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Tonix's TNX-1500 Shows Promise in Preventing Organ Transplant Rejections of Either Human or Pig Organs; Autoimmune Diseases Also a Target

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CHATHAM, NJ / ACCESS Newswire / March 12, 2025 / On any given day, there are over 100,000 people in the U.S. alone waiting for an organ transplant. Of that group, approximately 17 will succumb to their illness each day without a transplant. That's why doctors and researchers have turned to non-human organs to make up for the shortfall. In March 2024 doctors performed the first ever transplant of a modified pig kidney into a living human. However, the rejection rate for non-human organs, otherwise known as xenotransplants, is much higher than in human transplants. Even with human organs, as many as 20% of kidneys, 30% of hearts and 35% of liver transplants are rejected

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Those are worrying statistics that Tonix Pharmaceuticals Holding Corp. (NASDAQ:TNXP), the biopharmaceutical company, is trying to change withTNX-1500,* a humanized monoclonal antibody that blocks the action of CD40-ligand (CD40L), also known as CD154. The promise of CD40L blockers is to modulate the immune system rather than suppress it. Traditional immunosuppression drugs work for transplant and autoimmune diseases, but they carry a number of liabilities related to how broadly they suppress immunity and also to how they damage kidneys and other organs at the doses required for efficacy.

"Despite advancements in the field of solid organ transplantation, there remains a significant need for new treatments with improved activity and tolerability," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Anti-CD40L modulates T cell function and has the potential to promote tolerance of transplanted organs."

TNX-1500 is a third-generation CD40L blocker that has been designed by protein engineering to maintain the activity of first generation CD40L blockers, while improving their tolerability. The hope is that agents like TNX-1500 may someday replace immunosuppressant drugs or at least reduce the dose of immunosuppressants to a point where they are safer.

The first generation of CD40L blockers were monoclonal antibodies that showed promise in reducing organ rejection and addressing autoimmune conditions, but their use was associated with an increased risk of thrombosis, or blood clots. The second generation of CD40L blockers included some biologics that were not monoclonal antibodies. Most of these reduced thrombosis risk, but sacrificed activity. The third generation of anti-CD40L blockers are based on learnings from the first two generations and are designed to retain the activity of the first generation, but with the reduced risk thrombosis. The promise of third-generation CD40L blockers is to translate the science into better patient outcomes with lower rates of rejection, and less reliance on traditional broad-spectrum immunosuppressants.

Proof is in the Studies
In February, 2025, Tonix reported the topline results of a first-in-human Phase 1 trial of TNX-1500. This was a single ascending dose escalation trial of TNX-1500 in healthy volunteers. Results of the Phase 1 trial are encouraging because TNX-1500 treatment blocked the ability of volunteers to respond to a test immunization. Also, the half-life of TNX-1500 in the blood stream supports monthly dosing in trials aimed towards FDA approval.

Earlier animal studies indicated that TNX-1500 is active at preventing rejection of organ grafts and preserving graft function, either as a single agent or in combination with low doses of traditional immunosuppressants. TNX-1500 is active whether the organ comes from the same species or from genetically engineered pigs. So far, TNX-1500 treatment in these animal transplantation studies has shown a dramatic reduction in thrombotic events, indicating that the protein engineering of TNX-1500's Fc region achieved its design goals.

Although the lead indication for Tonix's TNX-1500 product candidate is the prevention of rejection of transplanted human kidneys, Tonix is also pursuing development of TNX-1500 for preventing rejection of genetically engineered pig organs. Ultimately, Tonix also plans to develop TNX-1500 as a treatment for autoimmune diseases.

Recently, encouraging clinical data in three different autoimmune conditions have been reported with other CD40L blockers. **Sanofi SA** reported an encouraging Phase 2 study in relapsing multiple sclerosis with frexalimab[1], **Biogen** reported a positive Phase 3 study in systemic lupus erythematosus with dapirolizumab pegol[2,3], and **Amgen** reported positive results in two patient populations in a Phase 2 study of Sjogren's Syndrome with dazodalibep[4,5]. Like TNX-1500, Sanofi's frexalimab has traditional characteristics of a humanized monoclonal antibody. In contrast, Biogen's dapirolizumab pegol and Amgen's dazodalibep are different types of biologics that block CD40L. The half-lives of TNX-1500 and frexalimab are greater than the reported half-lives of the non-antibodies, which provides for convenient monthly dosing.

Growing Potential Multi-Billion Dollar Market
Reducing rejection rates of human and non-human organs would not only save lives, it is also a potential big opportunity for Tonix. According to one estimate, the organ transplant immunosuppressant drug market was valued at $5.5 billion in 2023 and is projected to reach $7.17 billion by 2030. Driving the need for these drugs is an increase in the prevalence of organ failures as well as an increase in organ transplants. Also boosting the market is the prevalence of autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis, which can potentially be treated with this new class of drugs.

One other CD40L blocker is in development for preventing organ transplant rejection, tegoprubart from **Eledon Pharmaceuticals Inc.**. A Phase 2 study of tegoprubart in kidney transplant has completed dosing of 120 patients[6] and data are expected in 2026. Tegoprubart is a non-covalent antibody with no heavy-light or heavy-heavy interchain disulfide bridges that is being studied with i.v. dosing every three weeks. Tonix's TNX-1500 has disulfide bridges and a half-life that supports i.v. dosing monthly.

With the number of needy people in the U.S. in excess of 100,000 and with the medical community turning to non-human organs to fill the void, developing drugs to make sure these organs take is imperative. Tonix believes it has a solution with TNX-1500. With Phase 1 trial results recently announced and with the organ transplant market seemingly poised to grow, Tonix's drug development is bringing hope to patients on the transplant waiting lists.

"Organ transplant is a stringent test of a CD40L blocker to modulate the immune system. The activity of TNX-1500 that we've observed in animal studies of human and pig transplants, and on blocking the response to a test antigen in the Phase 1 study encourages us to develop TNX-1500 for allotransplantation, xenotransplantation and also for the treatment of autoimmune conditions," said Dr. Lederman.

*TNX-1500 (Fc-modified humanized anti-CD40L monoclonal antibody) is an investigational new drug and is not approved for any indication

[1]Vermersch P, et al. N Engl J Med. 2024 Feb 15;390(7):589-600. doi: 10.1056/NEJMoa2309439. PMID: 38354138
[2]Gelman, M. Endpoints. "Biogen, UCB detail response rates in Phase 3 lupus trial after surprising Success" Nov. 19, 2024
[3]Biogen Press Release, November 19, 2024. https://investors.biogen.com/news-releases/news-release-details/dapirolizumab-pegol-phase-3-data-presented-american-college

[4]Horizon Press Release. September 12, 2022. https://www.biospace.com/article/releases/horizon-therapeutics-plc-announces-phase-2-trial-evaluating-dazodalibep-for-the-treatment-of-sjoegren-s-syndrome-meets-primary-endpoint/

[5]Horizon Press Release. January 18, 2023.

[6]www.nasdaq.com/articles/eledon-pharmaceuticals-completes-enrollment-phase-2-bestow-trial-tegoprubart-kidney

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