Value Proposition

We provide the first-ever antidotal therapy for carbon monoxide (CO) poisoning. CO poisoning is an illness caused by exposure to too much carbon monoxide, a colorless, odorless and tasteless gas. CO poisoning can lead to heart damage, permanent brain damage and even death. There are currently few treatment options with most of the therapies causing a significant portion of the patients to have long term neurological defects. Reducing the number of patients hospitalized and decreasing the amount of neurologic side effects of this condition are a pivotal, unmet clinical need. Our novel antidotal therapy will provide a portable alternative that may have significantly better outcomes over current standards of care.

Market Opportunity

CO poisoning is responsible for up to 40,000 ER visits and nearly 6000 deaths per year, making it one of the leading causes of poisoning death in the United States. The societal costs of CO poisoning are upwards of $6 billion per year.

In comparison, antidotal therapies, such as CroFab™ (BTG Pharmaceuticals) used in the treatment of 5000-7000 snake bites/year in the US, need to be stocked and immediately available before use in the ER, resulting in sales of $100 million per year. With 40,000 patients a year, our novel antidotal therapy could follow a similar model and achieve a potential market penetration of up to 5 times this size.

Competitive Landscape

The current treatments for CO poisoning include the use of high flow oxygen or hyperbaric oxygen therapy. While inexpensive, it is cumbersome and logistically challenging, as it cannot be used in the field and it only accelerates the rate of carbon monoxide elimination by a few fold. Less than 200 medical centers in the US provide hyperbaric chamber therapy, the standard of care. For critically ill patients it can be impossible. Even with the best of therapy, 20% of patients have long term neurologic deficits and 1% will die.

Our novel portable antidotal agent therapy will rapidly clear carbon monoxide within five minutes of effusion significantly improving time to reversal of CO poisoning.

Technology

Recombinant neuroglobin will be an infusible biologic agent that can be given either on site by first responders or on initial presentation to the Emergency Room. Neuroglobin is a naturally occurring human globin protein that we have modified to adjust its CO binding properties. When infused, it will immediately act as a sink for carbon monoxide, rescuing red blood cells from poisoning, enabling them to rebind and deliver oxygen. We have demonstrated proof of concept in small mammal studies and have preliminary toxicology data.

Stage of Development

We are now entering into preclinical GLP small mammal studies with GMP Recombinant Neuroglobin testing pharmacokinetics and pharmacodynamics of the agent. We have filed an Orphan Drug Application with the FDA, which, if approved, would provide patent protection benefits and a smaller sized clinical studies requirement for potential FDA approval.

IP Status

PCT Application has been filed.

Funding

NIH SMARTT Program Grant
NIH RO1 (under review)
Mark T Gladwin, MD

Division Chief, Pulmonary, Allergy, and Critical Care Medicine; Director, Vascular Medicine Institute

Dr. Gladwin has a long history of leadership of translational projects and programs, having served at the Intramural NHLBI as the Chief of the Pulmonary and Vascular Medicine Branch and as a principal or associate investigator on more than 30 human subjects protocols. He has held seven FDA INDs for the use of investigational therapeutic medications, including acetylcarnitine, nitrite, carbon monoxide, L-NMMA, and sildenafil. He has performed research successfully across all stages of the Bench-to-Bedside enterprise, from high impact bench biochemistry to drug development. He has developed and patented drugs that are at the NIH are currently licensed and in phase I-II development including inhaled nitrite for pulmonary hypertension, which is currently in phase II trial in 40 International sites with enrollment of 30 subjects to date. From a clinical trials perspective, he has been a PI on two large phase II clinical trials, the DeNOVO trial of NO therapy for acute pain crisis in patients with sickle cell disease, which successfully enrolled 150 patients at 13 Centers, and the Walk-PHASST trial of sildenafil for pulmonary hypertension secondary to sickle cell disease which successfully enrolled 700 patients in a screening study at 13 sites. He currently serves on the scientific advisory board for the multi-center trial of inhaled nitrite for Group I PAH patients. He continues to lead NIH funded translational research and training programs focused on translational medicine and pulmonary hypertension, including a PO1 entitled Vascular Subphenotypes of Lung Disease, and on two translational T32 training grants.

Dr. Gladwin's research activities focus on the discovery that the nitrite anion is a circulating storage pool for NO bioactivity (PNAS 2000) that regulates hypoxic vasodilation (Nature Medicine 2003) and the cellular resilience to low oxygen and ischemia (JCI 2005). His experience in hemoglobin and neuroglobin research (more than 150 listed publications in pubmed on the topics) form the basis for his new current studies on CO scavenging by recombinant neuroglobins.

Publications


Jesus Tejero Bravo, PhD

Research Assistant Professor of Medicine Pulmonary, Allergy, and Critical Care Medicine

Dr Terjero received his degree in Organic Chemistry at the University of Zaragoza, Spain in 1998 and earned his PhD in Biochemistry at the University of Zaragoza in 2004 with the thesis "Redesign of the coenzyme specificity of the ferredoxin-NADP+ reductase from Anabaena PCC 7119" under Prof. Carlos Gómez-Moreno and Dr. Milagros Medina. He moved to the United States in 2005 as a research fellow at the lab of Dr. Dennis Stuehr at the Cleveland Clinic, Lerner Research Institute. His work there focused on the structure and function of nitric oxide synthases. He joined the Gladwin lab at the University of Pittsburgh in May, 2009.

Publications


Jason J Rose, MD

Fellow Pulmonary, Allergy, and Critical Care Medicine

Dr Rose obtained his B.S.E. in Biomedical Engineering at the University of Michigan in 2006. In 2010, he received his M.D. from Wayne State University School of Medicine, where he worked in basic biochemical research with brain glia cells and inflammation. In 2013, he completed his Internal Medicine Residency training at Duke University Medical Center in Durham, NC. His research examined the association between an influenza gene expression model & cardiovascular outcomes under the supervision of Dr. Geoffrey Ginsburg. He also studied clinical outcomes in NSTEMI patients with LBBB at the Duke Clinical Research Institute under Dr. Christopher Granger. He joined the Fellowship in 2013. He is also a current student at the Tepper School of Business for an MBA.

Publications