LIPOSOMAL BUPIVACAINE USE IN STELLATE GANGLION BLOCKS
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 issues this RFP for a prospective clinical research study evaluating liposomal bupivacaine stellate ganglion block for clinical conditions including cardiac syndromes/procedures, complex regional pain syndrome, and Raynaud's syndrome. This RFP is funded through the investigator-initiated trial (IIT) grant program at Pacira. Funding is available for the fiscal year 2022 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 a stellate ganglion block.

TIMELINE

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

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

STELLATE GANGLION BLOCKS

The stellate ganglion

The stellate ganglion is formed by a group of sympathetic nerves located at the level of the seventh cervical vertebrae. The ganglia innervates to the head, neck, upper extremity, and a portion of the upper thorax (including the myocardium). The somatic branches of the stellate ganglion provide sympathetic fibers to the anterior rami of the C7, C8, and T1 while the visceral branchers contribute to the cardiac plexus.

Use of liposomal bupivacaine in stellate ganglion blocks

The literature contains few reports of liposomal bupivacaine stellate ganglion blocks (SGB) (1, 2). However, evidence suggests that the use of SGB blocks with liposomal bupivacaine is worth further exploration. In a case report, a patient with ventricular fibrillation arrest was treated with 5mL of 0.5% bupivacaine and 5 mL of liposomal bupivacaine (1.3%). The patient experienced no resulting episodes of ventricular fibrillation or ventricular tachycardia in the four days following the SGB (3).

Other published case reports include the use of liposomal bupivacaine SGB for headache after right internal carotid artery dissection and complex regional pain syndrome (CRPS). A case report from Qureshi et al. described a patient with recurrent headaches due to internal carotid artery dissection who was treated with a mixture of 4 mL (53.2mg) of liposomal bupivacaine and 16 mL preservative-free normal (0.9%) saline. Following the second block, the patient was pain free until Day 15 with return to peak pain intensity at Day 17, which was three folds longer duration than SGB with bupivacaine hydrochloride. Due to the success of the block a repeat block at a higher dosage of 8 mL (106.4 mg) of liposomal bupivacaine and 12 mL of preservative-free normal (0.9%) saline was performed. Following this block, the patient was pain free for 27 days with return to peak pain intensity by Day 28, which was more than 6 folds longer than with bupivacaine hydrochloride (1).

A case report detailed the experience of a patient diagnosed with CRPS type I of the arm. The patient initially received several SGB blocks with bupivacaine hydrochloride with or without lidocaine; symptom relief was approximately 7 days. The first liposomal bupivacaine SGB trial consisted of a 1 mL dose that resulted in 3 weeks of pain relief (at least 50% pain reduction) and increased function. Subsequently, the patient received repeated SGBs 3-5 weeks apart with 2.0-2.5 mL liposomal bupivacaine. Each liposomal bupivacaine SGB block provided 18-21 days of pain relief compared to 5-7 days of pain relief with bupivacaine hydrochloride (2).

SCOPE OF WORK

The successful applicant will prepare a research proposal for a feasibility study that adequately addresses the use of SGBs in cardiac syndromes/procedures, complex regional pain syndrome, or Raynaud's disease.

The study proposal should focus on patients with cardiac syndromes/procedures, complex regional pain syndrome, or Raynaud's disease who are scheduled to undergo a stellate ganglion block. The study will be a case series evaluating patients before and after SGBs for up to six months with a 3-month enrollment period. Outcomes may include pain (eg, NRS, VAS), number and severity of episodes, symptom abatement, physical function, and quality of life.

Grant recipients will 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 CONTACT INFORMATION

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

CONFIDENTIALITY

This Request for Proposal constitutes the confidential and proprietary information of Pacira BioSciences, Inc., and its respective subsidiaries 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. All information provided herein is proprietary to Pacira and is to be used only by your company in its response hereto. Any other use or communication of this information is prohibited.

REFERENCES

1. Qureshi AI, Waqas MA, Jadhav V, Saleem MA, Campbell J, Wallery SS. Long Acting Liposomal Bupivacaine for Percutaneous Sympathetic Stellate Ganglion Blockade: A Technical Note. Journal of vascular and interventional neurology. 2017;9(5):49-53.
2. Ferrillo MG. Treatment of complex regional pain syndrome with stellate ganglion local anesthetic blockade: A case report of one patient's experiences with traditional bupivacaine HCl and liposome bupivacaine. Clinical Case Reports. 2016;4(9):861-5.
3. Hutchins J, Aakre G, Habeck J, Berg A. Ultrasound-guided stellate ganglion block with liposome bupivacaine for malignant ventricular arrhythmia: A case report. Regional anesthesia and pain medicine. 2018;43(7):e68.