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Breathing in a new gene therapy to treat pulmonary hypertension

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Mount Sinai has partnered with Theragene Pharmaceuticals, Inc. to advance a novel airway-delivered gene therapy for treating pulmonary hypertension (PH), a form of high blood pressure in blood vessels in the lungs that is linked to heart failure. If the therapy succeeds in human clinical trials, it will provide patients for the first time with a way to reverse the damage caused by PH.

This gene therapy technique comes from the research of Roger J. Hajjar, MD, Professor of Medicine and Director of the Cardiovascular Research Center at the Icahn School of Medicine at Mount Sinai, and has been proven effective in rodent and pig animal models. PH is a deadly disease that disproportionately affects young adults and women; 58 percent of cases are found in young adults and 72 percent are women. There is currently no effective cure for PH, and about 50 percent of people who are diagnosed will die from the disease within five years.

PH is a rare (15-50 cases per million people), rapidly progressing disease that occurs when blood pressure is too high in vessels leading from the heart to the lungs. The high pressure is caused by abnormal remodeling of the lung blood vessels, characterized by a proliferation of smooth muscle cells and a thickening and narrowing of these vessels, and can lead to failure of the right ventricle of the heart and premature death. Abnormalities in calcium cycling within the vascular cells play a key role in the pathophysiology of pulmonary hypertension, along with deficiencies in the sarcoplasmic reticulum calcium ATPase pump (SERCA2a) protein which regulates intracellular calcium within these

vascular cells and prevents them from proliferating within the vessel wall. Downregulation of SERCA2a leads to the proliferative remodeling of the vasculature. This gene therapy, delivered via an inhaled aerosolized spray, aims to increase the expression of SERCA2a protein, and has been shown in rodents and pigs to improve heart and lung function, as well as reduce and even reverse cellular changes caused by PH.

"This is a devastating disease, and our work in collaboration with many laboratories across the country has allowed us to identify a specific molecular target and use gene therapy to improve cardiovascular and lung parameters in experimental models of PH. We look forward to starting first-in-human studies using this approach in affected patients," said Dr. Hajjar, the senior author of the studies, highlighting that clinical trials will be underway in the next two years. It may take several years before a product is commercially available for PH patients.

"We are excited about the potential for SERCA2a gene therapy as a new modality in treating this serious disease," said Jon Berglin, Chief Executive Officer of Theragene Pharmaceuticals, Inc. "We look forward to develop and advance this promising product into the clinic."

"This represents another critical advancement in a potentially transformative therapeutic breakthrough by Mount Sinai scientists, demonstrating our commitment to improving health outcomes. We are thrilled to be working with Theragene Pharmaceuticals, and continue to strengthen our expertise in partnering health care innovations with industry," said Erik Lium, PhD, Senior Vice President of Mount Sinai Innovation Partners, the commercialization arm of the Icahn School of Medicine at Mount Sinai.

Provided by The Mount Sinai Hospital