Sirnaomics
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Sirnaomics: a unique, clinical-phase RNA therapeutic innovator on the global stage

A pipeline of drug candidates includes two lead products that show promise in oncology and fibrosis applications.

Sirnaomics is a unique proposition. As the first clinical-stage RNA therapeutic company to have a strong presence in both the United States and China, Sirnaomics is poised to improve outcomes in therapeutic areas such as oncology and fibrosis with a pipeline of prospects built on proprietary delivery technology platforms able to deliver siRNAs and mRNA in vivo for novel RNA therapeutics.

In recent years, Sirnaomics has raised $280 million across series D and E rounds and its initial public offering (IPO), enabling it to grow into an organization with 186 employees, most of whom work in research and development (R&D). Sirnaomics raised the money to advance a pipeline of drug candidates underpinned by its polypeptide nanoparticle (PNP) and GalNAc (N-Acetylgalactosamine) technology platforms (Fig. 1).

PNP offers high delivery and packaging efficiency, validated safety, simple and stable formulation, and the ability to target beyond the hepatocytes of the liver. Those attributes led to PNP being used in the first positive phase 2a clinical trial of RNAi technology in a cancer indication. The GalNAc platform is made up of two approaches: GalAhead, which conjugates GalNAc moieties to unique RNAi trigger structures; and the peptide docking vehicle, which conjugates GalNAc moieties to a small peptide that connects up to two siRNAs.

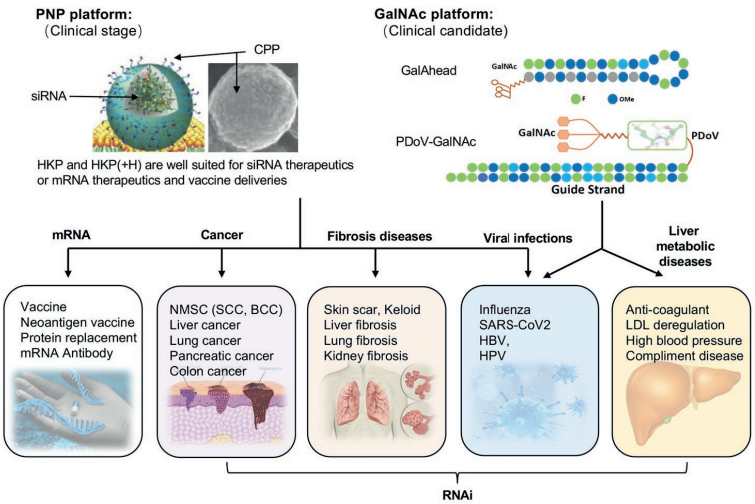

Fig. 1 | Delivery technology platform and therapeutic areas. The PNP and GalNAc platforms enhance siRNA and mRNA deliveries. BCC, basal cell carcinoma; GalNAc, N-Acetylgalactosamine; HBV, hepatitis B virus; HKP, histidine-lysine co-polymer; HPV, human papilloma virus; LDL, low-density lipoprotein; NMSC, non-melanoma skin cancer; PNP, polypeptide nanoparticle; SCC, squamous cell carcinoma.

Validating the polypeptide nanoparticle platform

The PNP delivery platform underpins Sirnaomics' lead candidates STP705 and STP707. Both STP705 and STP707 are made of two siRNA oligonucleotides that hit transforming growth factor beta 1 (TGF-β1) and cyclooxygenase 2 (COX-2) mRNA, gatekeeper targets for oncology and fibrosis. TGF-β1 regulates a range of cellular processes, including proliferation, and COX-2 is a proinflammatory and proliferative mediator. Using PNP, Sirnaomics developed a locally administered formulation for direct administration to diseased tissue (STP705).

In a phase 2 cutaneous squamous cell carcinoma in situ (isSCC) trial, Sirnaomics showed that STP705 silences expression of the two targets, leading to the suppression of cellular proliferation, tumor progression and development. Within the two high dose cohorts, 90% of subjects experienced complete histological clearance, encouraging Sirnaomics to move into a phase 2b clinical trial in the US in May 2021.

The US study, as well as a clinical trial in China, will evaluate the two most efficacious dosing regimens identified in the earlier program against placebo in up to 100 adults with isSCC. Sirnaomics expects to have initial data in the second half of 2022. In parallel, Sirnaomics is developing STP705 for use in basal cell carcinoma, an indication in which it has delivered phase 2 data, and pursuing an earlier-stage opportunity in the treatment of fat sculpting. A phase 1 fat sculpting—the cosmetic removal of excess fat cells—trial is scheduled to start in 2022.

Sirnaomics' other clinical-phase candidate, STP707, is in phase 1 testing in the treatment of solid tumors and a rare form of liver fibrosis. In common with STP705, STP707 consists of two siRNA oligonucleotides that target TGF-β1 and COX-2 mRNA. STP707 uses a different carrier peptide and is given intravenously, opening up opportunities to treat solid tumors and fibrotic liver diseases such as primary sclerosing cholangitis (PSC).

Expanding the pipeline

The two lead clinical candidates are the tip of a broad pipeline. Sirnaomics is running preclinical tests of 16 other products, including candidates based on its PNP and GalAhead delivery platforms. The lead GalAhead candidate is STP122G, which targets coagulation factor XI. STP122G triggered a long-lasting target knockdown effect and suggested a strong therapeutic benefit in preclinical tests, leading Sirnaomics to aim to file an investigational new drug (IND) application targeted for the second half of 2022.

The IND for STP122G will be the first of a series of filings for candidates based on the GalAhead platform. Sirnaomics has demonstrated that PNP can deliver siRNAs to the lungs when administered intravenously. In the first half of 2023, Sirnaomics plans to file an IND for a COVID-19 candidate that uses the PNP to deliver siRNAs against two highly conserved sequences present in most coronaviruses, including the Omicron and Delta variants of SARS-CoV-2 as well as the 2003 SARS virus. More filings will follow later in 2023.

The growth of Sirnaomics' pipeline is supported by its reproducible process for generating candidates and investment in a fill-and-finish facility in Guangzhou, China. Working out of the facility, Sirnaomics will be able to produce around 50,000 vials of lyophilized human injectables, giving it enough capacity to support its current clinical development plans.

Having laid those foundations, Sirnaomics is set to advance quickly in 2022 and 2023, with data readouts on STP705 and STP707 scheduled for the coming months ahead of the potential roll out of clinical trials of the lead candidate globally next year. The data drops will come amid a series of IND filings that will drive the rapid expansion of Sirnaomics' early-phase pipeline, positioning the Sino-American biotech to cement its status as an RNA therapeutic innovator on the global stage.

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