IOVERA° USE PECTUS EXCAVATUM CORRECTION
REQUEST FOR PROPOSAL

BACKGROUND

Pacira BioSciences, Inc. is committed to supporting independent research initiatives that foster the advancement of scientific and clinical information and improve patient care. To that end, Pacira extends a new grant opportunity by way of a request for proposal (RFP) focused on research trials that seek to result in optimized patient care. These research trials will provide valued information on the efficacy of the company's marketed products.

All proposals are reviewed for scientific merit, innovation, clinical impact on patients, and compliance with Pacira policy and requirements. If you are interested in applying for support of a research proposal, please review the submission process and apply online by clicking here. Pacira will review and consider all relevant research proposals but is not obligated to provide support for any research proposals received.

While the Pacira Grant Review Committee (PGRC) reviews all research proposals, the principal investigator (and ultimately the grantee) is responsible for the design, implementation, and conduct of the independent initiative supported by the grant. Pacira will not be involved in the conduct or monitoring of the proposed trial, including drafting the research study protocol.

PURPOSE AND INTENT

Pacira BioSciences, Inc. issues this RFP for a prospective clinical research study evaluating the iovera° system to treat pain associated with pectus excavatum correction procedures. This RFP is funded through the investigator initiated trial (IIT) grant program at Pacira. Funding is available for the fiscal year 2020 and may be extended at the company's discretion.

ELIGIBILITY

To be eligible for consideration, the requestor must be an independent third party. Examples of appropriate requestors include, but are not limited to:

- Academic medical centers
- Healthcare institutions, including private practice settings and ambulatory care facilities

Note: If the research involves multiple departments within an institution and/or between different institutions/organizations/associations, please note each institution's role in the grant application.

TARGET AUDIENCE

Health care professionals involved in the care of patients requiring procedures for pectus excavatum correction.

TIMELINE

The RFP application will remain open until the grant has been awarded.

Note: The PGRC may award multiple awards at its discretion.

BURDEN

Epidemiology of pectus excavatum
Pectus excavatum or funnel chest is a structural chest wall deformity characterized by a depression of the anterior chest wall; the condition represents 90% of all chest wall deformities (1). While there is some disagreement as to the etiology, the disorder may arise from an uneven growth of the rib cage (2). In severe cases, thoracic organ displacement and spinal deformities may result in difficulty breathing, chest pain, palpitations, arrhythmia, fatigue, and dizziness (2).

Globally, the prevalence of pectus excavatum ranges from 6.28 to 12 cases per 1000 with most diagnoses made within the first year of life (1, 3).

Economic impact of pectus excavatum
Pectus excavatum is reported to be the most common of the chest wall deformities and surgical repair is a common treatment method in severe cases (1, 3). In a query of The Healthcare Cost and Utilization Project Kids' Inpatient Database the average length of stay for patients undergoing pectus excavatum repair was over 4 days and postsurgical pain was the second most common surgical complication (4). Overall, the average hospital charges for a patient undergoing pectus excavatum surgery is $41,015.58 (4).

Postoperative pain management for pectus excavatum correction
Current surgical treatment options for severe pectus excavatum include both open repair (ie, Ravitch procedure), and minimally invasive repair (ie, Nuss procedure). Intraoperative cryoanalgesia for postsurgical pain management (3, 5). The procedures result in a significant amount of acute and chronic postoperative pain (5-7). Postoperative pain management primarily utilizes opioids and typically includes include thoracic epidurals, paravertebral regional blocks, intercostal blocks, intercostal infusion catheters, muscle relaxants, and multimodal analgesics, however an optimal regimen has not yet been established. Despite the use of multimodal strategies, opioid related side effects such as nausea and constipation due to the use of around-the-clock opioids (8-13).

Cryoanalgesia of the intercostal nerves for post-thoracotomy pain has been shown to improve postoperative pain control, as well as decrease postoperative opioid usage and improve pulmonary function. (14-27). More recently, cryoanalgesia has been applied to treat pain

following pectus excavatum repair. Studies have shown long-lasting pain control with reduced opioid consumption, reduced hospital stay compared to thoracic epidural. (28,29).

SCOPE OF WORK

The successful applicant will prepare a research proposal for a feasibility study that adequately addresses the postsurgical pain management of pectus excavatum with cryoanalgesia using the iovera° system.

The study proposal should focus on patients undergoing pectus excavatum correction. The study will be a case series evaluating patients before and after percutaneous cryoanalgesia treatment for up to six months with a 3-month enrollment period. Outcomes may include pain (eg, NRS, VAS), length of hospital stay, opioid consumption, physical functional outcomes (eg, voluntary ventilation, exercise tolerance, exercise induced dyspnea), and patient reported outcomes (eg, quality of life).

