Notice of Interest (NOI)- The effect of cell therapy and bone healing in Spine, Orthopedics, and Regenerative Medicine.

Isto Biologics is pleased to announce an opportunity for clinical investigators experienced with our solutions to request funding through our Investigator Initiated Study (IIS) program. Applications will be accepted to conduct retrospective and prospective studies for Spine, Orthopedics, and Regenerative Medicine.

What is an IIS

An Investigator-Initiated Study (IIS) is a research effort in which the investigator designs and implements the study, and the investigator or the institution acts as the study sponsor. As the sponsor, the Investigator assumes all responsibilities for complying with applicable regulatory requirements. These studies may be supported by Isto Biologics in the form of product, research grant, and/or technical input.

Investigator Responsibilities

- Designing and conducting the scientific investigation
- Complying with institutional requirements where the study will be conducted using all relevant laws, regulations and guidelines for clinical and pre-clinical research
- Reporting safety data to regulatory authorities and Isto Biologics as required
- Registering the clinical study on a public website such as www.clinicaltrials.gov, as applicable
- Providing Isto Biologics with interim and final research summary reports, a proposed publication plan and a draft manuscript, as applicable.

Isto Biologics Solutions

- Influx™ Bone Graft
- Lightning Aspiration Needle
- Magellan® Autologous Platelet Separator
- InQu® Bone Graft Extender & Substitute

Topics of Interest

The scope of this NOI is limited to clinical research and does not include in vitro laboratory based research. Applications for funding will only be considered in which all products/devices are to be used in accordance with standard of care techniques, as well as the FDA cleared Instructions For Use for the respective Isto Biologics product.

Application Review & Criteria for Selection

All application submittals will be reviewed by an internal, cross functional team. Applications will be reviewed and selected on the basis of the scientific merit of planned research, business alignment of research objectives, previous research experience, site capability and local fair market value costs. You will then be notified of the committee's decision regarding your study proposal.

Where applicable, Institutional Review Board (IRB) approval is required for all applications approved by Isto Biologics to ensure an appropriate oversight, consent process, and/or handling of personal health information. If assistance is needed with the IRB process, please notify Isto Biologics.

What Happens After my Study Proposal is Approved?

You will be notified and asked to submit additional documents for final review. These documents include:

- **IIS Agreement**: All approved applications will require a fully executed research agreement, based on local fair market value and delivery of agreed milestones.
- **IRB Approval Letter**: Where applicable all approved applications must provide Institutional Review Board (IRB) approval documentation.

Once these documents have been reviewed and approved, agreed-upon funding, product, and/or technical input will be released according to the terms and milestones in the funding contract. The study cannot commence until final approval is provided by the Isto Biologics team.

Upon completion of the study, findings are expected to be submitted to a peer-reviewed journal. The investigator will also provide Isto Biologics with the deliverable noted in the IIS Research Contract (e.g. final study report, draft manuscript, abstract, etc.)

All other factors being equal, preference will be given to applications which include the following:

Scientific Merit	• Level of evidence: Comparative research • Scientific hypothesis statement • Sample size appropriate to address research question • Quality of safety data that can be provided including type and frequency of adverse events • Explain management of potential variability in results if more than one physician/site will be used
Investigator Capability	• Proven clinical research track record • Quantity and quality of published research • Experience in using device/product
Logistics	• Study timeline-timing for delivery of evidence to a peer-review journal • Resource requirement

Application Process

If you are interested in submitting an application, you may request relevant application documents by sending an email to research@istobiologics.com

** The email subject line should be formatted as follows: [Isto-NOI-Year-PI Name].

Applicants are required to submit:

- A completed application form which must include all key milestones for study preparation/execution and manuscript submission expectations
- A detailed itemized budget
- A signed and dated CV