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Emerging Company Profile: Chinese siRNA Specialist Sirius All In On Cardiovascular Disease

Potential Once-Yearly Regimen

by Dexter Yan

Sirius has joined the race to develop China's first homegrown RNAi therapy and is backing its assets' potential in chronic cardiovascular disorders, including possible once-yearly dosing, the venture's CEO tells *Scrip* in an interview.

The first days of the new year witnessed multinationals including *Novartis AG* tie up with developers of small interfering RNA therapies from China, once regarded as a backwater for R&D into such a novel drug modality. (Also see "*Asia Deal Watch: Argo Partners RNAi Programs With Novartis In Major Biobucks Pact*" - Scrip, 8 Jan, 2024.) (Also see "*BI Gets Down To Business Early With Trio Of Pacts*" - Scrip, 5 Jan, 2024.)

Sirius Therapeutics, one of the emerging Chinese siRNA-focused contenders, has also been in the foreground in the race to globalize China's first homegrown RNA interference therapy.

With its US-based team responsible for discovery activities and its China team leveraging local clinical resources, Sirius stepped into the spotlight two years after its founding in 2021. Last October, the

Key Takeaways

- Sirius Therapeutics, a Chinese developer of siRNA therapies, is taking aim at cardiovascular diseases with a potential once-yearly treatment regimen.
- Its lead asset SRSD107, a Factor XI

fledgling biotech announced the closing of a $60m series B funding, taking the total raised in venture capital rounds to roughly $100m.

One key attraction to investors is a potential breakthrough in the design of RNA sequences and chemical modifications to oligonucleotides, Sirius CEO Qunsheng Ji told *Scrip* in an interview.

inhibitor for the prevention and treatment of thromboembolic disorders, entered the clinic in Australia in early January.

- SRSD101, a PCSK9 inhibitor for dyslipidemia, progressed into the clinical stage in China in November 2023.

Although the venture has yet to report any results from clinical trials, outcomes from preclinical primate studies with its lead assets have indicated the potential for a dosing frequency of just once a year.

"We have confidence in [the forecast based on the modeling]," Ji said, adding Sirius has a "highly efficient" RNAi platform he expects to spawn "a cascade" of preclinical candidates.

All In On Cardiovascular

To take full advantage of its RNAi technology's edge in dosing frequency, Sirius is currently focusing on chronic cardiovascular diseases with large patient populations.

"It is the best use for the siRNA modality," Ji said. "There are huge populations of patients with cardiovascular diseases, but few novel drugs have been developed in the past few years." Sirius's all-in approach hinges on the long-term treatments required in the area.

So far, the venture has disclosed details of two of its most advanced programs. In early January, an investigational new drug application for SRSD107 was approved in Australia, paving the way for the therapy to enter its first Phase I study worldwide, the executive said.

The Factor XI inhibitor targets the prevention and treatment of thromboembolic disorders and preclinical *in vivo* studies demonstrated a near 100% reduction of Factor XI levels for up to six months, without bleeding events after a single subcutaneous dose, the firm noted.

While SRSD107 stands a good chance of becoming the world's first RNAi therapy targeting Factor XI, it would face competition with more clinically advanced candidates globally, such as the small molecule Factor XIa inhibitors asundexian from *Bayer AG* and milvexian from *Bristol Myers Squibb Company*/*Johnson & Johnson*.

There is also a dual Factor XI/XIa inhibitor antibody, abelacimab, being developed by *Anthos*

Therapeutics Inc. and all three of these front-runners have already progressed into Phase III.

However, Ji told *Scrip* that Sirius plans to develop SRSD107 with a six-month or even potentially annual dosing regimen for patients on chronic treatment, and this along with related improved compliance is seen as conferring a possibly competitive upper hand. Abelacimab is being developed as a monthly injection, while asundexian and milvexian are administered orally daily.

"SRSD107 will be aimed at the global market," Ji added.

PCSK9 Inhibitor

As for the second program, SRSD101 is a PCSK9 inhibitor for dyslipidemia and an IND application was cleared in China in November 2023. According to Sirius, the durability of its pharmacology and safety profile exhibited in preclinical studies suggests the asset has the potential to be a new-generation therapeutic for the disorder.

Ji disclosed it will be locally developed for the China market, where the PCSK9 inhibitor space is becoming increasingly crowded. In August last year, Novartis/*Alnylam Pharmaceuticals Inc.*'s Leqvio (inclisiran) was approved in the country as the first-in-class, PCSK9-targeting siRNA therapy.

Previously, three PCSK9 antibodies from *Amgen, Inc.*, *Sanofi*/*Regeneron Pharmaceuticals, Inc.* and *Innovent Biologics, Inc.* had received approvals in China.

New, domestically-originated class entrants are also appearing on the horizon. *Jiangsu Hengrui Medicine Co., Ltd.*, *Shanghai Junshi Biosciences Co., Ltd.* and *Akeso Inc.*/*Dawnrays Pharmaceutical (Holdings) Limited* all filed new drug applications for their PCSK9 antibodies in the first half of 2023.