Fibrosis in IBD Research Initiative

Request for Proposals (RFP)

Program Guidelines & Policies

Effective January 13, 2023

Crohn's & Colitis Foundation
National Office
Research Department
733 Third Avenue
Suite 510
New York, NY 10017

Contact:

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Key Dates

RFP Announcement	**January 13, 2023**
LOI Application deadline	**March 30, 2023**
Notification to submit full proposal	**June 2, 2023**
Full proposal deadline	**July 24, 2023**
Notification of award	**December 2023**

1. Overview

Half of all Crohn's disease (CD) patients develop fibrotic strictures (fibrostenosis), leading to GI tract obstruction and severe disease course. Fibrostenosis is also a serious complication for ulcerative colitis (UC) with approximately 8% incidence over the lifetime. Currently there is no medical therapy for fibrostenosis in IBD. Therefore, there is a great unmet need to understand the biology of fibrotic complications in IBD and how to prevent and treat them. Fibrosis is a complex process, involving multiple types of cells, cytokines and other proteins. Based on the current knowledge, chronic inflammation, activation of stromal cells (particularly fibroblasts) and excessive deposition of extracellular matrix proteins (ECM) contribute to the development of fibrostenosis. Several Foundation-funded programs have resulted in major advances in this field, including the identification of prognostic biomarkers for fibrosis in pediatric CD through the RISK Consortium[1] and development of an iPSC-derived human intestinal organoid model of fibrosis[2].

Given the phenotypic heterogeneity of IBD, research focused on the identification of molecular endotypes driving intestinal fibrosis could lead to identification of molecular biomarker signatures for patient segmentation, thereby offering the opportunity for discovery and development of personalized anti-fibrotic treatments.

Through this RFP the Crohn's & Colitis Foundation (Foundation), in collaboration with Takeda Pharmaceuticals (Takeda), will support multidisciplinary approaches to define, based on human multiomics signatures, fibrotic patient segmentation/endotyping, and to better understand the biology of intestinal fibrosis in relevant experimental model systems. A particular interest will be related to the transmural interplay of fibroblasts and myofibroblast with other stromal cells and inflammatory cells in specific IBD patient populations to enable the future discovery of effective anti-fibrotic therapeutics.

2. Scope

The Foundation seeks to fund studies focused on investigating the biological mechanisms leading to and reverting or protecting from fibrosis in IBD. Interest will be on proposals that address one or more of the following areas:

- **Pathophysiology of fibrosis and patient segmentation/endotyping based on multi-omics analysis:** Research based on available multiomics datasets/samples (e.g. biopsies, resected tissue, etc) from IBD patient cohorts such as IBD Plexus or investigators' own data/samples from ongoing longitudinal studies, are expected to be utilized to identify molecular signatures for fibrotic patient stratification/endotyping and to elucidate biological drivers of fibrostenosis. Use of data sets derived from transmural bowel resections is encouraged (e.g. full thickness resections collected at pre-stricture or post-stricture event) and preferred if biopsies and resections are paired with blood samples (plasma and/or serum).

- Datasets and biosamples derived from demographically and ethnically diverse cohorts are also preferred.
- **Cell biological mechanisms of fibrosis:** Areas of interest could include investigation of the cell-cell interactions and molecular mechanisms of the interplay between human intestinal cells (epithelial cells), myofibroblasts, mesenteric fat, creeping fat, stem cells and inflammatory cells, leading to, or reverting or protecting from fibrosis in specific IBD patient populations, to enable the future discovery of effective anti-fibrotic therapeutics.
- **Role of microbiome:** Investigation of the role of the gut microbiome, their metabolites and host factors leading to, or reverting or protecting from fibrosis.
- **Evaluation of therapeutic potential of modulating specific fibrotic pathways:** Interventions could include pharmacological or genetic manipulation of targets predicted to play a role in fibrosis development and/or maintenance. Validation of previously described pathways, as well as interrogation of novel pathways, is encouraged.
- **Multidisciplinary approaches**: Multidisciplinary proposals that integrate analysis of patient cohorts/samples with *in vivo*, *in vitro* and *ex vivo* experimental systems that recapitulate patient-based observations are preferred, for example including *in vitro* models (*e.g.,* human intestinal organoids, stem cells derived from fibrotic patients), analysis of transmural bowel biopsies, animal models of fibrosis, biophysical studies, and imaging approaches.

