Xenikos Enrolls First Patient in Global Pivotal Phase 3 Study Evaluating T-Guard® in Patients with Steroid-Refractory Acute Graft-Versus-Host Disease

- *Study Designed to Evaluate Whether T-Guard is Superior to Ruxolitinib in Patients with Grade III or IV Steroid-Refractory Acute Graft-Versus-Host Disease*
- *Preliminary Results Expected First Half of 2023*
- *Results Expected to Provide the Basis for Both FDA and EMA Regulatory Submissions*

NIJMEGEN, the Netherlands – June 27, 2022 – Xenikos B.V., a privately-held biotechnology company that develops innovative immunotherapies for treating patients with severe immune disease and post-transplant rejection, today announced enrollment of the first patient in a global pivotal Phase 3 clinical study designed to evaluate T-Guard® versus ruxolitinib for the treatment of patients with Grade III or IV steroid-refractory acute graft-versus-host disease (SR-aGVHD) following allogeneic hematopoietic stem cell transplant (allo-HSCT).

Xenikos reached agreement with the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) on the design of this global, pivotal, randomized Phase 3 study, which is planned to enroll 246 patients and has been designed to test for superiority of T-Guard compared to ruxolitinib for the treatment of Grade III or IV SR-aGVHD. The study will be conducted at 75 transplant centers across the US and Europe and will be executed in collaboration with the Blood and Marrow Transplant Clinical Trials Network (BMT CTN). Patients will be randomized 1:1 to receive either T-Guard or ruxolitinib. Participants on the T-Guard arm will receive a 1-week course of treatment with T-Guard as a 4-hour infusion every other day. Each dose consists of 4mg/m^2 Body Surface Area (BSA). Participants on the ruxolitinib arm will receive 10mg of ruxolitinib twice daily for a minimum of 56 days. The primary endpoint of the study is complete response (CR) rate at Day 28, which is an important surrogate for long-term survival in patients with SR-aGVHD. Key secondary objectives include overall survival at Days 60, 90, 180, and 365, duration of complete response (CR), time to CR, overall response rate at Days 14, 28 and 56, GVHD-free survival, incidence of infections and safety.

There will be a safety run-in phase at the beginning of the study whereby the Data and Safety Monitoring Board (DSMB) will evaluate the first 24 patients. Xenikos expects to report results from the safety run-in phase during the first half of 2023. The trial will also include an interim analysis for futility after 46 patients become evaluable for the primary endpoint. A second interim analysis will be performed once 150 participants have reached Day 28.

Xenikos expects the data from this study to support the submission of a Biologics License Application (BLA) in the US based on Day 28 data from the first 150 patients. Data from the full 246 patients is expected to support the submission of a Marketing Authorization Application (MAA) in the EU.

"Standard first-line therapy for acute graft-versus-host-disease consists of corticosteroids, which are effective in approximately half of all patients. However if the condition is resistant to treatment or progresses there are currently limited treatments available that don't lead to broad and long-term immunosuppression," said Gérard Socié, Protocol Co-chair, Professor of the Department of Hematology-Transplantation at the Hôpital Saint-Louis, Paris, France. "This Phase 3 study is supported by very promising Phase 2 data and we look forward to further elucidating the potential of T-Guard versus ruxolitinib and helping bring this innovative new therapy through the next stage of development and to the physicians and patients who need it."

"Patient enrollment is now underway in our global, pivotal Phase 3 T-Guard study, and this initiation marks an important milestone for Xenikos," said Ypke van Oosterhout, PhD, Chief Executive Officer of Xenikos. "Since T-Guard's mechanism of action is fundamentally different from other agents, we believe it has the potential to provide an effective treatment option for patients battling steroid-refractory acute graft-versus-host disease, while avoiding long-term immunosuppression. Our dialogue with the FDA and EMA has led to this Phase 3 study design which we believe will demonstrate T-Guard's superiority and safety. We look forward to reporting the outcome of the safety run-in portion of the study during the first half of 2023."

