ADITX THERAPEUTICS, INC.

Executive Summary

Problem/Opportunity

Organ transplantation can be a lifesaving treatment option, but the immune system continues to pose the greatest challenge to transplantation becoming a routine medical treatment due to the rejection that occurs when the recipient's immune system recognizes the transplanted organ as foreign.

The discovery of immunosuppressants (anti-rejection drugs) over 40 years ago, such as cyclosporine, has allowed survival of transplanted organs by preventing acute or early rejection. **However, immunosuppressants fail to prevent the chronic or long-term rejection that occurs years after the initial transplantation procedure. About 40% of transplanted organs survive for no more than 5 years.** Furthermore, **immune suppression leads to significant undesirable side effects such as increased susceptibility to life-threatening infections and cancers** because it is not specifically targeted towards the transplanted organs; rather, it indiscriminately and broadly suppresses immune function throughout the body.

A New Approach

New, focused therapeutic approaches are needed that modulate only the portion of immune cells that are involved in rejection of a transplanted organ, as this will be safer for patients than indiscriminate immune suppression. Such approaches are known as immune tolerance, and when therapeutically induced, may not only be safer for patients, but could also potentially allow long-term survival of transplanted tissues and organs.

In the late 1990s, academic research on these approaches was conducted at the Transplant Center at Loma Linda University (LLU) in connection with a project that secured initial grant funding from the U.S. Department of Defense (DOD). The focus of that project was skin grafting for burn victims. Twenty years of research at LLU and an affiliated incubator led to a series of discoveries that have been translated into a large patent portfolio of therapeutic approaches that may be applied to the modulation of the immune system in order to induce tolerance to self and transplanted organs.

We have an exclusive worldwide license for commercializing this nucleic acid-based technology called Apoptotic DNA Immunotherapy™ (ADi™), which utilizes a novel approach that mimics the way our bodies naturally induce tolerance to our own tissues ("therapeutically induced immune tolerance").

While immune suppression requires continuous administration to prevent acute or early rejection of transplanted organs, induction of tolerance has the potential to retrain the immune system to accept the organ for longer periods of time. Thus, ADi™ may allow patients to live with transplanted organs with significantly reduced dependence on immune suppression.

Potential Key Differentiators

- Injected in minute amounts directly into the skin where targeted cells of immune system reside
- No additional hospitalization needed
- Potentially better safety profile as DNA based therapeutics are generally considered safe
- Streamlined manufacturing and storage

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ADi™ Technology Platform

ADi™ utilizes a novel approach that mimics the way our bodies naturally induce tolerance to our own tissues. It is a technology platform which we believe can be engineered to address a wide variety of indications.

ADi™ includes two DNA molecules which are designed to deliver signals to induce tolerance. The first DNA molecule encodes a pro-apoptotic protein that induces 'programmed' cell death. This is a core component of the technology because it is intended to greatly increase the recruitment of dendritic cells, which are implicated in regulating the immune system. The second DNA molecule encodes the protein of interest (guiding antigen), which is modified to promote a path of tolerance. The guiding antigen is intended to result in tolerance induction specific to the tissue where the protein is found.

ADi™ has been successfully tested in several preclinical models and its efficacy can be attributed to multiple factors:

- ADi™ does not rely on a single mechanistic approach. It has multiple components (target antigen, apoptosis, plasmid DNA) that affect different arms of the immune system, which can be manipulated.
- ADi™ activates key immune cells known to maintain tolerance in test animals and humans.
- ADi™ has been successfully applied to a stringent transplantation model.
- ADi™ is designed to be safely administered repeatedly to achieve its full potential therapeutic effect.