To ensure that the research stays focused on preclinical experiments that are related to IBD fibrosis experienced by patients, the research approach must demonstrate this relationship through a connection with clinical observations and/or published evidence in human fibrosis in general, and IBD fibrosis in particular. Studies including analysis of samples collected from IBD patients to validate clinical and/or *in vitro* and *in vivo* findings will be preferred.

3. Eligibility

Applications from a team with the relevant expertise are required, with one lead Principal Investigator (PI) and at least one Co-PI.

- The lead PI must be a senior faculty member (Professor, Head of Research, Associate Professor, etc) expert in fibrosis research preferably in IBD but experts in fibrosis in other therapeutic areas are encouraged to apply in collaboration with a Co-PI with expertise in IBD research (basic or clinical).
- Applications from multiple co-investigator PIs (co-PIs) are encouraged. At least one co-PI must be a junior Co-PI (Instructor or Assistant Professor, prior to receiving an independent RO1 grant or international equivalent) with experience in IBD research and who is committed to pursue a career in IBD research as a part of his or her career

development. Generally, junior Co-PI candidates should not be more than ten years beyond the attainment of their doctoral degree at the time of application.

- PI and Co-PIs must be employed by an institution (public non-profit or private non-profit) engaged in health care and/or health related research. Collaborations of lead PI with subcontracted for-profit organizations (e.g. CROs) are eligible. International applicants are also eligible to apply and there are no geographical restrictions regarding research site location(s).
- Applications are strongly encouraged from diverse teams of applicants that include women, underrepresented racial and ethnic groups, individuals with disabilities, and/or individuals from disadvantaged backgrounds.

4. Grant Terms

This award is a result of a collaboration between the Foundation and Takeda. All award terms must be consistent with the provisions of the Foundation/Takeda agreement, a summary of which is attached hereto at Appendix D. Awards will be granted for 1.5 years with a maximum amount of $300,000 per year per project, for a total maximum budget of $450,000 per project, inclusive of all indirect expenses. It is anticipated that the Foundation will support up to 2 projects. Milestones will be agreed upon prior to project onset, and continued funding for another 1.5 years (additional $450,000) could be considered and is dependent on exceptional progress towards specified milestones. Indirect expenses must not exceed 10%.

The proposal can be submitted by a multi-center consortium or by an individual research group; one institution should be identified as the primary applicant and will be expected to manage subawards to other institutions, if any.

5. How to apply

The investigators should submit the LOI by the specified deadline (see *Key Dates,* above). The LOIs will be evaluated competitively based on the alignment of the proposed study with the scope of the program and the feasibility of success of the study, as described in more detail in Appendix A (below). Only investigators who submitted an LOI and were invited to submit a full proposal are eligible to apply.

The investigators should provide a full research proposal and the accompanying document by the application deadline (see *Key Dates*, above) and according to the guidelines for proposal preparation and electronic submission (Appendix B, below).

All applications should be submitted through the proposalCENTRAL portal at the following URL: https://proposalcentral.altum.com/
Please refer to **Appendices A and B** for complete instructions of the application process.

6. Application Review and Selection Criteria

The investigators will provide a full research proposal and the accompanying document by the application deadline (see *Key Dates*, above) and according to the guidelines for proposal preparation and electronic submission (Appendix, below). The proposals will undergo peer review by a multidisciplinary review committee and evaluated based on the following criteria:

- **Alignment with the scope for this RFP** (see section 2 above).
- **Clinical relevance**: The proposed project should investigate pathophysiological mechanisms of fibrosis in human IBD, with the potential to inform eventual therapeutic strategies and/or identification of novel therapeutic targets. The hypothesis should be based on observations made in patients and/or address aspects of human pathophysiology.
- **Research strategy**: The proposal should have a translational approach, which is relevant for clinical application, sufficient preliminary data, well defined goals, clear experimental design and alternative strategies. The proposal must be well written and understandable by the scientific audience. The lay summary must clearly summarize the proposal and be understandable for non-scientific reviewers. (**Note*:*** scoring of the proposal by the non-scientific patient reviewer will depend on his/her understanding of a well written lay summary. A poorly written lay summary will negatively impact the score provided by the patient reviewer.)
- **Feasibility of success**: Demonstration of capabilities, personnel, and infrastructure to conduct the proposed study, organizational resources, collaborators.
- **Investigators' professional accomplishments**: The senior investigator must show a successful track record in acquiring funding and published research in the field of fibrosis. At least one investigator must be a proven expert in IBD research. The junior investigator should be on the clear trajectory for, and have prior accomplishments required to becoming an independent investigator in the field of IBD.

