Xenikos Announces T-Guard Phase 3 Clinical Update and Outlines 2021-2022 Corporate Objectives

Company Plans to Commence New Pivotal, Randomized Phase 3 Study Evaluating T-Guard Versus Ruxolitinib in Patients with Grade III or IV Steroid-refractory Acute Graft-Versus-Host Disease in Second Half of 2021

Positive Results Expected to Support Both FDA and EMA Regulatory Submissions

NIJMEGEN, the Netherlands – July 19, 2021 – 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 that it has reached agreement with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on the design of its pivotal randomized Phase 3 clinical study (BMT CTN 2002) 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). The primary endpoint will be Day 28 Complete Response (CR), which is the strongest surrogate for long-term survival in patients with SR-aGVHD. The study is expected to enroll 246 patients from several European countries and the US. Xenikos expects to commence this Phase 3 study in the second half of 2021. The study is being done in collaboration with the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a US National Institutes of Health (NIH) funded program focused on HSCT and other cell therapies.

“Severe acute GVHD remains a major threat to successful outcomes in allo-HSCT, and we are in desperate need of new agents. On behalf of patients, I am grateful to the Blood and Marrow Transplant Clinical Trials Network, the National Institutes of Health and Xenikos for supporting this first of kind trial in this vulnerable population,” said Gabrielle Meyers, Protocol Co-chair, Associate Professor of Medicine, Oregon Health and Science University, US.

Gérard Socié, Protocol Co-chair, Professor of the Department of Hematology-Transplantation at the Hôpital Saint-Louis, Paris, France, stated “Allo-HSCT remains the only curative therapy for several malignant and non-malignant hematologic diseases, but GVHD still represents a substantial obstacle to its ultimate success. High dose steroids are the only available first-line treatment option for acute GVHD, but for those patients who fail first-line steroid therapy, novel effective therapies are urgently needed. T-Guard’s mechanism of action appears to be fundamentally different from other agents used in the field and has the potential to provide great added value, especially if it avoids long-term immunosuppression.”

Assuming a positive outcome from the new Phase 3 study, 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. If the full 246-patient trial results show superiority of T-Guard over ruxolitinib, this will support the submission of a Marketing Authorization Application (MAA) in the EU.

“Our conversations with the FDA and EMA have enabled us to finalize the Phase 3 study design along with the appropriate safety and efficacy endpoints,” said Ypke van Oosterhout, PhD, Chief Executive Officer of Xenikos. “We look forward to commencing the new Phase 3. Over 75 hospitals in 11 countries will

participate in this study and preparations are well on track to open the study for patient enrollment in the second half of 2021."

Corporate Objectives for 2021-2023

- Initiate new Phase 3 study evaluating T-Guard versus ruxolitinib in patients with SR-aGVHD following allo-HSCT in the second half of 2021.
- Complete safety run-in phase of Phase 3 study mid 2022.
- Complete futility analyses portion of the Phase 3 study during the first half of 2023.

Details of the New Randomized Phase 3 Study

This Phase 3 study is expected to enroll 246 Grade III or IV SR-aGVHD patients across 75 transplant centers across the US and Europe and will be conducted in collaboration with the 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 4-hour infusions 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 minimal period of 56 days. The primary endpoint of the study is CR rate on Day 28. Secondary objectives include: overall survival at Days 60, 90 and 180, duration of complete response (DoCR), time to CR, overall response rate at Days 14, 28 and 56, GVHD-free survival, and incidence of infections.

At the beginning of the study, there will be a safety run-in phase where the Data and Safety Monitoring Board (DSMB) will evaluate 12 patients from each of the two treatment arms (~24 patients total). This trial will include an interim analysis for futility after 23 participants on the T-Guard arm (~46 across both treatment arms) become evaluable for the primary endpoint. A second interim analysis will be performed once 150 participants on combined arms have reached Day 28 and 100 participants on the combined arms have reached Day 180.

About the Prior Phase 3 Study

Following successful completion of Phase 1 and Phase 1/2 clinical studies, in 2019 a US-based, single-arm Phase 3 study was initiated to evaluate T-Guard for the treatment of SR-aGVHD in patients following allogeneic stem cell transplantation (NCT04128319). That study was put on hold by the FDA in February 2020 because the first three patients died within the first 30 days of the study. An in-depth investigation was conducted by the FDA and found no reason to stop further development of T-Guard. However, the FDA advised Xenikos to design a new randomized Phase 3 study which evaluates T-Guard against a comparator treatment (ruxolitinib) to serve as a safety benchmark and which includes a safety run-in phase. Eligibility for the new Phase 3 trial aligns with the trials of ruxolitinib in SR-aGVHD patients.

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, thereby significantly 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, and a randomized Phase 3 registration trial evaluating T-Guard for the treatment of SR-aGVHD is expected to commence in the second half of 2021.

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 44 Phase II and III trials at more than 100 transplant centers and enrolled over 14,304 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 expected to begin in the US and Europe in the second half of 2021.

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