ENDPOINTS NEWS

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**By Lei Lei Wu**

After co-founding two biotechs off virus-based therapies, one for pain and one for cancer, Ken Greenberg decided to go in a different direction for his newest biotech, SonoThera.

Based out of San Francisco, SonoThera announced Monday morning that it raised $60.75 million to develop new gene therapies — but delivered by ultrasound, which Greenberg says can address the major challenges facing more conventional viral gene therapies.

Greenberg previously co-founded Coda Biotherapeutics, which is developing an adeno-associated virus-based therapy for pain and Oncorus, which wants to use an oncolytic virus against cancer but laid off just under 20 employees last week.

"I've been working in the gene therapy space for about 20 years now. And during that time, the majority of the work was with viral vectors, whether it's AAV or [lentivirus], or herpes, or adenovirus, and as well as some non-viral systems … I got a good feeling for where things are working and where they don't, and where the shortcomings are of the current modalities that are used," he told Endpoints News.

SonoThera's Series A was led by ARCH Venture Partners, followed by the venture arms of a number of big companies — Illumina, Johnson & Johnson and Eli Lilly — and Medical Excellence Capital, Vertex Ventures HC

(separate from Vertex Pharmaceuticals), Alexandria Venture Investments, Lifespan Investments, Formic Ventures, Foothill Ventures and Wilson Sonsini.

The biotech was founded by Greenberg; Michael Davidson, the CEO of NewAmsterdam Pharma and co-founder of Corvidia Therapeutics, which Novo Nordisk bought in 2020 for $725 million; and Steve Feinstein of Rush University, who previously invented diagnostic imaging agents and will serve as SonoThera's CSO. Davidson is the chairman of SonoThera's board, where ARCH's Steven Gillis is now also a member.

University of California-Berkeley's David Schaffer, who also co-founded 4D Molecular Therapeutics, serves as a scientific advisor to the fledgling biotech.

Traditional gene therapies that are delivered in virus vectors have run into safety issues, including patient deaths, and approved therapies are pricey. Two weeks ago, the FDA approved Hemgenix, CSL's gene therapy for hemophilia B, which the company then priced at $3.5 million per treatment, making it the most expensive single-dose therapy in the US.

The size of the gene delivered is also limited by the size of the viral vector. AAV vectors, for instance, can carry max payloads of 4.7 kilobases, which limits what diseases they may be able to address. And because they use viral vectors, gene therapies can only be dosed once. After that, the body develops an immune response to the virus.

A plethora of new biotechs have been scurrying to develop alternative options that they say can address the limitations of the earlier gene therapies. Spanish biotech SpliceBio uses two AAVs to deliver bigger genes and is developing treatments for a rare eye disease. Hub-and-spoke startup Replay, led by Sangamo's former R&D chief Adrian Woolfson, uses an HSV vector which it says can hold bigger payloads.

Vector BioPharma touts a "gutless adenovirus" that it says can overcome the size limitation, immune response, and safety concerns. Deerfield-backed Apertura Gene Therapy is developing custom AAVs that can get into more difficult-to-reach organs, like the brain and kidney. And like SonoThera, Code Biotherapeutics is working on a non-viral option.

Greenberg said that SonoThera's platform can take on all four of what he sees are the main challenges of current gene therapies — the immune response, payload cap, cost, and choice of organ system. SonoThera co-infuses ultrasound contrast agents with DNA through an IV, and then uses an ultrasound probe at target organs where the acoustic energy disrupts the cell membrane to allow the genetic payload to enter into the cell and nucleus. Greenberg noted that since naked DNA degrades very quickly, the treatment and ultrasound happen "within the order of minutes."

SonoThera's new cash infusion will be used to spur preclinical development and help the biotech do the work needed to identify a lead candidate. He noted that SonoThera wanted to pick a lead program "where we can be unique in doing delivery to areas that others are simply challenged by, or our therapeutic will have features that we think will make it superior to others," though he declined to say anything further.

The biotech will also use the new money to build out its team. It currently stands at 13 full-time employees with nearly just as many consultants, but Greenberg hopes to bring that up to 20 employees by the middle of next year.

As for getting into the clinic, the biotech still has a ways to go. Greenberg hopes that SonoThera's first Phase I trial will be in 2025.