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Walden: targeting podocytes as linchpin for kidney function

Backed by Arch and UCB, Walden to enter the clinic next year with a mAb and small molecule targeting podocytes for kidney diseases

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Launched in October with $51 million in an Arch- and UCB Ventures-led series A, Walden aims to test its theory that targeting podocytes can make diseased kidney tissue healthy again.

Walden Biosciences Inc. President and CEO Blaine McKee and Arch Venture Partners Managing Partner Steve Gillis have a long history. The two met in the late 1990s when Gillis was CEO at Corixa Corp. and McKee was in BD at Genzyme Corp., where he spent 15 years, 1996-2011.

McKee left Genzyme following its acquisition by Sanofi (Euronext:SAN; NASDAQ:SNY) and spent three years at a Polaris-backed medical device start-up as CBO.

He then joined Shire plc in 2014-18, where Gillis was a board member. McKee said they interacted frequently.

McKee joined ImmunoGen Inc. (NASDAQ:IMGN) in 2018 as EVP and CBO but decided to leave after a trial failure in 2019. Gillis, who is chairman of Walden's board, approached McKee about the CEO position late that year, after which McKee assumed the role in January 2020.

Walden's founding science stems from the labs of Jochen Reiser, professor of medicine at Rush University's medical college and chairman of the Department of Internal Medicine at Rush University Medical Center; and Sanja Sever, associate professor of medicine at Massachusetts General Hospital and Harvard Medical School.

Both labs study podocytes, specialized epithelial cells in the kidney involved in blood filtration. If podocytes become damaged, they become less effective at filtration, which leads to proteinuria. Proteinuria is increased levels of protein in the urine and a primary indicator of kidney disease.

The two labs study different proteins involved in podocyte function. Reiser's lab studies the urokinase receptor suPAR, and Sever's lab focuses on the GTPase DMN.

High suPAR levels cause inflammation and are associated with acute kidney injury. suPAR is also involved in the pathogenesis of focal segmental glomerulosclerosis. "suPAR is produced in the bone marrow and then goes to the podocyte. When it binds to the podocyte, this results in a dysfunctional reorganization of the podocyte cytoskeleton, and they become less effective at filtration," McKee told BioCentury.

Walden is developing antibodies to inhibit circulating suPAR.

Dynamin helps podocytes form actin filaments, creating a supporting structure and glomerular filtration barrier. Loss of function of dynamin causes podocytes to become less effective at filtration.

Reiser and Sever were senior authors on a 2015 *Nature Medicine* paper that revealed that a small molecule that promotes dynamin oligomerization in podocytes led to improved kidney health and extended lifespan in mouse models of both transient and chronic kidney diseases.

Walden is developing small molecules that selectively accumulate in the kidney and activate dynamin.

Kidney disease can be split into acute and chronic, and Walden wants to tackle both.

Acute kidney injury is a sudden decrease in kidney function and can range from minor loss of function to complete kidney failure. It's often a complication of another illness, such as ischemia or infection.

"On the acute side, we see COVID-induced renal injury as perhaps one of our first indications for the suPAR program. Of patients hospitalized with COVID, 47% experience acute kidney injury," said McKee.

In an observational study of adult patients hospitalized for COVID-19 published in the *Journal of the American Society of Nephrology*, suPAR levels measured at admission were predictive of in-hospital acute kidney injury and the need for dialysis.

Walden's preliminary list of indications also includes focal segmental glomerulosclerosis, IgA nephropathy, polycystic kidney disease and lupus nephritis, which it chose based on the "scientific basis of our approach to the disease, regulatory features of the disease and competitive intensity," said McKee.

He added that the regulatory landscape has been challenging for renal disease. "Prior to 2018, for approval in renal disease, an agent had to show an improvement in glomerular filtration rate," which he says remains the gold standard but comes with many challenges.

For example, it takes about five years for a diseased kidney to show a 20% decline in GFR.

In 2018, the FDA adopted a new surrogate endpoint for orphan renal diseases: reduction in proteinuria. Walden's programs are designed to reduce proteinuria, and the company is planning to start clinical trials for both programs next year.

McKee said he is unaware of any other company working on dynamin agonism or renal-specific suPAR therapeutics.

According to BioCentury's BCIQ database, Monopar Therapeutics Inc. (NASDAQ:MNPR) is the only other company developing antibodies targeting suPAR. Its MNPR-101 is in preclinical development to treat solid tumors, and MNPR-101RIT, the same mAb conjugated to a radionuclide, is in preclinical development for solid tumors and severe COVID-19 in collaboration with NorthStar Medical Radioisotopes LLC.

COMPANY PROFILE
Walden Biosciences Inc.
Cambridge, Mass.
Technology: Small molecule DMN agonists, antibodies against suPAR
Origin of technology: Massachusetts General Hospital and the University of Miami
Disease focus: Renal
Clinical status: Preclinical
Founded: 2019 by Sanja Sever and Jochen Reiser
Academic collaborators: None
Corporate partners: None
Number of employees: 17
Funds raised: $51 million
Investors: Arch Venture Partners, UCB Ventures, Huizenga Capital Management
CEO: Blaine McKee
Patents: 11 issued; 6 covering suPAR and 5 covering DMN