7. Reporting

Oversight and progress reports

The funded investigators will be required to submit progress reports every six months via proposalCentral using the Foundation's progress report template. In addition to the progress reports, as PI, you will be expected to present progress in oral presentations, including:

a. Mid-year oversight teleconference with Foundation staff, Takeda and members of the relevant oversight committee.
b. Translational research Initiatives oversight meeting, including all Research Initiatives PIs and members of the oversight committees, to be held annually in person in New York in early December. **Travel expenses for this meeting should be included in the submitted budget proposal**.

Intellectual property
The Foundation requires notification of any intellectual property (IP) arising out of or resulting from this scientific proposal within 30 days of receiving an invention disclosure or other notice indicating existence of intellectual property. Grantee shall provide the Foundation with written notice, via proposalCentral, of all inventions and patents as required by the Foundation Patent and Intellectual Property Policy (Appendix C). Upon accepting the award and signifying this Grant Agreement, both Principal Investigator and Authorized Institutional Officer express agreement and compliance with the terms of the Foundation Patent and Intellectual Property Policy as well as any applicable provisions of the Foundation/Takeda agreement referenced in Appendix D.

Additional award requirements
Funded investigators will be expected to submit financial reports and to report project outcomes using the ResearchFish portal. For additional information regarding the Foundation's post-award policies, including reporting, please refer to the Foundation's website: https://www.crohnscolitisfoundation.org/research/post-award-policies

8. Contact Information

For more information and questions please contact Drs. Andrés Hurtado-Lorenzo and Ji-eun Oh at: ibdfibrosis@crohnscolitisfoundation.org

9. Cited Literature

1) Kugathasan S, *et al*. (2017). "Prediction of complicated disease course for children newly diagnosed with Crohn's disease: a multicentre inception cohort study." *Lancet* 389: 1710-1718.

2) Estrada HQ, *et al*. (2022) Development of a Personalized Intestinal Fibrosis Model Using Human Intestinal Organoids Derived From Induced Pluripotent Stem Cells. Inflamm Bowel Dis. 4;28(5):667-679.

APPENDIX A: Letter of Intent (LOI) Submission Guidelines

The LOI should be submitted electronically on **March 30, 2023**.
The LOI application should be submitted
to proposalCENTRAL at: https://proposalcentral.altum.com

The LOI electronic submission form will include the following fields:

Paper copies of the application are not accepted.

a. If you are a first-time user, register by clicking on “First time user.” This will generate a confirmation number, which will be emailed to the email connected to this account. Confirm your registration by submitting this number when prompted.
b. Once you are a registered user, please click on “Grant opportunities” on the far right of the page and select Crohn’s & Colitis Foundation under “Filter by Grant Maker” drop down menu on the upper left of the page.
c. Locate the “Fibrosis in IBD” announcement and click “Apply now”.
d. To activate the navigation bar on the left, enter the title of your proposal on the title page and “save” the application. The navigation bar on the left will now become interactive for you to continue your application.
e. Once completed, please validate and submit the application.

