First UK Clinical Trial Site Open for Recruitment of Diabetic Patients with Chronic Limb-Threatening Ischemia Using Novel Patient-Specific Regenerative Cell Therapy

Phase III SALAMANDER Trials of Rexgenero's REX-001 Open and Recruiting Patients at the University Hospital of Wales in Cardiff

London, UK, 4 December 2019: The first UK clinical trial site for the treatment of diabetic patients with chronic limb-threatening ischemia (CLI) using a novel patient-specific regenerative therapy has opened for patient recruitment at the University Hospital of Wales in Cardiff. The site will be evaluating Rexgenero's REX-001 in two Phase III trials, codenamed the SALAMANDER trials. The trials are being led by Mr Ian Williams, a Consultant Vascular Surgeon and the Principal Investigator at the site.

The University Hospital of Wales is participating in the trials through a consortium, the Midlands-Wales Advanced Therapy Treatment Centre (MW-ATTC), part of the Advanced Therapy Treatment Centre Network (ATTC) which aims to bring pioneering advanced therapy medicinal products (ATMPs) to patients. THE MW-ATTC has been working in collaboration with the Cardiff & Vale University Health Board to progress the initiation of the two SALAMANDER trials and is planning to activate new clinical trial sites in the Midlands in England shortly.

CLI is a chronic disease and the most serious form of peripheral arterial disease (PAD), a common condition in which a build-up of fatty deposits in the arteries reduces the blood flow to the legs and feet. CLI is characterized by chronic ischemic at-rest pain, ulcers or gangrene in one or both legs. CLI is a common condition in Europe and the United States affecting 1-1.5% of the population aged over 40[1]. It represents an area of high unmet medical need as there are currently no approved therapies that successfully treat the CLI patient population. Patients with CLI have a very negative prognosis. A year after initial diagnosis, around 12% of patients have had an amputation. Five years after diagnosis the situation is even worse with mortality at 50%, rising to 70% after ten years[2].

REX-001 represents a new class of regenerative medicines. It is an autologous cell therapy manufactured using the patient's own bone marrow and consists of immune cells (lymphocytes, monocytes and granulocytes) and progenitor cells involved in immune modulation and tissue regeneration. It is administered as a single dose within 4 days after collection of bone marrow cells.

Ian Williams, Consultant Vascular Surgeon and Principal Investigator commented, "Chronic limb-threatening ischemia is a serious disease with severe consequences and limited treatment options. There is a high unmet need for novel and innovative therapies – such as REX-001 – that have the potential to be a highly effective treatment and to reduce amputation and mortality rates amongst the patient population."

Chris Fegan, Consultant Haematologist, Cardiff and Vale University Health Board said, "We have brought together many highly specialized teams from diabetes, surgery, radiology and stem cell transplantation to participate in the pioneering "SALAMANDER" study here at Cardiff and Vale, which we hope will revolutionize treatment options for patients with chronic limb-threatening ischemia."

Rexgenero, the company pioneering the development of REX-001, says that the experimental product has already demonstrated efficacy in Phase I/II studies. In the Phase II clinical trial, 82% of patients with non-healing ischemic ulcers were healed within the first 12 months after a single administration dose of REX-001.

Joe Dupere, CEO of Rexgenero added, "Treating our first patient with REX-001 in the UK will be an important milestone for our Phase III program in diabetic patients with chronic-limb threatening ischemia, a severe condition with high unmet need. With clinical trial sites and manufacturing bases now open across multiple countries in Europe, we are one step closer to completion of the Phase III studies and potential regulatory and market approval for an innovative and much-needed product."

Rexgenero is planning to treat a total of 60 patients with CLI and rest pain and 78 patients with CLI and non-healing ischemic ulcers in two independent Phase III SALAMANDER trials in approximately 25 hospitals across Europe. In addition to the trial sites in the UK, Rexgenero is also recruiting patients for both trials at sites in Spain, Austria, Portugal, Poland, Hungary, the Netherlands and the Czech Republic.

For more information about the REX-001 Phase III SALAMANDER trials, and how to participate, please visit the clinical trial website.

