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Big Data: CT bioscience companies use AI to speed up life-saving drug discoveries



BioXcel Therapeutics CEO Vimal Mehta PHOTO STEVE LASCHEVER

BY NATALIE MISSAKIAN
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New Haven's BioXcel Therapeutics has been a company for only three years, yet it's on track to have its first commercial drug by the end of 2021 — a dissolving film that's similar to a mouthwash strip and can quickly calm agitated patients.

"We went from first-in-human [dosing] to completion of the phase 3 trial in a 19-month time period, which is unheard of in our industry," says CEO Vimal Mehta, who announced the drug's successful phase 3 trial results in July.

In fact, industry experts say it typically takes 10 to 12 years, and as much as $2.6 billion, to bring a new drug from lab to market. And that's only if that drug is one of the few that make it all the way through clinical trials.

But BioXcel is one of a growing number of drug companies trying to slash that timeline by more than half — and increase the return on their R&D investment — by using artificial intelligence and machine learning to assist with drug development.



The company, which spun off from data analytics firm BioXcel Corp. in 2017, uses proprietary machine learning algorithms to sift through tens of millions of pages of scientific research hunting for older drugs that have been overlooked or discarded, but can be repurposed to treat new diseases.

Mehta says there are more than 5,000 new research papers published in medical journals every day, while one study shows the average scientist can read only 314 in an entire year.

"Even if you're a Nobel laureate you can't keep all of that information in your head. It's humanly impossible," he says. "With a machine we can grind 40 million to 50 million publications in a few hours, literally."

By focusing on drugs that have already been found safe in human testing, BioXcel saves time by jumping directly into later-stage clinical trials.

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Its agitation drug is a reformulated version of a 20-year-old Pfizer drug, marketed under the brand name Precedex, that had previously been used as an intravenous sedative in the operating room.

Growing trend

Nationally, the number of AI-focused biotechs is growing. In 2014, there were only 30 U.S. biotech startups claiming to use sophisticated AI platforms for drug research and development; today there are 150, according to Deep Knowledge Analytics, which has studied the trend.

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companies or tech firms, according to DKA.

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While there's currently no FDA-approved drug on the market developed solely using AI, the technology has the potential to revolutionize the drug industry over the next five to 10 years, says DKA Director Alex Creshnev.

He says companies are using AI not only to find new disease treatments, but also to design clinical trials, predict their outcomes and even monitor how well their commercial products are performing with patients.

"In the long run, when we collect more data about biology itself, when we know all of the biochemical processes, genetic patterns and all that, AI will be able to model the entire cellular systems and even organisms," says DKA's Creshnev. "When this becomes reality, we will be able to develop drugs without animal models, and much faster and better."

BioXcel isn't the only New Haven area drug company leveraging AI. Guilford's AI Therapeutics, a company founded by Connecticut serial entrepreneur Jonathan Rothberg, says it uses artificial intelligence to mine clinical, genomic and literature-based data to identify drug candidates that have already demonstrated evidence of clinical safety in patients. The computer then matches them with diseases for which they are likely to be effective.

The company has already identified four drug candidates to treat diseases such as lymphoma, leukemia and amyotrophic lateral sclerosis (ALS).

One of its drugs, apilimod, has shown promising anti-viral activity against COVID-19 and is now in human testing, says Dr. Murat Gunel, a Yale neurosurgeon who chairs the company's scientific advisory board.

Meanwhile, BioXcel's sister company, InveniAI, also based in Guilford, has used its AI platform, AlphaMeld (which discovered BioXcel's agitation drug before the two companies split from their parent) to help companies like Alexion, Takeda, Axcella and others find new drugs.

InveniAI also inked a partnership this summer with drug giant GlaxoSmithKline to help its consumer health division stay abreast of new innovations.

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Kant.

The company has just started working with a Japanese biopharma to build out a pipeline of new drugs to treat gut-related disorders, he says.

Connecting the dots

Experts say one of the biggest benefits of AI is the potential to improve the industry's high failure rate, which can lower drug costs since the losses are often baked into the pricing of new pharmaceuticals. Industry statistics show 90 percent of experimental drugs fail in clinical trials.

"Even if you can move the needle 20 to 30 percent, that's significant in terms of bringing more drugs to the market at a faster pace — and obviously at a reduced cost because now your probability of success has gone up," says Kant.

Kant says machine learning can improve the odds not only by predicting the diseases for which a drug is most likely to be effective, but also by alerting companies early on to potential safety concerns that could sink its chances for approval.

For instance, he says InveniAI helped Centrexion, a Boston biotech founded by retired Pfizer CEO Jeff Kindler, to rule out any safety issues and find the best indications for three of its preclinical pain drugs before the company invested millions to advance them into clinical trials.

Pharma giant Eli Lilly has since paid Centrexion $47.5 million upfront for the licensing rights to one of those drugs, a non-opioid treatment for chronic pain.

While AI won't replace human expertise, it can help detect patterns and come up with hypotheses that aren't always apparent, says AI Therapeutics' Gunel.

He says the company's AI platform, Guardian Angel, turned up three very different diseases as likely matches for its drug apilimod: lymphoma, ALS and the Ebola virus.

"That initially makes no sense," he says. "How can you have a drug that can be important for cancer, be important for neurodegeneration and be important for viral infection?"

The research team later determined that the drug played a role in the cell's recycling and garbage removal system, which impacts all three of those diseases.

It began human testing on the drug as a possible COVID-19 treatment this summer after discovering that the virus used the very same pathway as a means of infecting cells.

"And AI predicted this [antiviral activity] before any other experimental evidence," says Gunel. "That's the beauty of the platform. It makes those connections that are not immediately obvious. It gives you the lead, but then you have to follow the lead."

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While acknowledging its promise, some caution that AI is not a magic bullet for the drug industry. One major challenge is the lack of quality data and incomplete scientific understanding, says Derek Lowe, a drug discovery researcher based in Boston who writes a blog about the industry.

"We have a lot of questions for which we don't have enough data, or for which the answers are not in the data that we have," he says. "We simply don't know enough about human biology and the biology of disease."

For example, he says, no machine learning program is going to find a cure for Alzheimer's, because scientists still don't understand what causes the disease.

Biotech leaders like Mehta and Gunel acknowledge the limitations, but point out that machines are constantly learning, and their predictions will only improve as scientific knowledge advances.

"The thing about AI is that it keeps getting smarter and smarter as you feed it more data and as you test the data," says Gunel.

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