



WORLD'S FIRST GENE THERAPY STUDY FOR FATAL LUNG DISEASE PLANNED FOR CANADA

TORONTO, ON, January 12, 2005 - The world's first-ever human trial to establish the safety of cell-based regenerative gene therapy for individuals with pulmonary arterial hypertension (PAH), a fatal lung disease, was just announced at the Canadian Pulmonary Hypertension forum in King City, Ontario, following a review by Health Canada.

Pioneered by scientists at Northern Therapeutics Inc., a Canadian biotechnology company with research laboratories at St. Michael's Hospital in Toronto, Ontario, the single-centre **PHACeT** Trial (**P**ulmonary **H**ypertension: **A**ssessment of **C**ell **T**herapy), represents a landmark study which will test the benefits of genetically-modified endothelial "precursor" (stem-like) cells* harvested from the patient's own blood for the treatment of this fatal respiratory disease. Cell and gene therapy offer the potential to restore lung vascular function in severe pulmonary arterial hypertension, by repairing damaged blood vessels in the lung and possibly even inducing the regeneration of blocked arteries, resulting in reversal of the disease.

"This trial represents the first time in the world that gene therapy will be used to treat this rare but fatal lung disease that unfortunately often afflicts the young, mostly affecting women. Our preclinical research indicates that transplanting genetically engineered stem-like precursor cells into the lungs can reverse established pulmonary hypertension by regenerating small blood vessels in the lung. These findings show tremendous promise for people suffering from severe PAH, who until now, have had little hope that the pathology underlying this devastating disease could be effectively treated," said Dr. Duncan Stewart, Associate Director of Research, St. Michael's Hospital in Toronto, Dexter Man Chair and Director of the Division of Cardiology at the University of

Toronto, Director of Regenerative Medicine, McLaughlin Centre for Molecular Medicine and the Chief Scientific Officer of Northern Therapeutics.

Pulmonary Arterial Hypertension (PAH)

PAH is a rare blood vessel disorder of the lung in which the pressure in the small pulmonary arteries rises above normal levels, resulting in the narrowing and loss of small lung arteries. Eventually, the right side of the heart becomes enlarged, caused by vascular insufficiency of the lungs, leading to severe heart failure and ultimately death. While the underlying cause of the disease may be linked to a genetic abnormality in some people, others may develop PAH associated with connective tissue disease (scleroderma), congenital heart disease, the use of diet pills, HIV or numerous other diseases.

PHACeT Trial

The PHACeT trial represents a novel approach pioneered by scientists at St. Michael's Hospital in which a therapeutic gene is delivered into the lung by transplanting genetically engineered endothelial precursor cells into the lungs to engraft the small pulmonary arteries which are severely damaged in this disease. These cells can be thought of as “building blocks” for new blood vessels as well as representing small ‘factories’ for the production of chemicals that orchestrate blood vessel repair and growth.

The phase one PHACeT trial will involve up to 18 patients in total from across Canada. Although the primary endpoint is safety and tolerability, data will be collected to establish the potential efficacy of this innovative approach.

Incidence and Treatment

Despite new pharmacological approaches, PAH is nearly universally fatal. In fact, most patients continue to progress with an expected survival of only three to five years after first diagnosis. While there is no patient database available, the incidence rates from other countries suggest that PAH affects 7,000 Canadians¹, with women between the ages of 20 and 40 being most at risk.²

Lung transplantation is a final resort for some patients. However, only 20 per cent of patients receive a transplant and of those, half are expected to die due to transplant rejection within five years of transplantation.³

Economic Burden of the Disease

The disease also has a significant economic cost attached to current treatment. According to Roy Romanow's final report on *The Future of Health Care in Canada*, pulmonary hypertension treatment can cost patients more than \$100,000 a year. In some provinces, patients must exhaust all their savings, including their RRSPs, before being eligible for government aid to cover the cost of treatment.⁴

About Northern Therapeutics

Northern Therapeutics is a privately held Canadian biotechnology company whose mission is to develop a unique cell and gene therapy platform technology for the therapy of chronic and life-threatening cardiopulmonary diseases. Northern Therapeutics is the distributor for a number of United Therapeutics Corporation (NASDAQ: UTHR) products in Canada including Remodulin[®], an infusion therapy for the treatment of pulmonary arterial hypertension.

** Please note: This research does NOT involve fetal or embryonic tissue.*

References:

¹ European Public Assessment Report (EPAR): Scientific discussion on Ventavis[®] (iloprost), CPMP/1066/03, EMEA, 2003.

² <http://www.cincinnatichidrens.org/health/heart-encyclopedia/disease/pph.htm>

³ N Engl J Med. 2004 Sep 30;351(14):1425-36

⁴ <http://www.hc-sc.gc.ca/english/care/romanow/hcc0086.html>