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Prof. Andreas Fouras
Australian Lung Health Initiative

Letter of Support for the Medical Research Future Fund Frontier Health and Medical Research Program, Stage 1:

4D FUNCTIONAL IMAGING: A NEW FRONTIER IN LUNG HEALTH

Dear Prof. Fouras,

Our research group at the University of Pennsylvania is delighted to support and participate as a Project Supporting-Partner, in your proposal titled: *4D FUNCTIONAL IMAGING: A NEW FRONTIER IN LUNG HEALTH* for the Stage One component of the Medical Research Future Fund's Frontier Health and Medical Research Program.

We understand the application is led by a joint venture consortium known as the Australian Lung Health Initiative Pty Ltd (ALHI), sited in Adelaide, and to comprise of 4Dx Ltd, the University of Adelaide, the South Australian Health and Medical Research Institute (completing negotations), Monash University, the University of Western Australia, and Micro-X Ltd, as the lead Project Partners.

Your proposed Partnership offers a unique opportunity for ground breaking world-leading research and clinical application in respiratory medicine, with the clear potential to transform the health of children and adults with inherited or acquired respiratory diseases, achieve substantial economic benefit in the Australian health, business and industrial spheres, and make a truly global impact on how airway diseases can be detected, treated and monitored.

Our specific interest is in Cystic Fibrosis and its disease progression following application of gene therapeutics. We have a long-standing interest in immune responses against the CFTR gene that is expressed in the lungs following gene therapy and their implication in hampering the success of gene therapy. This pioneering technology will allow us to study in relevant animal models of CF the impact of successful expression of the CFTR and the consequences of immune cell activation on the structure and function of the airways in real time. We were the first to demonstrate the activation of CFTR specific T cells in mouse models of CF and later partnered with the UK Cystic Fibrosis Gene Therapy Consortium to study CFTR T cell immune responses in the CF subjects of their gene therapy clinical trial using liposomes to express CFTR.

We would offer expert advice to the research teams led by Prof. Parsons and Prof. Fouras on how best to design animal studies to evaluate and examine the likelihood of immune cell activation *in vivo* in response to successful CFTR gene therapy and its impact on the integrity of the CF lungs.

We are delighted to participate in this Program and excited at the significant impact this Program may have on the development and clinical translation of therapeutics for lung diseases, with an emphasis on CF.

Sincerely yours,

Maria P. Limberis