

Newco News

Cardior takes heart from preclinical miRNA data

By Cormac Sheridan, Staff Writer

Cardior Pharmaceuticals GmbH will have a full dance card when it shows up in San Francisco for the JP Morgan Healthcare Conference this week. The young German biotech is attracting plenty of big pharma interest for its lead program, a microRNA (miRNA)-targeting oligonucleotide in development for heart failure, which is entering a first-in-human phase Ib trial in patients shortly.

Although miRNAs have largely fallen out of favor as drug targets, Hanover-based Cardior hopes to lead a resurgence in the field. “I think we have learned a lot from all the errors the others have made,” the firm’s co-founder and chief scientific officer, Thomas Thum, told *BioWorld*. Thum is director of the Institute of Molecular and Translational Therapeutic Strategies at Hannover Medical School and an authority on the role of miRNA regulation of gene expression in cardiac disease.

The company’s lead molecule targets mir-132, which regulates the remodeling of cardiac tissue that follows a heart attack.

Earlier efforts to target miRNAs in a variety of indications were undone by poor chemistry and delivery challenges. Cardior is employing a third-generation chemistry, based on locked nucleic acid technology, which avoids the toxicities seen with previous approaches.

“This is, I think, relatively well known in the field. There are less side effects than with the older chemistries,” Thum said. But what has really sparked interest in the company’s lead program is the extraordinarily extensive preclinical dataset it has generated. It has conducted studies in some 200 pigs, the gold-standard animal model in cardiology, given the anatomical similarities between human and porcine hearts. “It’s probably the world’s largest ever pig study in the field,” he said.

That work, which has yet to be published, has enabled the company to develop a rich understanding of its drug’s profile, its mode of action and its dosing requirements. Although remodeling is a compensatory mechanism that decreases stress and assists the functioning of a damaged heart, excessive tissue growth or hypertrophy leads to heart failure. It is driven by two miRNAs, mir-132 and mir-212, whose expression is induced in hypertrophic conditions, resulting in the down-regulation of a transcription factor, FoxO3, which normally keeps hypertrophy in check. “What we block is this pathological remodeling,” Thum said. “We also block fibrosis.” The drug also has effects on cardiomyocyte contractility.

Patients who have experienced myocardial infarction will receive two doses of the drug. It is administered intravenously. “We know that a good percentage of the drug ends up in the heart,” Thum said.

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Thomas Thum
Co-founder/CSO, Cardior Pharmaceuticals

Cardior was spun out from Hanover Medical School in 2016 and raised €15 million (US\$17.1 million) in series A funding in 2017. Its investor roster includes Bristol-Myers Squibb Co., of New York, and the venture capital arm of Boehringer Ingelheim GmbH, of Ingelheim, Germany, as well as Biomedpartners, Life Science Partners and High-Tech Gründerfonds. Its scientific advisory board includes Arthur Levin, a pioneer of oligonucleotide-based drug development while at Ionis Pharmaceuticals Inc., Santaris Pharma (now part of Roche Holding AG) and Miragen Therapeutics Inc., who is now based at Avidity Biosciences LLC, of La Jolla, Calif. “He’s advising us on toxicity and drug delivery strategy,” Cardior CEO and co-founder Claudia Ulbrich told *BioWorld*.

It’s more than a decade since the first miRNA-targeted drug entered the clinic, but progress since then has been distinctly patchy. Miravirsin (SPC-3649), which Santaris developed to target mir-122 to prevent hepatitis C virus replication in the liver, was first into the clinic, although it failed to get beyond phase II. In 2017, Regulus Therapeutics Inc. discontinued development of RG-101, which also targeted mir-122, following the development of jaundice in a number of patients. Mirna Therapeutics Inc. halted a phase I cancer trial of its miRNA mimic, MRX-34, in 2016 because of severe immune reactions. It subsequently completed a reverse merger with Cambridge, Mass.-based synthetic biology firm Synlogic Inc. (See *BioWorld Today*, Sept. 22, 2016.)

Although all but deserted by investors – its market cap is less than \$10 million – La-Jolla-based Regulus still has a live collaboration with Paris-based Sanofi SA. The pharma firm recently took on development responsibility for RG-012, a miR-21-directed oligonucleotide in phase II development for Alport syndrome, an inherited kidney condition. Miragen, of Boulder, Colo., is still in the game, with three clinical-stage drug candidates, cobomarsen (MRG-106), remlarsen (MRG-201) and MRG-110, in development for hematologic cancers, fibrosis and heart failure, respectively. The latter drug is the subject of an alliance with Les Laboratoires Servier SAS, of Suresnes, France. ♦