Title (100 characters limit)
Priority area and relevance to IBD (3000 characters limit): State what population of IBD patients the study will potentially benefit (Crohn’s disease / Ulcerative colitis). Explain the relevance of the main objective of the study for the IBD field and the scope of the Fibrosis in IBD RFP (See Section 2). Explain how the proposed study is aligned with the focus areas of 2019 Challenges in IBD research.
Total Budget: State the total requested budget for a **3 year performance period including a a budget for the first half of the project (1.5 years) and the second half (1.5 years)** of the proposed study. Estimate is acceptable and may be revised if a full proposal is submitted.
Primary Investigator (PI) and Institution, as defined by the primary performance site and the primary point of contact for budget management, and for research progress and financial reporting.
Co-PI and Other Key Personnel: If the primary PI is a junior investigator the co-PI should be a senior faculty member and primary investigator in an NIH-funded laboratory (or national equivalent funding agency for international applicants). **If PI and junior co-PI are not full-time fibrosis researchers, the team must include an additional co-PI who is a scientist with proven record of a career devoted to fibrosis research in IBD or another therapeutic area.**
Abstract (3000 characters limit): Briefly describe the main goal or the problem that the study will address, state hypothesis, specific aims, research approach (including preliminary data), types of samples and/or the model methods that will be used, expected outcomes and the translational potential of the study. Please clearly state how the proposed study aligns with the scope of the Fibrosis in IBD RFP.
Scientific rationale and research plan: This section should provide a clear concise overview of the proposed work **(3 years plan with clearly defined 18 months milestones and 36 months milestones)**, including the background, objectives, hypothesis, and supporting rationale, specific aims, and proposed methodology. Space limit 3 pages (12,000 characters).
Research team (1000 characters limit): Briefly describe your team and explain how the PI’s and the co-PI’s expertise will contribute to the successful performance of the proposed work. Explain which team members meet the criteria in the RFP (e.g. junior Co-PI, established fibrosis researcher, etc.)
PDF Attachments:

a. NIH Biosketches for key personnel (required)
b. References cited in application (required)
c. Publications (optional)
d. Other Supplemental Information (optional)

Selection criteria

Reviewers of LOIs are asked to comment on the following selection criteria:

a. Alignment of the proposed study to the scope of the Fibrosis in IBD RFP and with the 2019 *Challenges in IBD Research* publication
b. Scientific strength of research proposal, rationale, specific aims and methodology
c. Study approach: integrating patient-based retrospective or prospective studies and preclinical studies using humanized models (*in vitro and/or in vivo and /or ex vivo)*
d. Strength of the scientific team, research environment and resources
e. Translational potential of the study to impact the quality of life of IBD patients

APPENDIX B: Full Application Submission Guidelines

General information

Applicants will be notified on June 2, 2023, if their proposal will be considered for full application. The full application is due on **July 24, 2023.**

The application should be submitted to proposalCENTRAL at: https://proposalcentral.altum.com

Paper copies of the application are not accepted.

f. If you are a first-time user, register by clicking on "First time user." This will generate a confirmation number, which will be emailed to the email connected to this account. Confirm your registration by submitting this number when prompted.
g. Once you are a registered user, please click on "Grant opportunities" on the far right of the page and select Crohn's & Colitis Foundation under "Filter by Grant Maker" drop down menu on the upper left of the page.
h. Locate the "Fibrosis in IBD" announcement and click "Apply now".
i. To activate the navigation bar on the left, enter the title of your proposal on the title page and "save" the application. The navigation bar on the left will now become interactive for you to continue your application.
j. Once completed, please validate and submit the application.

The Full Application form will include the following fields:

Title Page: Enter your title and "save" the application

Templates and Instructions: PI Biosketch and a New Vendor Form are available for download.

New Vendor Form *Required (part of Attachments section): Complete this form to authorize your institution to receive payment from the Foundation. This document contains instructions on how payment will be transferred to your institution and should not include information on the Investigator. This is required even if institution has received Foundation funding in the past.

Enable other Users to Access the Proposal: Add personnel that can have access to review and edit the proposal.

Applicant /PI: Principal Investigator (PI) is defined as the one person responsible to report to the Foundation for scientific and technical direction of the project. Although Co-PI is required, only one person can be indicated as the main point of contact. Note: If the research (entirely or partially) is to be conducted in the Co-PI's laboratory, a subcontract budget needs to be proposed.

Institution and Contacts: Provide contact information of the signing staff officials at the institution where the lead PI is located and where the study will take place.

Co-PI(s), Collaborator and Key Personnel: Add the roles and the contact information for Co-Principal Investigator (Co-PI) and key personnel whom you would like to include in this application. Effort: Percentage Estimation of Amount of Time Allocated to this Project: Describe how the time (in percentages of full-time effort) is allocated in your current position at this institution.

Summary

Lay Summary

The Foundation has instituted a Stakeholder Reviewer Program, in which selected lay patients or caregivers participate as voting members of the various review committees. The Lay Summary should provide a clear, concise overview, in a lay language, of the proposed work, including the main goal(s) or the central hypothesis of the study, the aims, the relevance to IBD and the alignment of the study with Challenges in IBD; In addition, please provide a brief impact statement describing the potential of the study to impact IBD research and/or healthcare; explain how the results of the study will potentially provide a novel solution or improve the current practices in IBD healthcare and disease management. Also include a brief glossary of any scientific terms included in your lay summary.

