Timmerman Report

Blazing a Trail With High-Tech Treatments of the Future

By Tim Hay / June 5, 2018

Pear Therapeutics is a company fortunate enough to describe its work and its accomplishments with superlatives like "first" and "only."

That's because in the past five years, as hundreds of thousands of mobile app developers raced to offer health and wellness apps that can be marketed without regulatory approval, Pear ran in the opposite direction. The company engaged a regulatory agency that many in the medical-technology business have long criticized for being risk-averse, unpredictable and poorly equipped to evaluate a new generation of digital medical products.

Now Pear Therapeutics is the first—and only—company in the world that can say its software has been cleared by the Food and Drug Administration to treat a disease with efficacy claims.

"We actually want to be the first, second and third …" company to make that claim, Chief Executive Dr. Corey McCann said.

"We believe there are 50 different indications that present an opportunity to redesign standards of efficacy. There are opportunities in oncology, cardiovascular and respiratory. Going forward, we'll act like the Genentech of prescription digital therapeutics."

Running in the opposite direction of the herd can be exhilarating, but also scary, said one of Pear's lead investors, Andy Schwab, a managing partner with 5AM Ventures, which has been backing Pear since its earliest days.

"(Approaching the FDA) was risky," he said. "There's no playbook here. It was walking into a potential lion's den. We didn't know how they'd respond."

They responded, he said, by "leaning toward innovation," and evaluating something new with its existing trial structures.

The Pear Therapeutics Pipeline

Pear Therapeutics makes patient-facing smartphone apps and Web interfaces for physicians, some of which are meant to be used in conjunction with prescribed medication and others that will be marketed as monotherapies, or standalone software offerings, with proven efficacy.

In September 2017, the FDA approved the company's reSET application to treat alcohol, cocaine, marijuana and stimulant abuse. The app delivers cognitive behavioral therapy to treat substance abuse, which the FDA defines as "when an individual's recurrent use of alcohol and/or drugs causes clinically and functionally significant impairment, such as health problems, disability, and failure to meet major responsibilities at work, school or home." ReSET is intended to increase abstinence from substance abuse and boost retention in outpatient therapy programs.

Also in Pear Therapeutics' pipeline is reSET-O, a drug-and-software combination to treat opioid addiction and the first piece of software granted Breakthrough Designation by the FDA. ReSET-O is currently under FDA review.

Sandoz, Novartis' generics and biosimilar division, has partnered with Pear to commercialize both reSET and reSET-O.

Pear is also developing a monotherapy for insomnia with comorbid depressive symptoms called 003, which is currently in the submission stage, McCann said.

Pear has also partnered with Novartis on Thrive, a software-and-drug combination meant to treat schizophrenia, and which is in the proof-of-concept stage. The company also has a partnership with Novartis/NIBR for development of an multiple sclerosis product.

The company's earlier stage assets include treatments for post-traumatic stress disorder and generalized anxiety disorder.

Clinical Trials

How does the FDA's Center for Devices and Radiological Health evaluate the efficacy claims of software?

According to Schwab of 5AM Ventures, "They evaluated the data as (they would for any) therapeutic. (The process) was somewhere between a medical device and a drug pathway. It was a bit of a hybrid between a PMA, a 510(k) and an NDA. It was none of those specifically, but a hybrid. All of us are figuring this out on the fly."

According the FDA's own description, the agency reviewed data from a multi-site, unblinded 12-week clinical trial of 399 patients who received either standard treatment or standard treatment with the addition of a desktop-based version of ReSET which could be accessed at the clinic or at home.

"The data showed a statistically significant increase in adherence to abstinence for the patients with alcohol, cocaine, marijuana and stimulant SUD in those who used reSET, 40.3 percent, compared to the patients who did not, 17.6 percent."

The clinical endpoint — abstinence — was verified with urine tests, McCann said.

ReSET-O, in development with Novartis to treat opioid addiction, has demonstrated in clinical trials it improves abstinence and increased program retention when used together with opioid replacement therapies, according to a report on Pear Therapeutics' website.

Three separate randomized clinical trials with a total of 465 patients completing outpatient buprenorphine or methadone maintenance treatment for opioid use disorder received standard face-to-face treatment or reduced standard treatment with reSET-O. Abstinence was again measured by urine analysis and self-reporting, according to Pear.

Patients in the trial received either the current standard of care or reSET-O with limited clinician exposure. ReSET-O plus pharmacotherapy increased abstinence, reduced dropout rates, and decreased number of required clinician interventions, materials from Pear said.

Thrive, which will be offered by Novartis alongside medication in a bid to better treat schizophrenia, is undergoing trials now. The software will offer real-time interventions targeting positive symptoms of schizophrenia including hallucinations and delusions and provide support for schizophrenia-related mood disorders.

Thirty-three patients on anti-psychotic medications were given access to Thrive and their symptoms were evaluated for 30 days. After 30 days of therapy, patients showed an average 8% reduction in Positive and Negative Syndrome Scale (PANSS), which is how the symptoms of the condition are assessed. Patients interacted with the app an average of 5.2 times per day, and 63% of the use was initiated by patients, materials from Pear said.

"Thrive works kind of like a choose-your-own adventure book," McCann said. "When patient reports symptoms he/she goes through (various levels of digital) treatment options to learn coping skills."

Pear's academic partners are also conducting trials of the software. According to materials from the company, a three-year multi-site/multi state study is underway in which more than 400 patients with schizophrenia will receive Thrive for 6 months of treatment post-discharge from an episode requiring hospitalization.

The Future

Pear Therapeutics, which has raised more than $70 million in venture backing, and has also been funded by Arboretum Ventures, Temasek Holdings, Jazz Venture Partners, Bridge Builders Collaborative, EDBI and other investors, will be a cornerstone of the pharmaceutical business a decade from now, Schwab said.

Their success, he said, will be determined by the strength of its partnerships and its adoption by pharma giants.

Whatever ultimately happens with the digital therapeutics offered by Pear, the company is already contributing to the new regulatory framework being built for the high-tech treatments of the future.

Pear is one of nine companies — a group that also includes Apple, Fitbit, Johnson & Johnson, Phosphorus, Roche, Samsung, Tidepool and Verily — that are taking part in the FDA's Pre-Certification program, which is designed to spur innovation. The agency aims to establish a standard of excellence for different types of technology developers.

McCann is unique among company founders, and Schwab differs appreciably from other investors, many of whom have gotten behind health and fitness applications specifically because they don't require the painstaking regulatory work that Pear Therapeutics is engaged in.

"We're data-driven, both Corey and I," Schwab said. "So many of the consumer apps have died off by now. We really want to prove in clinical trials we're effective in treating disease. We want to prove it with data."