IOVERA° USE IN POSTHERPETIC NEURALGIA
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 in the treatment of pain due to postherpetic neuralgia. 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 postherpetic neuralgia.

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 postherpetic neuralgia
Postherpetic neuralgia is a frequent complication of herpes zoster. Herpes zoster or "shingles" is the reactivation of the varicella zoster virus that generally remains dormant in the nerve root. This condition is characterized by persistent pain (ie, 90 days) after the onset of rash (1, 2). The rash and subsequent pain follows a defined dermatome, most often in the trunk, but can also travel along the trigeminal nerve affecting the eye (2).The associated pain frequently results in sleep disturbance, interference with activities of daily living, depression, chronic fatigue, and weight loss (1).

The total number of herpes zoster cases in the U.S. is estimated at one million with approximately 43,000 progressing to postherpetic neuralgia (3). Globally the incidence of herpes zoster is between 3 and 5/1000 person-years with the risk of developing postherpetic neuralgia at 5-30%, where both rates increasing with age (4).

Economic impact of postherpetic neuralgia
The economic impact of herpetic neuralgia and its complications are significant with total costs estimated to exceed $2.4 billion and 67,000 quality-adjusted life years (QALYs) lost (3). Productivity loss (ie, absenteeism and presenteeism) in herpes zoster and postherpetic neuralgia can be significant. For example, in a trial assessing productivity losses in workers with herpes zoster and postherpetic neuralgia, authors reported an average of 27 hours of absenteeism and 34 hours of presenteeism (5).

Postherpetic neuralgia treatment
Current treatment of postherpetic neuralgia includes anticonvulsants, tricyclic antidepressants, topical lidocaine patches, opioids, steroids, and cryoanalgesia (1, 6). While there is a scarcity of evidence for cryoanalgesia for postherpetic neuralgia the reported outcomes are worth exploring further. For example, a retrospective study evaluating cryoanalgesia for postherpetic thoracic pain reported 50% pain relief at 3-months (7).
Cryoanalgesia has also been applied in a number of pain disorders including occipital and trigeminal neuralgia. Kim et al. (2015) reported outcomes of 38 patients who received local anesthetics in addition to cryoanalgesia to the occipital nerve (ON) to treat occipital neuralgia who experienced ≥50% benefit following local anesthetic injections (8). The average improvement of pain relief with cryoanalgesia was 57.9% with an average duration of 6.1 months.

Stogicza et al (2019) reported on the safety of an ultrasound-guided technique to target the greater ON with cryoanalgesia (9). The authors had performed this procedure on more than 50 patients in their clinic and reported no major complications and rare minor complications (post-procedure soreness), which resolved spontaneously in 1 to 3 weeks (9).

Nally et al (1984) reported outcomes of 211 patients with paroxysmal trigeminal neuralgia (10). The report included 42 patients who were treated with open nerve cryoanalgesia and followed for 3 years. This cohort showed no return of pain in the distribution of the 54 (out of 55) nerves treated with cryoanalgesia. In 16 patients, the pain migrated from its original source 3 to 9 months after the initial treatment (10).

SCOPE OF WORK

The successful applicant will prepare a research proposal for a feasibility study that adequately addresses the management of pain due to postherpetic neuralgia with cryoanalgesia using the iovera° system.

The study proposal should focus on patients with postherpetic neuralgia who have failed conservative therapies. The study will be a case series evaluating patients before and after cryoanalgesia treatment for up to six months with a 3-month enrollment period. Outcomes may include pain (eg, NRS, VAS), pain interference (eg, Brief Pain Inventory (BPI), Zoster Brief Pain Inventory (ZBPI)), sleep interference (eg, The Medical Outcomes Study Sleep Scale (MOS-Sleep), The Pittsburgh Sleep Quality Index (PSQI)), and adverse events.

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 *postherpetic neuralgia RFP*.

CONFIDENTIALITY

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