Please note that a lay summary that is not clearly written using lay language could affect the score provided by the Stakeholder Reviewer.

Scientific Summary of the Project

The Scientific Summary should provide a clear, concise overview of the proposed work, including the background, objective(s), specific aims, research approach (including preliminary studies, if available, types of samples and/or the model methods that will be used), expected outcomes and the translational potential of the study. Please include references and upload a Cited References document as an attachment.

Relevance to IBD:

Re-state, what population of IBD patients the study will potently benefit (Crohn's disease/ Ulcerative colitis). Explain the relevance of the main objective of the study for the IBD field. Explain how the proposed study is aligned with the scope of this RFP.

Budget Period Detail

Start and End Dates

Specify the date on which you expect to start this project. Enter dates for 3 years in 1-year increments.

Complete the e-form total budget.

The budget requested per year may not exceed $300,000 inclusive of 10% indirect cost (Direct costs: $272,727; indirect costs: $27,273).

Budget Summary Detail: The total budget request for year 1 must not exceed $300,000 inclusive of 10% indirect cost. Salaries are capped at NIH limits. The total budget for 1.5 year is $450,000 inclusive of 10% indirect costs (Direct costs: $409,091; indirect costs: $40,909). Justification of the budget for the 1.5 year period must be provided.

Current and Pending Financial Support: Please provide information on additional ongoing funding that currently supports this research project.

Organization Assurance: Human/Animal Studies Approval/Recombinant DNA

All activities involving human subjects or vertebrate animals must be approved by an appropriate institutional review board (IRB/IACUC) or equivalent prior to the start date of award. Indicate with "Yes" or "No" response, and if yes indicate date of approval and attach approval in that Attachments Section.

Copies of the IRB approval should be provided to the Foundation's Research Department. If approval is not available at the time of application, provide a date of anticipated approval. **This approval must be received before the start date of the approved grant.**

Human and/or Animal Approvals: Upload IRB/IACUC approvals for human and animal research

Upload Attachments:

- **Cover page**
  Describe background and expertise of the PI, Co-PI and the relevant investigators, and the role/ tasks to be performed by each investigator
- **Research Plan/Protocol**
  The description of the proposed research project must include the following items in sufficient detail to permit evaluation of the scientific merit of the study. This cannot exceed 10 pages, single spaced. The page limits distribution indicated below are included as a guideline and not required.
    - Overall Objectives and specific aims (no more than 1 page)
        - Briefly outline the general scientific objectives
        - Describe concisely and realistically what the specific research described in this application is intended to accomplish. Specifically outline Aims for 1.5 year, 6-month-interval milestones and timelines. State any hypotheses to be tested.
    - Background -including preliminary data (no more than 3 pages)
        - Outline the previous work in the area by others, and the preliminary data or previous studies by the investigator(s). Enough preliminary data should be included in the application to demonstrate that the project is feasible, and that the investigator is likely to complete the project successfully in the duration of the grant. Provide evidence that supports clinically relevant observations made in patients
    - Detailed description of methods and materials to be used (no more than 5 pages)
        - Provide a detailed discussion of the experimental design, procedures, and materials to be used to accomplish the Specific Aims.
        - Describe protocols, including methods for new techniques, and explain the advantages over existing methodologies.
        - Discuss the kinds of data expected to be obtained and the means by which data will be analyzed and interpreted.
        - Justify the use of any animal models (i.e., choice of species, number used, etc.).
        - Discuss potential difficulties and/or limitations of the proposed procedures and alternative approaches to achieve aims.

- Significance and relevance of the proposed research to Crohn's disease and/or ulcerative colitis and to the Fibrosis in IBD RFP (no more than 1 page).
  - Justify the significance of the results of this project to the understanding of the etiology, pathogenesis, therapy, and prevention of fibrosis in IBD. Specifically identify the gaps this project is intended to fill related to the Fibrosis in IBD RFP.
- Facilities Available to carry out the Proposed Studies (one or two paragraphs)
  - Describe the facilities available, including square footage, equipment, animal care facilities, and other environmental factors. Pay particular attention to those items required for successful completion of this proposal. Include a description for each facility to be involved.
- References (no more than 2 pages)
  - Literature citations should be listed in this section, at the end of the Research Plan. ***These are not counted as part of the 10-page limit.

