

Urearetics:

Inhibiting Urea Transport to Treat Cardiovascular Complications of Chronic Kidney Disease



EXECUTIVE SUMMARY

TEAM

Jeff Sands, MD

Clinical Lead
Emory University

Janet Klein, PhD

Technical Lead
Emory University

Xiaonan Wang, MD, MS

Technical Lead
Emory University

FUNDING

\$104k Biocivity Grant

INTELLECTUAL PROPERTY

Invention disclosure on file with Emory University Office of Technology Transfer

Technology available for licensing and partnership

STATUS

Lead candidate discovery

TECHNOLOGY

The Urearetics team is developing novel inhibitors of urea transport to treat cardiovascular complications of chronic kidney disease, including uremic pericarditis, pericardial effusions, and heart failure with preserved ejection fraction (HFpEF). Currently, uremic pericarditis is treated by intensive hemodialysis (4 treatments over 5 days), and there is no therapy for uremic pericardial effusions or uremic cardiomyopathy.

MARKET NEED

Chronic kidney disease (CKD) is characterized by a gradual decline in kidney function over a period of a few months to years. There are five stages of CKD, and they are segmented based on the rate at which the kidneys filter blood (glomerular filtration rate, GFR). End-stage renal disease (ESRD) refers to the final stages of CKD (stages 4 and 5) that require either renal transplantation or chronic hemodialysis.

CKD is remarkably prevalent, with over 38% of U.S. adults over age 65 affected by CKD at any stage. In 2018, there were roughly 1,276,000 patients in the US with CKD stages 4/5, with approximately 840,000 of them developing pericardial effusions. The presence of cardiovascular disease is an important predictor of mortality in patients with CKD, as it accounts for nearly 45% of all deaths associated with CKD.

If left untreated, pericardial effusion can develop into uremic pericarditis, a major complication of ESRD that is demonstrated by inflammation of the pericardium due to the accumulation of metabolites and waste products, such as urea, due to kidney failure. Uremic pericarditis is characterized by diastolic dysfunction, left ventricular hypertrophy (LVH), and ventricular fibrosis, and it is treated with conventional hemodialysis therapy; however, uremic cardiomyopathy can persist or even worsen after conventional hemodialysis is initiated. Despite advances in dialysis treatment and improved management of hypertension, hypervolemia, and anemia, patients with CKD or ESRD continue to have myocardial remodeling, leading to an increased risk of morbidity and mortality due to cardiovascular disease.

STATUS

The Urearetics team has demonstrated proof-of-concept of their mechanism of action using a known urea transport inhibitor, dimethylthiourea (DMTU), and is currently generating compounds to be screened for efficacy. The team will advance promising compounds toward lead candidate designation by testing in *in vivo* models of uremic cardiomyopathy and pericardial effusion in mice with CKD, as well as a rat model of HFpEF.

For more information on this technology email biocivity@gatech.edu or contact:

Jeff Sands, M.D.: jeff.sands@emory.edu

Janet Klein, Ph.D.: janet.klein@emory.edu

Xiaonan Wang, M.D.: xwang03@emory.edu

Hyeon (Sean) Kim (Licensing Associate, Emory University): hyeon.s.kim@emory.edu