ACS Green Chemistry Institute
Pharmaceutical Roundtable

2025 ACS GCI Pharmaceutical Roundtable Research Grant for Increasing the Breadth and Utility of Enzymes in Pharma Manufacturing

The ACS Green Chemistry Institute Pharmaceutical Roundtable (GCIPR) is a partnership between the ACS Green Chemistry Institute® and pharmaceutical-related corporations united by a shared commitment to integrate the principles of green chemistry and engineering into the business of drug discovery and production. Current members are AbbVie, Amgen, AstraZeneca, Bayer, Biogen, Biohaven, Boehringer-Ingelheim, Bristol-Myers Squibb, F. Hoffmann-La Roche Ltd., Ferring, Gilead, GSK, Ipsen, Johnson & Johnson, Lilly, Merck & Co., Merck KGaA, Darmstadt, Germany, Neurocrine, Novartis, Novo Nordisk, Pfizer, Sanofi, Takeda, UCB Pharma, Vertex, and the ACS Green Chemistry Institute®. Associate members are Asymchem, Axplora, Bachem, CatSci, ChemExpress, Codexis, EuroAPI, Hikal, Hongene, Hovione, InnoSyn, Nitto Avecia, PharmaBlock, Pharmaron, Polypeptide, Porton, Sai Life Sciences, ST Pharm, Syngene, and WuXi AppTec. Affiliate members are Aralez Bio, Corteva Agriscience, FMC, PHT and Zoetis.

The ACS GCIPR is seeking a one-year R&D commitment to assist the Roundtable its aim to further develop enzymes for scalable API manufacture. The focus of the proposal should be to identify areas of either:

a) enzymatic C-C bond formations that are currently underrepresented in literature, to explore new enzymes or modify existing ones to fill this gap. We will particularly welcome applications that address the discovery and development of novel C-C bond formation through C-alkylation and proposals which address C-C bond formation with a cascade approach (e.g., via enzymatic halogenation-alkylation).
b) atom efficient enzymatic amide bond formation

Proposals are invited from public and private institutions of higher education worldwide. This collaborative project is intended for a student within the selected Principal Investigator's research group. One grant is planned to be awarded, and the total award is limited to $80,000 for a grant period of 12 months. Interested PIs are required to provide a written proposal describing the investigator's capability to carry out the Roundtable's proposed research. Deadline for receipt of proposals is **May 16, 2025, at 11:59 p.m. EDT**. All submissions must be made in our application portal: https://gci.acs.org. The Principal Investigator with the selected proposal will be notified by **September 1, 2025.** It is expected that research will commence in the principal investigator's lab no later than **October 2025** and last 12 months.

Requirements for Submission

Proposals will only be accepted from public and private institutions of higher education. The grant is not limited to institutions in the United States. Proposals must be submitted in our application portal https://gci.acs.org through the appropriate institutional office for external funding. For international

submissions, if there is no comparable office, submit a PDF of a letter signed by an appropriate university official recognizing the terms of the grant.

Detailed Project Description

The exquisite enantio- and regio-selective nature of enzymes makes them extremely attractive catalysts for API synthesis. Additionally, enzymes can often be used in combinations, in cascade reactions allowing complex transformations in one pot. With increased sustainability becoming a prominent goal for synthetic chemists in the industry, the inherent biorenewability and biodegradability of enzymes, coupled with their high evolvability and native activity in water, has increased their desirability. However, even with the ability to engineer enzymes to have the desired characteristics for their intended process, there are gaps in their applicability. An internal survey within the members of the GCIPR has highlighted two areas of interest to the pharmaceutical industry for which efficient enzymatic alternatives would be desirable

The areas of interest identified by the GCIPR are as follows but not limited to:

- C-C bond formation
- Atom efficient methods for enzymatic amide bond formation

The members of the GCIPR would be interested in receiving proposals that utilize both natural enzymes and those that incorporate noncanonical amino acids to facilitate more challenging non-traditional enzymatic reactions.

Key Considerations:

- Safety: All reactions considered should have the appropriate safety considerations taken into account, especially those involving oxidation with air, oxygen or other oxidants
- Co-factors: For enzymes requiring co-factors that are depleted per turnover, recycling methods should be considered and presented.
- Substrates and Reactions: Heterocyclic compounds are abundant in the pharmaceutical industry. Substrates and/or reactions of study should be selected based on a pharmaceutically relevant profile to prioritize activity against these compounds.
- Greenness: To ensure that chemistry in water and flow chemistry continue to stay at the frontier of sustainability, applications should be reflective of the key research areas described by the GCIPR:

  https://acsgcipr.org/funding-awards/research-grants/

  https://doi.org/10.1039/C8GC01276H

  and of the principles of both green chemistry and green engineering:

- Processing: Standard pharmaceutically relevant manufacturing operations such as liquid-liquid extractions, distillations, crystallizations, and membrane separations have limitations when operated in the presence of large quantities of protein. As such, the ability to engineer enzymes in the proposals to sufficient activity to be suitable for use in a manufacturing environment should be considered

Project Goal

Promote innovation at the interface of chemistry and biochemistry/enzymology to overcome enzymatic activity, selectivity, substrate scope limitations, allowing broader application and scale-up of enzymatic reactions of the defined reaction type below

- C-C bond and amide bond forming reactions that are traditionally underserved in the biocatalysis literature.