- **Biosketches for Key Personnel**
  - Biosketch (NIH format) for PI, Co-PI, and fibrosis research expert (required), and additional key personnel (optional).
- **Letters of Collaboration**
  - Attach supporting letter(s)
- **References/ Appendices (optional)**
  - Uploaded reference material may include, but not limited to:
    a. Article references
    b. Abstracts
    c. Original Pictures
    d. Other Letters of Support

- **Signed Signature Pages**
  This document is generated by the PDFs and Signature Pages module after submitting all the forms and uploading all the required documents. Module PDFs and Signature Pages are located on the navigation bar on the left-hand side.
- **Timeline and Milestones**
  Timeline for completion of project (Gantt chart or similar format): List of milestones projected for every six months of the project period.

Validate: Click *Validate* to check for any missing REQUIRED information or files. All missing required information will be listed on the screen.

PDFs and Signature Pages

Click *Print Signature Pages* to be signed by the applicant and the organization officials. Upload the signed document on the Upload Attachments module.
Click *Print Signature Pages and Attached PFD Files* if you would like to save the full application for your records. Do not upload the full application with the signed signature pages in Upload Attachment module.

Submit

Only the primary PI is authorized to submit the application.

APPENDIX C: IP policy

All inventions or intellectual property ("Property") that results from research supported, in whole or in part, by grant awards from the Foundation must be reported in writing at the earliest possible time to Foundation. The grantee institution agrees to notify the Foundation within a reasonable time, preferably within 30 days, of receiving an invention disclosure or other notice indicating existence of a Property and to notify the Foundation immediately of the decision to apply for letters of patent or other legal protection for the Property. The Foundation agrees to keep all information confidential and not to release any information relating to such inventions, intellectual property or applications for protection to any third party, except as specifically set forth below or upon written agreement with the grantee institution, which consent cannot be unreasonably withheld. All patenting expenses or intellectual property application expenses shall be borne by the grantee institution.

Title to all Property shall reside with the grantee institution to the extent that such title is claimed by the institution under its institutional patent policy or procedure. If a grantee institution has no established institutional patent policy or procedure for administering inventions or intellectual property, or if the institutional patent policy or procedure does not claim rights for the institution or individual inventor, then Foundation shall have the right to determine the disposition of the Property rights in accordance with the provisions set forth below.

Distribution of income derived from any Property, which might include equity disposition, shall be shared by the grantee institution and the Foundation on mutually agreeable terms, such terms to be determined as soon as practicable, preferably prior to any licensing or commercial exploitation of the Property, and in any event no later than six months after first receipt of income. Such distribution shall be guided by the principle that the Foundation's proportion of the income shall be reasonably related to the Foundation's proportion of support for the research leading to the Property. The grantee institution agrees to notify the Foundation within a reasonable time of beginning negotiations with potential licensees and to notify the Foundation upon execution of any license or other agreement to commercialize the Property. The grantee institution will provide a copy of the license or other agreement, or an excerpt of the financial terms relevant to the Foundation's right to income from the Property together with the name of the licensee, the subject matter of the license and any other terms relevant to the foundation, including without limitation whether such license is exclusive or nonexclusive.

If any Property is made with or results from the joint support of the foundation and another organization, that organization, the grantee institution, and the Foundation will confer, in good faith, to arrive at a mutually satisfactory disposition of the Property rights guided by the principle that distributions of income be made in proportion to each party's contribution of support for the research leading to the Property.

No patent, patent application or other type of protection for a Property shall be abandoned without first notifying the Foundation and giving the Foundation a reasonable opportunity to take title to the Property.

If grantee institution does not effectuate a license to Property within four (4) years from the date that such Property is disclosed in writing through an invention disclosure or similar form to the grantee institution by the principal investigator, then the Foundation shall have the right to

introduce to the grantee institution one or more bona fide potential licensees and the grantee institution shall enter into good faith negotiations for license of the Property with such potential licensee(s). Upon consummation of any such license, the Foundation's introduction of the licensee to the grantee institution shall be counted to the benefit of the Foundation in calculating its share of any income from the Property.

