IOVERA° USE IN MUSCLE SPASTICITY
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 for treatment of pain in patients with muscle spasticity (ie, upper limb spasticity and cervical dystonia). 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 muscle spasticity.

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 muscle spasticity
Spasticity is a motor disorder characterized by increased muscle tone and deep tendon reflexes (1). Spasticity is present in many neurological conditions, including cerebral palsy, brain injury, multiple sclerosis, stroke, spinal cord injury, and rare conditions like tropical and hereditary spastic paraparesis (2). Spasticity can affect any muscles, including upper and lower limbs, as well as the neck in a severe condition causing prolonged contraction of the neck muscles. The condition is referred to as cervical dystonia or spasmodic torticollis. Spasticity in any area can lead to significant bone and joint deformities and subsequent disability.

The incidence and prevalence of muscle spasticity vary depending on the region of the body and etiology. For example, the prevalence of spasticity after the first episode of stroke was reported to be between 17-25% in an observational study where spasticity was more severe in the upper limbs (4, 5). Cervical dystonia is thought to affect between 57 and 280 people per million (6).

Economic impact of muscle spasticity
While the economic impact of muscle spasticity differs based on the severity of contracture, the individual and societal costs can be substantial. A study published in 2001 evaluating the overall individual costs of managing focal spasticity after stroke and traumatic brain injury (TBI) found that the mean per-case costs for upper limb muscle spasticity following a stroke was $5,131 (range: $1,314-$15,776) and $14,615 (range: $1,799-$58,002) following a TBI (7).

Muscle spasticity is not only painful but can also be debilitating, affecting activities of daily living and mood. Consequently, many with muscle spasticity will require continued support and physical assistance. A study found that employed caregivers spent an average of 27.4 hours of a normal work week caring for a stroke survivor. Furthermore, the mean number of hours spent per week caring for the stroke survivor with mild, moderate, and severe disability was 19.0, 38.0, and 49.0 hours, respectively. The study also reported a mean absenteeism rate of 9% and presenteeism rate of 27%, and an overall caregiving-related work restriction of 32%. The mean number of lost work hours [per week] was 8.8 hours leading to opportunity costs of $5,669 per caregiver per year and total lost productivity costs of greater than $10,000 per employed caregiver (8).

Muscle spasticity treatment

Current treatment options for spasticity include intrathecal baclofen, local injections of phenol, alcohol, or botulinum toxin, oral medications, surgery, and cryoanalgesia, (9-13). Non-invasive treatment options might also include daily exercise and muscle stretching, bracing/orthoses, casting, or splinting. A case report and proof of concept study evaluating cryoanalgesia in lower and upper limb spasticity have shown some promise with patients reporting improved pain and function (9, 12, 14). Unfortunately, current evidence does not support the use of one intervention over another, and as with all interventions, the least invasive methods with the greatest safety profile should be employed first.

SCOPE OF WORK

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

The study proposal should focus on patients with muscle spasticity 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), and functional outcomes (eg, Modified Ashworth Scale (MAS), Tardieu Scale/Modified Tardieu Scale), patient reported outcomes (eg, Leeds Adult Spasticity Impact Scale, Goal Attainment Scaling, Penn Spasm Frequency Scale (PSFS)) 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 *spasticity RFP*.

CONFIDENTIALITY

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