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EMERGING COMPANY PROFILE

Cardior: targeting microRNAs to treat heart failure

BY DANIELLE GOLOVIN, STAFF WRITER

Cardior plans to build on early clinical data for its antisense oligonucleotide in heart failure patients by moving the RNA therapy into niche indications where it believes the product can help dysfunctional hearts pump more efficiently.

Cardior Pharmaceuticals GmbH spun out of Hannover Medical School in 2016 to develop non-coding RNA-based therapeutics and diagnostics for cardiovascular diseases. Its lead candidate, CDR132L, is a locked nucleic acid (LNA) antisense oligonucleotide inhibitor of miR-132 to treat heart failure.

miR-132 disrupts signaling pathways that regulate key cardiovascular processes including hypertrophy, contractility and autophagy by blocking transcription of targets such as FOXO3 and ATP2A2. The microRNA is activated and upregulated in cardiomyocytes under and after various forms or cardiac stress.

"Once we block miR-132, we can normalize those pathways and make a dysfunctional heart pump more efficiently and reverse the pathological remodeling process," said CSO Thomas Thum.

Thum believes Cardior's preclinical data — in which it saw reduced cardiac mass and ventricular dilation and improved ejection fraction — should translate to humans well because miR-132 has a 100% identical nucleotide sequence between the species.

In November, the Cardior team published data from a Phase Ib study showing CDR132L led to early signs of improved cardiac function in heart failure patients. Two doses of the LNA therapy given four weeks apart led to a 23% median reduction of the heart failure marker NT-proBNP vs. a 0.9% increase in the control group.

Cardior plans to begin a Phase II trial testing a two dose regimen in about 300 heart failure patients by mid-2021. It expects the double-blind, placebo-controlled trial to run for three years.

"We would like to start with niche indications of patients that can be easily identified — patients that develop heart failure within weeks after myocardial infarction," Thum said. "We see this as an entry point to broaden, later on, our clinical development into more chronic heart failure patients."

COMPANY PROFILE
Cardior Pharmaceuticals GmbH

Hannover, Germany

Technology: Non-coding RNAs

Origin of technology: Hannover Medical School

Disease focus: Cardiovascular

Clinical status: Phase I completed

Founded: 2016 by Thomas Thum, Sandor Batkai, Claudia Ulbrich, Ascenion GmbH, Max Planck Innovation

University collaborators: Harvard Medical School, Washington University School of Medicine, University of Mississippi Medical Center, University of Lorraine, Hannover Medical School

Corporate partners: None

Number of employees: 20

Funds raised: €25 million ($30.6 million)

Investors: Life Science Partners, BioMedPartners, Boehringer Ingelheim Venture Fund, Bristol Myers Squibb, HighTech Founders Fund

CEO: Claudia Ulbrich

Patents: 5 issued patents covering composition of matter and use of the lead compound and miR-132 target as well as technology for several other non-coding RNA therapeutic targets and diagnostic markers for cardiovascular diseases

In future studies, Cardior plans to deliver CDR132L to chronic heart failure patients on a monthly basis for one year, then assess long-term safety and efficacy. "What we know from large animal studies is that even if we stop the treatment for three months, we still see very beneficial effects."

The company developed a system to monitor the plasma level of miR-132 and can deliver additional injections on an as-needed basis after the first year of treatment. The company also aims to investigate the use of miR-132 as a companion diagnostic in the Phase II trials.

At least one other company, Regulus Therapeutics Inc. (NASDAQ:RGLS), is developing a miR-132 inhibitor. Its therapy is also an antisense oligonucleotide, and is in preclinical testing for non-alcoholic steatohepatitis (NASH).

Cardior CEO Claudia Ulbrich says CDR132L may have the potential to treat other indications, but for now, Cardior is focused on cardiovascular diseases. The company is developing a second compound to treat an undisclosed cardiovascular orphan disease.

Cardior aims to close a series B round by mid-2021 for which Ulbrich said the company hopes to attract a new lead investor as well as a U.S. investor.

The heart failure field has seen a series of setbacks, with the most recent being omecamtiv mecarbil from Cytokinetics Inc. (NASDAQ:CYTK) and partners Amgen Inc. (NASDAQ:AMGN) and Servier, but there are at least 18 programs in the clinic. Five programs — all involving new mechanisms — are expected to read out over the next year.

RNA therapies are showing promise in other indications related to cardiovascular health as well. Last year, the European Commission approved antisense oligonucleotide Waylivra volanesorsen to treat familial chylomicronemia syndrome and this month siRNA therapy Leqvio inclisiran from Novartis AG (NYSE:NVS; SIX:NOVN) to treat hypercholesterolemia or mixed dyslipidemia.

TARGETS

ATP2A2 (SERCA2A) – ATPase Ca++ transporting cardiac muscle slow twitch 2
FOXO3 (FOXO3a) – Forkheadbox O3
miR-132 – MicroRNA-132
NT-proBNP – N-terminal pro-brain natriuretic peptide

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