

Kymab and Seattle Children's Research Institute publish impressive results using Kymab's KY1005 in a model of Acute Graft versus Host Disease (aGVHD) in *Science Translational Medicine*

- KY1005 in combination with sirolimus has potential to set a new standard of care for aGVHD prevention
- First time investigators have successfully controlled aGVHD for the entire trial period of this model
- KY1005 is an antagonist of OX40-Ligand with the potential to treat a number of autoimmune disease
- KY1005 is Kymab's most advanced clinical stage antibody currently being trialled in healthy volunteers and patients with an autoimmune disease

Cambridge, UK, 21 September 2017 – Kymab, an emerging biopharmaceutical company focused on the discovery and development of fully human monoclonal antibody drugs, announces that new data published in *Science Translational Medicine* indicate that Kymab's most advanced clinical stage antibody, KY1005, could play an important role in blood-system transplants, such as the treatment of leukemia. This preclinical model of a haematopoietic cell transplant (also known as bone marrow transplant) demonstrates, for the first time, that acute graft versus host disease (aGVHD) has been controlled for the entire trial period.

Researchers from Kymab worked with a team led by **Dr. Leslie Kean, Associate Director of the Ben Towne Center for Childhood Cancer Research at Seattle Children's Research Institute** "KY1005, in combination with sirolimus, sets a new standard for aGVHD prevention," commented **Dr. Kean**. "These results in the complex and clinically relevant animal model suggest this regimen is an exceptional candidate for clinical translation."

Dr David Chiswell, CEO of Kymab, said: "Kymab is searching for therapeutic antibodies that answer significant medical needs and solve challenging clinical problems. Transplant medicine has brought tremendous advances, but rejection and graft-versus-host disease remain two very difficult challenges. Our new results show that our antibody KY1005 could provide a biologically valid approach to managing transplant immunology better, with improved outcomes for patients."

In this study, KY1005 was administered in combination with sirolimus prophylactically and was able to potently control T-cell activation yet still support successful haematologic reconstitution and donor engraftment post-transplant. On its own, KY1005 produced a longer period of freedom from disease than controls, comparable to the effect of sirolimus. However, it was the combination of both treatments that gave impressive results: recipients remained healthy and free from aGVHD signs for the length of the study (100 days post-transplant) and even when they had been weaned off KY1005. Importantly, the work was supported by biological evidence that gene activity in T-cells is normalised, combined with the reduction of the characteristic signs of aGVHD.

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Notes to Editors**About KY1005**

KY1005, a fully human monoclonal antibody, is a potential first-in-class therapeutic that may address an underlying immune system imbalance in patients with many autoimmune conditions. It binds to OX40L and blocks it from activating OX40, a protein that induces a prolonged response in T-cells of the immune system, which can lead to diseases of the immune system and damaging effects on patients. By blocking this activation, K1005 may act to bring the immune system back into balance. This could lead to a profound clinical impact and restoration of healthy organ functions in autoimmune conditions. Current treatments for these diseases tend to suppress the immune system on a broad basis, leading to significant side effects. One of the potential advantages of KY1005 is that it has the potential to be a more targeted treatment.

KY1005, which is in Phase 1 trials in healthy volunteers and patients with an autoimmune disease, blocks an interaction between proteins OX40 and OX40L that stimulates the immune system. KY1005-CT01 clinical study is targeting a total enrollment of 88. Primary completion is expected in 1H 2018. The study is a single and multiple ascending dose, placebo-controlled, double-blind, Phase 1 study to evaluate the safety and tolerability of KY1005 in healthy volunteers and patients with a mild-to-moderate immune system disease.

About OX40/OX40L

OX40 (CD134) and its binding partner, OX40L (CD252), are members of the TNFR/TNF superfamily and are expressed on activated CD4 and CD8 T cells as well as a number of other lymphoid and non-lymphoid cells. Costimulatory signals from OX40 to a conventional T cell promote division and survival, augmenting the clonal expansion of effector and memory populations as they are being generated to antigen. OX40 additionally suppresses the differentiation and activity of Treg, further amplifying this process. OX40 and OX40L also regulate cytokine production from T cells, antigen-presenting cells, NK cells, and NKT cells, and modulate cytokine receptor signaling. In line with these important modulatory functions, OX40/OX40L interactions have been found to play a central role in the development of multiple inflammatory and autoimmune diseases, making them attractive candidates for intervention in the clinic.

About immune and inflammatory disorders / autoimmune diseases

Immune and inflammatory disorders (autoimmune diseases) affect up to 50 million Americans, according to the American Autoimmune Related Diseases Association (AARDA). These diseases develop when the immune system, which defends the body against infections, treat healthy cells as foreign. As a result, the immune system attacks healthy cells. Depending on the type, an autoimmune disease can affect one or many different types of body tissue and can result in tissue damage, altered tissue growth, and impaired organ function. This can be highly painful and debilitating. There are over 80 types of immune system diseases, including GvHD, rheumatoid arthritis, psoriasis, atopic dermatitis, multiple sclerosis (MS), lupus and inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis. Currently, treatment for these diseases focuses on dampening or rebalancing the immune system and relieving symptoms because there is no curative therapy.

About Acute Graft versus Host Disease (aGVHD)

The immune response must balance between insufficient and excessive response: too little and the immune insult might not be resolved; too much and the immune system can cause damage to host organs. In each case, the host's wellbeing can be compromised. This need for balance is particularly acute in transplant medicine: in an organ transplant, such as kidney or liver, the recipient receives cells that are imperfectly matched to their own tissues and might appear as 'foreign'. In the case of a bone marrow transplant, the cells from the donor can recognise the recipient cells as foreign and attack them. This deadly complication is known as "Graft-versus-host disease".

The mainstay of immunosuppression are drugs that inhibit activity of the protein calcineurin, which normally activates T-cells. But these drugs are blunt instruments that damage all T-cells, including regulatory T-cells. Sirolimus, which inhibits a protein that activates T-cells, also acts against the immune response, but spares regulatory T-cells to a greater degree than calcineurin inhibitors. However, it cannot prevent GVHD on its own. These new results suggest that the combination of KY1005 and sirolimus may represent a new and efficacious strategy for successful immunomodulation.

About *Science Translational Medicine*

Science Translational Medicine is an interdisciplinary medical journal established by the American Association for the Advancement of Science. It covers translational, and clinical research on human diseases. *Science Translational Medicine* publishes original, peer-reviewed, science-based research articles that report successful advances toward the goal of improving patients' lives. The editors and an international advisory group of scientists and clinician-scientists as well as other experts hold articles to a high-quality standard.

About Kymab

Kymab is an emerging biopharmaceutical company focused on the discovery and development of fully human monoclonal antibody drugs using its proprietary antibody platform which contains a full diversity of human antibodies, making it the most comprehensive antibody development platform available.

Kymab's platform has been designed to maximise the diversity of human antibodies produced in response to immunisation with antigens. Selecting from a broad diversity of fully human antibodies assures the highest probability of finding drug candidates with best-in-class characteristics quickly and efficiently.

Kymab is using the platform for its internal drug discovery programmes and in partnership with pharmaceutical companies. Kymab was founded in 2010 and has raised over US\$220m of equity financing which includes \$100m Series C financing. It has an experienced management team with a successful track record in drug discovery and development and a broad pipeline of therapeutic antibody programmes in immune-oncology, auto-immunity, haematology, infectious disease and other areas.

For more information please see <http://www.kymab.com>

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