References

1. Sigvant et al. A population-based study of peripheral arterial disease prevalence with special focus on critical limb ischemia and sex differences. *J. Vasc. Surg.* **45,** 1185-1190 (2007).
2. Varu, V. N. et al. Critical limb ischemia. *J. Vasc. Surg.* **51**, 230–241 (2010).

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About Rexgenero

Rexgenero is a clinical-stage regenerative medicine company developing innovative cell-based therapies targeting serious diseases with unmet medical needs.

The Company's lead candidate, REX-001, is a highly innovative autologous cell therapy that is being studied in a Phase III clinical programme in patients with chronic limb-threatening ischemia (CLI) with diabetes, a poorly treated disease with a high risk of amputation and death. REX-001 has been shown to be effective in Phase I/II and Phase II trials, alleviating CLI in the majority of patients, offering the potential to increase the quality of life of CLI patients by reducing pain, alleviating ulcers, increasing mobility, improving sleep and reducing the need for amputation. Rexgenero is developing REX-001 in a range of indications and, pending approval, intends to launch and market this specialty product in major territories.

Rexgenero is a privately-owned company, which draws on an exceptional understanding of the fundamental science of cell therapies developed by the Andalusian Health Authority (Servicio Andaluz de Salud) and Andalusian Initiative of Advanced Therapies.

The Company was founded in 2015 and is headquartered in London (UK) with R&D and manufacturing operations in Seville (Spain) and Frankfurt (Germany).

For more information, please visit: www.rexgenero.com

Connect with us: Twitter: @_Rexgenero; LinkedIn: https://www.linkedin.com/company/rexgenero-limited/

About the REX-001 Phase III SALAMANDER Trials

REX-001 has shown efficacy in 70% of patients in Phase I and I/II studies and is currently progressing through two Phase III SALAMANDER trials in Europe being conducted at approximately 30 sites, with plans to enrol a total of 138 patients. The trials are given the name SALAMANDER in reference to the amphibian's ability to regenerate its tail and limbs.

The Phase III study in patients with Rutherford stage 4 CLI will assess the efficacy and safety of REX-001 with a primary endpoint of complete relief of ischemic rest pain.

The Phase III study in patients with Rutherford stage 5 CLI will assess the efficacy and safety with a primary endpoint of complete ulcer healing.

Amputation-free survival is included as a secondary endpoint in both studies. The trials are expected to produce interim analysis in early 2021 with full results expected later that year; all dependent on the speed of patient recruitment.

For more information about the REX-001 Phase III SALAMANDER trials, please visit: https://www.cli-treatment.com

About the Midlands and Wales Advanced Therapy Treatment Centre (MW-ATTC)

The Midlands and Wales Advanced Therapy Treatment Centre (MW-ATTC) consists of a large regional network with the necessary commercial and NHS infrastructure required to facilitate the delivery of advanced therapy treatments to patients. The centre includes a wide range of specialists in advanced therapy manufacturing including academic and commercial partners, logistics companies, specialists in clinical trial delivery and teams focussed on IT solutions and health economics.

For more information, please visit: https://www.theattcnetwork.co.uk/centres/midlands-wales

The ATTC Network Programme is a world-first, UK system of Advanced Therapy Treatment Centres (ATTC) operating within the NHS framework and coordinated by the Cell and Gene Therapy Catapult to address the unique and complex challenges of bringing pioneering advanced therapy medicinal products (ATMPs) to patients. The centres include Innovate Manchester Advanced Therapy Centre Hub (iMATCH), Midlands-Wales Advanced Therapy Treatment Centre (MW-ATTC, comprising Birmingham, Wales and Nottingham) and Northern Alliance Advanced Therapies Treatment Centre (NA-ATTC, comprising Scotland, Newcastle and Leeds).

The network is initially supported by the Industrial Challenge Strategy Fund with the aim to develop first-of-a-kind technologies for the manufacture of innovative medicines across areas including blindness, cancer, heart failure, liver disease, neurological conditions and rare paediatric diseases.

For more information, please visit: https://www.theattcnetwork.co.uk/