John Levine, Protocol Co-chair, Director of BMT Clinical Research, Mt. Sinai School of Medicine and Gabrielle Meyers, Protocol Co-chair, Associate Professor of Medicine, Oregon Health and Science University added, "Patients with GVHD that is both severe and resistant to standard treatment are in urgent need of new and better therapies. It is our hope that this study will show that T-Guard can help meet that need. We appreciate that the NIH funded BMT CTN and Xenikos are supporting this trial."

Acute Graft-Versus-Host Disease

Following allogeneic stem cell transplantation, most patients have a high risk of developing graft-versus-host disease (GVHD). With GVHD, the donor's immune cells attack the patient's cells. Acute GVHD occurs early after transplantation and can be relatively mild or quite severe, even life-threatening, if not treated. Although GVHD can often be treated successfully with steroids, few options are available if the disease progresses or becomes resistant to steroid treatment, and the long-term survival of patients with steroid-refractory acute GVHD (SR-aGVHD) is less than 20%, highlighting the urgent need for effective new therapies.

T-Guard®: Helping Reset the Body's Immune System

T-Guard is designed to safely and swiftly reset the body's immune system in life-threatening T cell–mediated conditions, including transplant-related rejection, acute solid-organ rejection, and severe autoimmune disease. T-Guard consists of a unique combination of toxin-conjugated monoclonal antibodies that target CD3 and CD7 molecules on immune cells. Preclinical and early clinical testing have shown that T-Guard can specifically identify and eliminate mature T cells and NK cells with tolerable treatment-related side effects. Importantly, T-Guard's action is short-lived and allows for a swift recurrence of a diverse T cell population, potentially reducing the patient's vulnerability to opportunistic infections

compared to currently available therapies. In a Phase 1/2 study, just one week of T-Guard treatment induced a remarkably high complete response rate and a doubling of the 6-month overall survival rate as compared to institutional historical controls in patients being treated second-line for steroid-refractory acute graft-versus-host disease (SR-aGVHD) following hematopoietic stem cell transplantation (HSCT). These results were published in the peer-reviewed journal Biology of Blood and Marrow Transplantation (Groth, et al. Nov 2018). T-Guard has been granted Orphan Drug Designation in both the EU and the US.

About the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)

The BMT CTN conducts rigorous multi-institutional clinical trials of high scientific merit, focused on improving survival for patients undergoing hematopoietic cell transplantation and/or receiving other cellular therapies. The BMT CTN has completed accrual to more than 50 Phase II and III trials at more than 100 transplant centers and enrolled over 16,000 study participants.

BMT CTN is funded by the National Heart, Lung, and Blood Institute and the National Cancer Institute, both parts of the National Institutes of Health (NIH) and is a collaborative effort of 20 Core Transplant Centers/Consortia, the Center for International Blood and Marrow Transplant Research (CIBMTR), the National Marrow Donor Program (NMDP)/Be The Match and the Emmes Company, LLC, a clinical research organization. CIBMTR is a research collaboration between the NMDP/Be The Match and the Medical College of Wisconsin.

The BMT CTN 2002 study is being led by Drs. Mehdi Hamadani, Protocol Officer, Scientific Director of CIBMTR, Medical College of Wisconsin; John Levine, Protocol Co-chair, Director of BMT Clinical Research, Mt. Sinai School of Medicine; Gérard Socié, Protocol Co-chair, Head of Hematology- Transplantation, Hôpital Saint-Louis; and Gabrielle Meyers, Protocol Co-chair, Associate Professor of Medicine, Oregon Health and Science University. More information about the BMT CTN can be found at www.bmtctn.net.

About Xenikos

Xenikos develops innovative immunotherapies based on conjugated antibodies. This novel therapeutic approach helps reset the immune system in patients who have a severe immune disease or have developed post-transplantation rejection. A randomized Phase 3 registration trial evaluating the Company's flagship product, T-Guard® for the treatment of steroid-refractory acute graft-versus-host disease (SR-aGVHD) is underway in the US and Europe.

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