

NEWS

# Biotech downturn hurts companies targeting autism-linked conditions

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Richard Novak realized that things were, in his words, “tanking” in December 2022. He was working to shore up a second round of funding for his company, **Unravel Biosciences**. But nothing was panning out. One potential partner told him they would love to collaborate with Unravel, which uses a computational model to identify new drug targets for conditions such as **Rett syndrome**, but they had no budget. A potential investor admitted that, at that moment at least, they weren’t interested in rare diseases.

This felt different from the rejections **Novak** had become used to since co-founding Unravel in 2020. Those usually came after a formal conversation. Now he was getting evasive responses or swift no’s. Larger pharmaceutical companies had faced financial strain for much of the year, but by December, Novak realized the funding challenges had come for smaller drug companies like his, too.

Just one year earlier, investment in the field had run rampant. Money had poured into biotechnology companies — investments buoyed by an intense pandemic-driven interest in biotech, plus fiscal stimulus and a low interest rate. Data from BioCentury, which tracks biotechnology investments, show that venture capital investment in biotech hit a record high of \$51 billion in 2021, and the NASDAQ Biotechnology Index reached an all-time peak in September of that year.

Since then, however, the mood has soured. Between September 2021 and mid-February of this year, the same NASDAQ index dropped by 23 percent. Venture investing in biotech fell to a more routine \$37 billion last year, a trend that has so far continued into 2023. Funding for companies targeting brain-based conditions — including autism and Rett syndrome, which saw unprecedented

numbers of financings in 2020 and 2021 — has dipped back down to pre-boom levels.

This was the environment in which Novak was trying to find additional backing for Unravel, a company primarily focused on central nervous system conditions. After its initial seed funding, the team had rented lab space and hired staff, but as investments slowed down during 2022, Unravel — like everyone else seeking the attention of investors — was competing in a much tighter field.

Faced with this downturn, many biotech companies began cutting costs or closing up shop — at least 29 have **announced layoffs** since the start of this year. Others, however, are turning to new partnership and funding models that have the potential to reshape the field.

The current funding correction is reaching all corners of the biotech space. But it might affect companies that target autism and other brain-related conditions more than others.

**Ovid Therapeutics**, **Neurona Therapeutics** and **Finch Therapeutics**, all of which have treatments underway for neurodevelopmental conditions, have cut staff in the past year. So has **Taysha Gene Therapies**, which said in March 2022 that it would focus resources on three gene-therapy programs and **minimize activity** for more than a dozen other programs, including those on Angelman syndrome and SLC6A1 disorder, both of which are linked to autism. It has been worse yet for **Vyant Bio**, a biotech company based in New Jersey, which **announced** earlier this month that it is delaying its **clinical trial** for a new treatment for Rett syndrome and taking steps to “preserve cash for the execution of an orderly wind-down process.”

Treatments for neurological conditions tend to be seen as particularly risky investments, says **Andrew Whiteley**, vice president of business development and technology transfer at Cold Spring Harbor Laboratory in New York, and the reason has to do with biology. Many of these drugs have to overcome the blood-brain barrier to be effective. And autism’s heterogeneity makes clinical trials of treatments for the condition more susceptible to failure.

“It’s going to delay things, but it doesn’t mean that the great ideas aren’t continuing to live on.” Andrew Whiteley

Treatments for rare and ultra-rare diseases of all kinds are also at a disadvantage, says **Emil Kakkis**, founder and chief executive officer of **Ultragenyx**, which is developing treatments for Angelman syndrome and CDKL5 deficiency disorder, a rare form of epilepsy. Those monogenic diseases have a clear single-gene target and should, in theory, draw attention from drugmakers. But the market for such treatments can be small; fewer than **1 in 10,000 girls** are born with Rett syndrome each year, for example. (Boys with the condition typically do not survive past birth.) Having so few people to sell the treatment to can scare away some companies, Kakkis says.

Also, though monogenic diseases may be easier to target than other conditions, the interventions,

such as gene therapies, carry their own unique safety risks, Whiteley says. That, too, can keep companies from pursuing them.

The good news, Whiteley says, is that even as the biotech sector contracts, the underlying science that powers it continues to progress. Early-stage academic research programs, largely funded by government grants, are mostly insulated from short-term downturns in venture capital investment. Some research institutes, such as Cold Spring Harbor Laboratory, where Whiteley works, also have partnerships with investment firms to advance translation of research even before companies are founded.

And patient advocacy groups sometimes fuel their own programs, Kakkis says. The Foundation for Angelman Syndrome Therapeutics, for example, developed a drug to boost **UBE3A**, the protein missing in people with the condition, and funded it through preclinical testing. Ultragenyx partnered with the company to develop the drug and is now running the clinical trials.

Also, this kind of contraction has happened before, Whiteley says. He acknowledges the tragedy of the layoffs this past year but notes that biotech investing is cyclical by nature.

During the 2008 housing crisis, for example, the field saw a similar boom and bust, with the NASDAQ Biotechnology Index peaking that August and then plummeting in the following months, before eventually bouncing back to its pre-boom level. Another rise and fall happened over 2015 and 2016. During dips, companies sell off or license non-core assets and cut their spending to focus on their most promising ideas and ongoing clinical trials, Whiteley says. When the market recovers, those companies that survive look to expand again.

The current downturn, therefore, isn't a death knell. "It's going to delay things," he says, "but it doesn't mean that the great ideas aren't continuing to live on."

Still, companies can exist only as long as the money lasts, as Novak is acutely aware. He and his team landed a partnership earlier this year, only to find out, as Unravel was preparing to announce the big news, that the supposed partner was going out of business. The deal evaporated.

Novak remains optimistic, saying that he senses a shift on the horizon. In the United States, the latest **jobs report** was positive, and the economy is looking strong. "People kind of breathed a sigh of relief" when those reports came out, he says.

He is also hopeful that new approaches to partnering and investment will take hold. Tough times make companies reexamine themselves, and that can force innovation. For example, Novak and other executives at cash-strapped companies are discussing how they can partner in more strategic ways, or how they might share datasets and discovery platforms. On the other end of the equation, investors are experimenting with new funding models. The new venture capital firm **Curie.Bio**, for example, is providing companies with smaller investments up front in return for

letting company founders hang onto their equity stake longer.

Novak likens these new strategies to soldiers “breaking step” when they march over a bridge. If they all march in rhythm, the theory goes, the pounding of their boots can cause the bridge to resonate at a frequency that leads to its collapse.

Breaking step during tough times, Novak suggests, is what led to more decentralized clinical trials during the pandemic and enabled ongoing data collection as studies progressed. That innovation has stuck, and that’s now the way many trials are run. It’s still early, but time will reveal what might come out of the current downturn.

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