



## 2023 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 Pharmaceuticals, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company, F. Hoffmann-La Roche Ltd., Gilead, GlaxoSmithKline, Ipsen, Johnson & Johnson, Merck & Co., Neurocrine, Novartis, Novo Nordisk, Pfizer, Takeda, UCB Pharma, Vertex, and the ACS Green Chemistry Institute. Associate members are Ampac Fine Chemicals, Asymchem, Bachem, CatSci, Codexis, Hikal, Hovione, InnoSyn, Kaneka, Novasep, Pharmaron, Polypeptide, Porton, Sai Life Sciences, Solara Active Pharma Sciences Ltd., and WuXi AppTec. Corveva Agriscience, EnzyTag, and PHT International Inc. are affiliate members.

The ACS GCIPR is seeking a one-year R&D commitment to assist the Roundtable's Biocatalysis initiative. The focus of the R&D will be toward overcoming enzymatic activity, selectivity, substrate scope limitations, allowing broader application and scale-up of enzymatic reactions. Proposals are invited from public and private institutions of higher education worldwide. This 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 \$50,000 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. The deadline for receipt of proposals is **May 15, 2022 at 5 p.m. EDT**. Proposals must be received by the deadline to be considered. Submissions must be a single PDF file submitted to [gcipr@acs.org](mailto:gcipr@acs.org). GCIPR will notify the selected PI by **September 6, 2022**. It is expected that research will commence in the Principal Investigator's lab no later than **October 3, 2022** and last approximately 12 months.

### **Requirements for Submission**

Proposals will 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 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**

Enzymes are natively active under aqueous conditions and are enjoying increased utility due, in part, to their often very high selectivity for specific reactive sites and high enantioselectivity. Additionally, enzymes can often be used in combinations, in cascade reactions allowing complex transformations in one pot. With sustainability becoming a prominent goal in synthetic chemistry, the inherent biorenewability and biodegradability of enzymes, coupled with their high evolvability, makes them

very desirable catalysis. However, even with the ability to engineer deficiencies in an enzyme's activity or selectivity, gaps in enzymes' repertoire do exist.

An internal survey within the members of the GCIPR has highlighted that there are areas within the realm of C-C bond formation that are far less well served with currently available enzymes.

Some areas of interest identified by the GCIPR are as follows, but also not limited to:

- Alkylases – both of the aliphatic or aromatic nature. This can also be potentially combined with halogenases in a cascade reaction to set up the key C-C bond forming transformation
- Halohydrin dehalogenases
- Diels-Alderases
- Pictet-Spenglerases
- Reductive coupling of carbon monoxide
- Aldolases

#### *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: The pharmaceutical industry prominently features heterocycles and very bulky water insoluble materials. Substrates and/or reactions of study should be selected based on a pharmaceutically relevant profile.
- 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://www.acsgcipr.org/advancing-research/> and <https://pubs.acs.org/doi/abs/10.1021/op100327d>) and of the principles of both [green chemistry](#) and [green engineering](#).
- Processing: New enzymes may start with low, but novel activities, which require high protein loadings. Standard pharmaceutically relevant 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 to achieve a long-term target activity of the enzyme, and therefore low protein loading, should be taken into consideration.

#### **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 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 anticipated that one year of research support will be sufficient to provide progress toward intended goals.

### **Proposal Format** (Maximum 3 pages as described below + CVs)

All of the information below must be submitted as a single PDF file. All components described in sections A, B, and C must be included in the same PDF file to assure the proposal is reviewed in its entirety.

#### A) Title Page (*1 page, 12 pt. font, 1-inch margins*)

1. Project Title:
2. Principal Investigator:
3. Title / Position(s):
4. Telephone Number(s):
5. Fax Number(s):
6. Postal Mailing Address:
7. Email Address:
8. Research Group Website:

#### B) Proposed Plan of Work (*2 pages, 12 pt. font, 1-inch margins*)

1. Objectives: Briefly state the project objectives
2. Project Approach: Include specific aims and investigations planned
3. Proposed milestone deliveries with brief description of the manner in which the researcher intends to achieve them
4. 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
5. 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 available with the freedom to use.

C) Detailed Estimated Budget: The total amount requested would include all direct costs, student assistantships, etc. The total award is limited to \$50,000 for a grant period of up to 12 months. This does not count toward your page limit.

1. Institutional overhead costs (indirect costs) should not be more than 10% of the total budget.
2. Post-doctoral associate salary and benefits are supported.
3. Student stipend and benefits are supported. Proposals for support of advanced graduate students are highly favored.
4. PI salary supplements will not be supported.
5. Laboratory supplies and instrument use charges are supported.
6. No funds may be allocated for travel, equipment purchase or repair, or administrative support.

D) Curriculum Vitae of Project Team Members: Please submit a curriculum vitae of each project team member (up to two pages per team member). This does not count toward your page limit.

### **Report Requirements**

- Progress reports or updates are due monthly or bi-monthly from initiation of research and will be discussed in arranged web-conferences. Reports will be shared with the member companies of the Roundtable.
- Reports are to 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](mailto: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 with the guidance of member companies of the ACS GCIPR.

### **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](http://www.acsgcipr.org)). The ACS GCI is a not-for-profit organization whose mission is to catalyze 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.acsgciper.org](http://www.acsgciper.org)

Email: [gciper@acs.org](mailto:gciper@acs.org)

