **Data and code sharing:** All datasets and code, either curated or generated through the project, must be made publicly available and easily accessible online, as early as possible, when feasible. This includes metadata, documentation, and intended computational use cases, as appropriate. Funded teams are expected to share data with others in the network on an annual basis at minimum, prior to publication. BD² scientific leadership will work with grantees to identify appropriate data platforms.

- **Tool and reagent sharing:** All tools or reagents funded by and resulting from awarded projects must be made readily available to the broader scientific community through an accessible community repository, such as Addgene for plasmids, DNA reagents, viruses. This requirement applies to cell lines, transgenic models, plasmids/clones, antibodies, and other tools and reagents.
- **Reporting requirements:** Progress reports with financial report-outs are due annually or at other times as deemed necessary by the scientific leadership for project evaluation. Progress report forms will be provided by the BD² program staff.
 - Quarterly progress discussions will be held between BD² program staff and the PIs and PM of each team as needed. Where necessary or helpful, follow-up could be expected.

Intellectual Property

Intellectual property resulting from, created, developed, conceived, or reduced to practice in whole or in part with funding from BD², including all patent, copyright, trademark, trade secret, and other rights therein (Grant IP) would be subject to obligations on the recipient organization to:

- Commercialize any Grant IP that has the potential to benefit patients who have bipolar disorder;
- Allow BD² or its sublicensee to commercialize any such Grant IP that the grantee is unwilling or unable to commercialize;
- Widely disseminate through publication the results of research funded with grants from BD²; and
- Grant a research license to BD², the founding funders of BD², and all of their respective non-profit grantees to use and to practice Grant IP in the field of bipolar disorder.

Funding Awarded in BD²'s Discretion

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

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 spam filters, then contact DiscoveryGrants@BipolarDiscoveries.org.

For inquiries about scientific priorities, eligibility requirements, application submission, as well as general and media inquiries, please contact: DiscoveryGrants@BipolarDiscoveries.org.