The grantee institution agrees that when it licenses a Property, it will use reasonable efforts to obligate the licensee to exert its best efforts to commercialize or cause to be commercialized the Property as rapidly as practical, consistent with sound and reasonable business practices and judgment, and reserve the right to terminate the license upon a failure by licensee to do so. If the grantee institution relicenses any Property, the Foundation shall be entitled to a share of any relicensed Property income according to the principles set forth above.

The Foundation reserves the right to public acknowledgment for Property resulting from research supported by the Foundation. However, the Foundation's name and logo may not be used in association with any Property without the prior written approval of the Foundation.

The Foundation shall have use of the Property without payment of royalties or license fees solely for the use by the Foundation for its own intramural or public education purposes, but not for any of its grantee institutions.

Awardees and grantee institutions are responsible for ensuring that there are no inconsistencies in their consulting or business agreements that conflict with this policy

APPENDIX D: Summary of Key Terms

The Foundation and Takeda have entered into an Alliance Agreement dated October 6, 2022 governing a Program with the overarching aim of advancing science in the field of fibrosis as they relate to inflammatory bowel diseases. Any Projects conducted under the Program (and their associated Project Funding Agreements) will be consistent with the provisions of the Alliance Agreement, a partial summary of which is included below. All capitalized but undefined terms have the meanings established in the Alliance Agreement.

1. Foundation and the Grantee may disclose Confidential Information of the other party to Takeda for use in connection with the Project. Foundation shall include in each Project Funding Agreement confidentiality and non-use obligations with respect to Takeda's Confidential Information that are no less restrictive than the confidentiality and non-use provisions of the Alliance Agreement.
2. Any Project may be extended (or otherwise amended) only with the written consent of the Grantee, Foundation, and Takeda.
3. Takeda may assume Foundation's rights and obligations under the Project Funding Agreement if Grantee terminates or intends to terminate such Project Funding Agreement as to Foundation, and Foundation will notify Takeda of such termination upon receipt of a termination notice from the Grantee.

4. Takeda may, following Foundation's termination of the Alliance Agreement, enter into an agreement with the Grantee on the same terms and conditions as the applicable Project Funding Agreement, mutatis mutandis, pursuant to which Takeda would assume all rights and obligations of Foundation with respect to any Project.
5. Foundation may assign its rights and obligations under the Project Funding Agreement to Takeda.
6. Takeda will be expressly identified as a third-party beneficiary under each Project Funding Agreement.
7. Grantee will expressly acknowledge and agree to comply with the Alliance Agreement.
8. Grantee will acknowledge Takeda's rights to exercise the Option to negotiate with Grantee towards a License Agreement containing an exclusive license to any Project IP generated by Grantee in connection with the Project, as well as a license to any Blocking Grantee IP (to the extent any such Blocking Grantee IP is necessary or reasonably useful for Takeda's practice of the Project IP, and to the extent any such Blocking Grantee IP exists).
9. If Grantee and Takeda do not enter into a License Agreement, Takeda will have a non-exclusive, perpetual, royalty free, fully paid, sublicensable license to exploit the Project IP for research purposes only.
10. If Takeda exercises its Option, but Takeda and the Grantee fail to execute a License Agreement within the Negotiation Period, then for a period of time beginning on the expiration of the Negotiation Period and ending on the first (1st) anniversary of that expiration, Grantee(s) may not sell, license, or enter into any transaction with any third party for Project IP on terms more favorable (when taken as a whole) to that third party than the terms offered to Takeda, without first offering those third-party terms to Takeda.
11. Grantee may publish the results of the Project, subject to Takeda's right to review for its Confidential Information and patentable information. If Takeda requests the removal of its Confidential Information, Grantee will remove that Confidential Information before publication or disclosure. If Takeda requests a delay in the publication or disclosure to seek patent protection for Inventions, Grantee will so delay the publication or disclosure.
12. Grantee will not engage in any Publicity about the Program or Project without Takeda's prior written approval.
13. Grantee will not have the right to terminate a Project Funding Agreement or a particular Project for any reason other than the material breach of such Project Funding Agreement by Foundation or Foundation's insolvency.
14. Project Funding Agreements will include other terms and conditions as are necessary to enable Foundation to comply with this Agreement.