



## REQUEST FOR PROPOSALS

# Clinical Trials of Desensitization in Solid Organ Transplantation

The Immune Tolerance Network (ITN) develops, implements, and conducts trials of novel immune tolerance therapeutics in transplantation, autoimmune diseases, and allergy and asthma. ITN trials look beyond the traditional endpoints of safety and efficacy, actively investigating the mechanisms of tolerance induction and maintenance by integrating hypothesis-driven, mechanism-based research into all its clinical trials. The goal is to improve our understanding of tolerance in the human clinical setting and to establish new biomarkers of tolerance in human disease. Supported by a diverse array of core facilities offering state-of-the-art genetic, cellular and immunologic assays, the ITN is generating some of the first combined clinical and mechanistic data on immune tolerance induction in humans.

**The ITN is currently seeking proposals for clinical trials for *novel therapeutic approaches* to induce B cell tolerance in patients who are donor-sensitized and/or to prevent sensitization. The therapeutic strategy must test specific immune mechanisms and must provide a clear pathway to future immune tolerance trials in solid organ transplantation. Proposals need to meet the following four criteria:**

- 1. The proposed study must have a mechanistic endpoint relevant to alloantigen specific tolerance. Examples include but are not limited to approaches that test for deletion/inhibition of donor reactive B cells, induction of regulatory B cells, or blockade of signals required for donor reactive B cell activation. The mechanistic endpoint must pre-specify the definition of specific signals that indicate durable “unresponsiveness.” The absence of DSA by itself is not sufficient; rather, a defined and testable mechanistic endpoint is needed to explain the absence of DSA. Parallel testing of T cell tolerance may also be proposed.**
- 2. Protocols for desensitization, or prevention of sensitization, must delineate specific criteria for the development of a subsequent tolerance trial. Prespecified definitions of success in the mechanistic study will determine whether the proposed strategy can proceed to the next step.**
- 3. Proposals do not need to include solid organ transplant.**
- 4. All biologic or pharmacologic agents to be used must be either be FDA approved, or have a clear safety record in early phase clinical studies and a commitment to development for clinical use (not necessarily in organ transplantation).**

**Immune Tolerance Network  
Request for Proposals**

Preliminary data to support the proposed novel therapeutic concept may derive from human clinical use, robust pre-clinical models, and/or studies using samples collected during prior tolerance trials. ITN trials and associated samples are available at *ITNTrialShare.org*.

The ITN is particularly interested in proposals for early phase studies (with approximately 5-20 patients); the ITN does not support larger phase 3 trials. The proposal review process will focus on evaluating the conceptual framework of the proposed trial and its significance and suitability for further development. We do not require submission of a detailed clinical protocol at this stage.

Proposals are welcome from academic, government and industry-based investigators throughout the year. Funding will vary based on the type and scope of the trial. The proposal should be no longer than 5 pages and should include:

- Name, title, and institution of principal investigator, co-investigator and/or key collaborator(s);
- Brief description of the proposed clinical trial, including the scientific basis and rationale that address the outlined criteria, in particular, the proposed clinical and mechanistic endpoints;
- References to published or preliminary (preclinical and pilot human study) data.

Responses are due *August 17<sup>th</sup>, 2018*. Please direct all proposal submissions and any questions concerning this RFP to:

**Philip Bernstein, PhD**

Director of Strategic Review and Planning

Tel: (240) 235-6132

Email: [pbernstein@immunetolerance.org](mailto:pbernstein@immunetolerance.org).

**About the Immune Tolerance Network ([www.immunetolerance.org](http://www.immunetolerance.org))**

The Immune Tolerance Network is a clinical research consortium dedicated to the development of immune tolerance therapies for transplantation, autoimmune diseases, and asthma and allergy. The ITN currently supports over 20 clinical trials, each with integrated investigations of the clinical mechanisms of tolerance. The ITN consortium is led by several institutions, including the Benaroya Research Institute at Virginia Mason, Seattle; University of California, San Francisco; and the Massachusetts General Hospital, Boston and is sponsored by the National Institute of Allergy and Infectious Diseases, with support from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Juvenile Diabetes Research Foundation.