Nanotechnology treatment reprograms immune cells to reverse autoimmune disease

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Parvus Therapeutics today announced the publication in *Nature* of a seminal paper describing the discovery and applications of a novel therapeutic approach employing nanomedicines, referred to as "Navacims", to reprogram white blood cells to become regulatory cells capable of blunting autoimmune responses and restoring the equilibrium of the immune system. Navacims are nanoparticles (NPs) coated with disease-relevant peptide-major histocompatibility complexes (pMHCs) that alter the behavior of pathogenic T lymphocytes by binding directly to their antigen receptors. The peer-reviewed article, titled "Expanding antigen-specific regulatory networks to treat autoimmunity" reports on a body of work, including results in multiple in vivo disease models, built on more than eight years of research by Parvus Founder and Chief Scientific Officer, Pere Santamaria, M.D., Ph.D.

Dr. Santamaria commented, "Autoimmune diseases, including type 1 diabetes, multiple sclerosis, and rheumatoid arthritis, are extraordinarily complex responses of our immune system against some of our own tissues (e.g. pancreas, brain and joints, respectively), leading to chronic organ inflammation, organ dysfunction, and, in some cases, premature death. Blunting these incompletely understood immune responses without suppressing the normal components of our immune system that protect us against infection and cancer is not currently possible."

"However, our work offers a pharmaceutical solution to this fundamental problem," Dr. Santamaria continued. "Navacims essentially re-program disease-causing white blood cells to become disease-

suppressing cells, known as regulatory cells, leading to sustained therapeutic effects in various spontaneous and experimental autoimmune diseases, as reported in our article in *Nature*. Essentially, we have found that Navacims can be tailored to treat a wide range of autoimmune diseases, while sharing a common structure. Importantly, they have been shown to affect human white blood cells in the same manner as they do murine cells. Furthermore, Navacims have shown promising safety findings in preclinical in vivo models. Based on our results to date, we believe Navacims represent a therapeutic platform with broad-ranging health care implications."

Findings being reported in *Nature* include:

- pMHC class II Navacims expanded cognate CD4+ T-cells that consistently have a TR1-like, regulatory T cell surface phenotype, transcriptional pattern and cytokine profile (mouse=human TR1 cells) systemically.
- pMHC class II-Navacims designed to target T cells in newly diabetic nonobese (NOD) mice restored normoglycemia (normal blood sugar regulation) in the majority of the mice tested.
- Tailored pMHC class II Navacims restored motor function to paralyzed C57BL/6 mice at the peak of Experimental Autoimmune Encephalomyelitis (a model of Multiple Sclerosis).
- pMHC class II Navacims, targeting disease-causing T cells in joints, resolved joint swelling and destruction in arthritic mice.

"The findings being reported in *Nature* represent a scientific advance for Parvus and also a major achievement in the field of Immunology," said Janice M. LeCocq, CEO of Parvus. "We believe that Dr. Santamaria's work has the potential to transform the treatment of many of the more than 80 major autoimmune diseases affecting humankind, alleviating the suffering of millions of patients and their families. Over the coming year, we will be dedicating much of our in-house efforts to the

advancement of our two lead programs for type 1 diabetes and multiple sclerosis."

"Dr. Santamaria's work to target the immune system dysfunction that causes type 1 diabetes represents the kind of innovative work that JDRF believes will eventually get us to a cure for this disease," said Juvenile Diabetes Research Foundation Vice President of Discovery Research Julia Greenstein, Ph.D. "He and his colleagues have made exciting progress towards possibly developing a new class of drugs that could rebalance certain T-cells and ultimately provide a cure for type 1 diabetes and other autoimmune diseases as well." The JDRF has funded the work of Dr. Santamaria and his colleagues at Parvus to explore Navacim-based treatments for diabetes.

Parvus' strategy is to establish partnerships with major pharmaceutical companies to undertake the clinical and commercial development of many of its product pipeline candidates while also reserving rights to others suitable for its own development and commercialization. Parvus currently is engaged in late stage discussions with multiple pharmaceutical companies with regard to the type 1 diabetes (T1D) program. Manufacturing scale-up is now underway to supply upcoming preclinical and clinical studies.

The work being reported in *Nature* was led by Dr. Pere Santamaria and largely executed at the University of Calgary, Cumming School of Medicine (animal models of disease) and the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) (humanized mouse work), with significant contributions from investigators at Institutions in Europe and the US. Further, Innovate Calgary, the technology-transfer and business-incubation center for the University of Calgary, provided early support for the transfer of the Navacims technology to and incubation of Parvus Therapeutics, which was organized as a separate entity in 2012.

More information: Xavier Clemente-Casares et al. Expanding antigen-specific regulatory networks to treat autoimmunity, *Nature* (2016). DOI: 10.1038/nature16962