Grant recipients will receive training on the use of the iovera° system and agree to provide data to Pacira at the time of study completion.

The Pacira Grant Review Committee will consider funding awards inclusive of indirect costs for the conduct of the study based on a budget within fair market value.

PROPOSAL SUBMISSION REQUIREMENTS

All requestors must submit a written proposal that addresses the following topics and includes required supporting documentation including:

- Organization's contact information
- Primary contact name, title, address, phone, and email
- Describe the organization's current activities relevant to the proposal including current standard of care and patient volume
- Project description and specific proposal objectives
- Available data/information relevant to proposal submission (eg, pilot data)
- Describe how the proposal will improve patient care in alignment with grant objectives
- Proposed timeline for completion with associated deliverables. If possible, attach a flow chart outlining the operational steps of the proposed program.
- Proposed budget that is within fair market value and reflects the scope of responsibilities to accomplish the goals of this project. No funding match is required; however, requestors will need to identify any other sources of funding, both in-kind and monetary, that will be used.

To apply for a grant, please click here.

A letter of intent on organizational letterhead should be included. The letter of intent should be single-spaced and not exceed four pages (not including the reference page).

The RFP process

Pacira maintains a stepwise process for review of RFPs. In brief, after registering on the online grant portal, the principal investigator submits a brief concept proposal and if accepted after a review by the PGRC, will be invited to submit a full proposal. Details on brief and full proposal contents are below.

Brief concept proposal:

A brief concept proposal must contain an adequate amount of information for the PGRC to determine interest in requesting a full study proposal. When submitting a brief concept proposal, the following information will be requested (if applicable):

- Principal investigator contact information
- Brief background for the study
- Method of administration of the marketed product
- Primary study objectives/endpoints
- Estimated study timelines
- Estimated total study budget
- Estimated study drug or device(s)
- Preliminary grant request: funding, drug, device, or a combination thereof
- Experience as sponsor-investigator
- Letter of intent on the requesting institution's letterhead
- Curriculum vitae from the principal investigator dated within the last calendar year

The PGRC will review all concept proposals for scientific merit, innovation, clinical importance/potential impact on patients, and compliance with company policy and requirements. The PGRC will extend contingent approval to individual applicants to proceed to the second step of the process, which is the submission of a full study proposal. Applicants will be notified of the PGRC's decision via email, and the status will also be available on the portal. Please note that an invitation to submit a full study proposal does not guarantee the approval of funding.

Full study proposal:

A full study proposal submission must contain enough detail about the research study to enable the PGRC to make an evaluation on support. When submitting a full study proposal, the following information will be requested (if applicable):

- Principal investigator contact information
- Study type: non-clinical or clinical
- Objectives: primary and secondary
- Key inclusion and exclusion criteria
- Study design
- Efficacy variables/measures
- Safety variables/measures
- Adverse event/Serious adverse event reporting
- Decision points/statistical methods/interim analysis

- Study product regimens
- Ethical rationale for the study
- Study deliverables
- Value of the study
- Applicable scientific references
- Publication plan
- Research Setting: single-site or multi-site
- Detailed budget
- Grant request: funding, product, or a combination thereof

Pacira reserves the right to reconsider its support if the research objectives outlined in the final protocol are materially different from the approved full study proposal. Pacira will not compensate for any work performed before the execution of a final contract or for impermissible costs, which include:

- Construction funds to build new facilities
- General education and training activities
- Hiring of staff that are not dedicated to the proposed research study
- Study to involve new investigational products or devices
- Studies that are designed to generate business for Pacira
- Purchase of capital equipment unrelated to the study or that would generate revenue
- Requests for support for ongoing or new research without an associated research study protocol
- Start-up funds to establish new clinical or research programs or to expand existing programs
- Support for ongoing clinical programs that are part of an organization's routine operations

PACIRA BIOSCIENCES, INC. CONTACT INFORMATION

If you have questions regarding this RFP, please email grants@pacira.com and include in the subject line *pectus excavatum RFP*.

CONFIDENTIALITY

This Request for Proposal constitutes the confidential and proprietary information of Pacira BioSciences, Inc. and may not, in whole or in part, be copied, reproduced, or otherwise used in any manner whatsoever without the prior express written permission of Pacira BioSciences, Inc. All information provided herein is proprietary to Pacira BioSciences, Inc. and is to be used only by your company in its response hereto. Any other use or communication of this information is prohibited.

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