In addition, the GCIPR requests the following, if appropriate:

- Perform the necessary screening of enzymes for the proposed transformation
- Evolution or engineering of enzymes for a specific reaction class
- Perform a substrate scope to better understand if there are significant limitations to the specific enzyme class
- A lab-scale demonstration of a select few transformations that show promise at a reasonable scale to show potential for scalability for the pharmaceutical industry.

Project Timeline

It is expected that one year of research support will be sufficient to provide progress toward intended goals.

Proposal Format

Please be prepared to provide the following information in the application portal:

1. Name and email of grant officer
2. Name, title, phone, email and address of the Principal Investigator
3. Project Title
4. Research Group website
5. PDF of Proposed Plan of Work *(2 pages, 12 pt font, 1-inch margins)*
   - Objectives: Briefly state the project objectives
   - Project Approach: Include specific aims and investigations planned
   - Proposed milestone deliveries with brief description of the manner in which the researcher intends to achieve them
   - Brief description of the PI's research facilities and summary of the student's (undergraduate, graduate student and /or postdoc) capabilities to perform the proposed work
   - References (does not count toward your page limit)

Note: The PI should list any existing background intellectual property and/or collaborations they are aware of that might limit the freedom to operate any of the results arising from any research funded by ACS GCIPR. The priority of the Roundtable is to encourage research utilizing reaction conditions that are commercially viable with the freedom to use.

6. PDF of Detailed Estimated Budget: The total amount requested would include all direct costs, student assistantships, etc. The total award is limited to $80,000 for a grant period of up to 12 months.
   - Institutional overhead costs (indirect costs) should not be more than 10% of the total budget.
   - Post-doctoral associate salary and benefits are supported.
   - Student stipend and benefits are supported. Proposals for support of advanced graduate students are strongly encouraged.
   - PI salary supplements will not be supported.
   - Laboratory supplies and instrument use charges are supported.
   - No funds may be allocated for travel, equipment purchase or repair, or administrative support.

7. Curriculum Vitae of Project Team Members: Please submit a curriculum vitae of each project team member (up to two pages per team member, combined into the same PDF document as the project description). This does not count toward your page limit.

Report Requirements

- Progress reports/research updates are due monthly or bi-monthly from initiation of research and will be discussed in arranged web-conferences. All reports/updates will be shared with the member companies of the Roundtable.
- Reports/updates should include research milestones/significant outcomes, summary of progress to date noting any deviations from the proposal, and research plans for upcoming months.
- A final comprehensive report is due one month after the end of the grant period. This report must be submitted as a PDF document electronically to gcipr@acs.org. In addition, the content of the report should be targeted for publication in a peer-reviewed technical journal. The paper will be co-authored by the principal investigator and student(s) performing the work. Representatives of member companies who make intellectual contributions to the project should be recognized as authors.

Intellectual Property, Publication Acknowledgement, and Terms of the Grant

- The primary purpose of this grant is the public dissemination of research through publication.

- Every patent, United States or foreign, that results from research funded (in part or in its entirety) by the ACS GCIPR Research Grant shall be immediately dedicated to the public, royalty free.
- Publication of results is expected within 6 months of work completion.
- Each publication prepared in connection with the ACS GCIPR Research Grant shall make acknowledgement in the following manner: "This manuscript was developed with the support of the American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable (www.acsgcipr.org). The ACS GCI is a not-for-profit organization whose mission is to stimulate interest in and enable the implementation of green and sustainable chemistry throughout the global chemistry enterprise. The ACS GCI Pharmaceutical Roundtable, composed of pharmaceutical and related industries, was established in 2005 to encourage innovation while catalyzing the integration of green chemistry and green engineering in the pharmaceutical industry. The activities of the Roundtable reflect its member's shared belief that the pursuit of green chemistry and engineering is imperative for business and environmental sustainability."
- Acceptance of a Roundtable Grant will be conditional upon agreement by the grantee institution that in the event the Principal Investigator is unable for any reason to conduct the research proposed, the funds, if previously paid by the Roundtable, shall, upon demand, be returned in full to the Roundtable, and further, that in the event the PI is unable for any reason to continue with the research after it has commenced, this grant shall be terminated forthwith and the unexpended and unencumbered balance of any funds theretofore advanced shall be returned to the Roundtable.
- The grantee institution, by acceptance of this grant, provides assurance that support normally provided by the institution for research of the faculty member will not be diminished.
- Applicants may have only one research grant with the ACS GCIPR at a time. In order to close a grant, the ACS GCIPR must receive and approve the required reports.

For additional information:

Website: www.acsgcipr.org
Email: gcipr@acs.org