EXPAREL USE IN HIP FRACTURE REPAIR

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 safety, efficacy, pharmacology, and tolerability 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 EXPAREL (bupivacaine liposome injectable suspension) use in hip fracture repair. 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 with hip fracture.

TIMELINE

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

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

BURDEN

Hip fracture epidemiology

Hip fractures are prevalent among certain groups (eg, the elderly) in the US and can lead to disability. A recent study evaluating data from the Health and Retirement Study found that among ten health conditions, hip fractures accounted for 17,660 disability-adjusted life years (DALYs) (1). While the risk of fracture differs across countries, regions, and race, the estimated lifetime risk of a hip fracture is 15.6-17.5% in white women, 5.2-6.0% in white men, 5.6% for black women and 2.8% for black men greater than 50 years (2, 3).

Hip fractures are often age-dependent with risk factors including decreased bone mineral density, fall, nutrition, chronic medication use, cigarette smoking, lack of physical activity, low body weight and fractures are classified by the anatomical location of the fracture relative to the hip capsule and level of displacement. Hip fractures are characterized as intracapsular (ie, at the femoral neck), extracapsular (ie, intertrochanteric or subtrochanteric), displaced (ie, significant separation at the site of the fracture), and nondisplaced (ie, little separation at the site of the fracture) (4). Femoral neck fractures are further classified as types I-IV based on the level of displacement and impaction (4).

In 2002, the overall hip fracture incidence (95% confidence interval (CI)) was 931 (912, 950) per 100,000 and 730 (712, 748) per 100,000 in 2015 (5).While the incidence of fractures is decreasing because of drug and non-drug interventions, a societal burden still remains.

Economic impact of hip fractures

In a study using published cost data, the authors reported the lifetime attributable cost of hip fractures in 1997 was estimated at $81,300 of which 11% are attributed to hospitalization costs (6). A retrospective database analysis of the 2014 Medicare database found an overall annual economic burden of $2.63 billion to the U.S. healthcare system (7).

Hip fracture management

A recent meta-analysis found that patients who underwent surgery within 48 hours had a 20% lower risk of mortality (risk ratio (RR) 0.80, 95% confidence interval (CI) 0.66–0.97) and 18% lower in patients who underwent surgical intervention within 24 hours (RR 0.82, 95% CI 0.67-1.01) (8). However, some suggest that reducing the time from admission to surgery to 6 hours is associated with fewer complications (9). While there is no agreed upon standard for managing pain

after surgery, an evidence review conducted for the Agency for Healthcare Research and Quality (AHRQ) safety program recommends regional analgesic techniques (eg, femoral nerve/fascia iliaca blocks) for the management of postsurgical pain (10). Consequently, innovative postsurgical pain management solutions are required.

Effective postsurgical pain control is a critical element in patient recovery following surgery, as the majority of patients may experience significant pain, particularly in the first few days. Improved postsurgical pain management contributes to better healing, faster patient mobilization, shortened hospital stays, and reduced healthcare costs (11).

SCOPE OF WORK

The successful applicant will prepare a research proposal that adequately addresses postsurgical pain associated with hip fracture repair.

The study proposal should include a focus on adults undergoing hip fracture repair and may include pain (eg, visual analog scale (VAS) or numeric rating scale (NRS)), functional outcomes (eg Timed Up and Go Test), total opioid consumption, length of hospital stay, discharge readiness, hospital discharge disposition, patient reported outcomes (eg, Barthel Index) and adverse events.

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 primary mission and/or current activities relevant to the proposal
- 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 *hip fracture 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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