180 Therapeutics Announces Positive Results from a Phase 2a Clinical Trial of Anti-TNF Therapy in Dupuytren's Disease

--- Potential New Treatment Option for a Severe and Disabling Inflammatory Hand Disease ---

Cambridge, Mass, July 31, 2018 – 180 Therapeutics LP, a clinical stage biopharmaceutical company focused on the discovery and development of novel biologic therapies for the treatment of fibrosis, a process of excessive undesirable scarring which is a major unmet medical need in many different human diseases, today announced positive results from a Phase 2a clinical trial of the anti-TNF monoclonal antibody, adalimumab, in patients suffering from Dupuytren's disease. The results were published in the journal *EBioMedicine*, published by *The Lancet.*

Research by the scientific founders of 180 Therapeutics, Professors Sir Marc Feldmann and Jagdeep Nanchahal, MD, PhD uncovered the role of tumor necrosis factor (TNF) in driving the development and activity of myofibroblasts, the cells responsible for the fibrosis that cause the fingers of patients with Dupuytren's disease to curl irreversibly into the palm.

The Phase 2a clinical trial was conducted by researchers at the Kennedy Institute, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK, working with clinicians at NHS Lothian, Scotland. The dose ranging study found that injection of the anti-TNF drug, adalimumab, into Dupuytren's disease nodules results in the reduction of key cellular markers of fibrosis. The study was supported by the Wellcome Trust, UK Department of Health and 180 Therapeutics. Based on these clinical Phase 2a findings, the company, together with the Wellcome Trust and Department of Health, is now supporting a Phase 2b clinical trial of adalimumab injected directly into the fibrotic nodules of patients with early stage Dupuytren's disease, which will assess efficacy to retard disease progression over 18 months.

"Our study has demonstrated that the anti-TNF drug, adalimumab, injected directly into the diseased tissue of patients may be effective in targeting the pro-fibrotic myofibroblast cells responsible for Dupuytren's disease," said Jagdeep Nanchahal, MD, PhD, University of Oxford Professor of Hand, Plastic and Reconstructive Surgery, who led the study. "This brings new hope to people who suffer from this common disabling condition, with its frequent recurrences, who currently have few treatment options other than surgery or collagenase for late stage disease".

"Based on results so far we are very optimistic about the likelihood of clinical efficacy in our ongoing Dupuytren's Phase 2b clinical study. This is because our approach has been based on investigating human diseased tissue in the lab, the same approach which provided the rationale for the translational path we pioneered in rheumatoid arthritis which showed the first dramatic clinical benefit of anti-TNF in patients afflicted with rheumatoid arthritis," said Professor Sir Marc Feldmann, co-founder of 180 Therapeutics and a Lasker Award winner.

About the Phase 2a Trial

The randomized, dose response, placebo-controlled Phase 2a trial recruited 28 patients with Dupuytren's disease who were scheduled to receive elective surgery to remove diseased tissue from their hands. Two weeks prior to surgery, patients received a single injection of the anti-TNF drug, adalimumab, at various dose levels, or placebo. The tissue removed during surgery was then analyzed in the laboratory. Adalimumab, at a dose of 40mg, reduced expression of the fibrotic markers, α-smooth muscle actin (α-SMA) and type I procollagen proteins, at 2 weeks post injection, suggesting

anti-TNF therapy may have utility in treating early Dupuytren's disease by preventing activity of disease causing myofibroblast cells. The treatment was found to be well-tolerated. The Phase 2a study publication is available on line in the journal *EBioMedicine*, published by *The Lancet*: https://www.ebiomedicine.com/article/S2352-3964(18)30229-9/fulltext

About Dupuytren's Disease

Dupuytren's disease is a common fibrotic condition of the hand that causes the fingers to curl irreversibly into the palm, leading to discomfort, pain and loss of hand function. In severe cases, digit amputation may be necessary. The disease affects approximately 4% of the population of Western Europe and the USA. Pharmaceutical treatments are extremely limited and there are no approved treatments for preventing progression of the disease.

About 180 Therapeutics

180 Therapeutics' is a clinical-stage company with a unique scientific approach and therapeutic drug pipeline for fibrosis, based on the ground-breaking science pioneered by Sir Marc Feldmann, a prestigious Lasker Award recipient for his work which led to the discovery of the utility of anti-TNF therapeutics. The discovery of TNF as a mediator of numerous immune mediated diseases, originated from the unique approach of analyzing human disease tissue from patients with rheumatoid arthritis, to identify the key mediators of disease. This approach has been used again for the analysis of human Dupuytren's disease tissue from patients with active fibrosis to identify a novel therapeutic target. Our areas of interest include fibrosis of the liver (NASH) and the musculoskeletal system, including Dupuytren's disease. http://www.180therapeutics.com/

Company Contact
Martin Williams
mwilliams@180Therapeutics.com

Media Contact
George E. MacDougall
MacDougall Biomedical Communications
gmacdougall@macbiocom.com
781-235-3060

###