simply be down to chance, or it could have been triggered by a fundamental asymmetry in nature. But Steven Benner, at the Foundation for Applied Molecular Evolution in Alachua, Florida, says it's unlikely that creating a mirror form of biochemical life could shed light on this question. Almost every physical process behaves identically when viewed in a mirror. The only known exceptions, called 'parity violations', lie in the realm of subatomic physics. Such tiny differences would not show up in these biochemical experiments, says Benner. (He is also interested in making DNA that can avoid unwanted degradation by natural enzymes or viruses, but rather than using mirror-DNA, he has created artificial DNA with non-natural building blocks.)

Church's ultimate goal, to make a mirror-image cell, faces enormous challenges. In nature, RNA is translated into proteins by the ribosome, a complex molecular machine. "Reconstructing a mirror-image of the ribosome would be a daunting task," says Zhu. Instead, Church is trying to mutate a normal ribosome so that it can handle mirror-RNA.

Church says that it is anyone's guess as to which approach might pay off. But he notes that a growing number of researchers are working on looking-glass versions of biochemical processes. "For a while it was a non-field," says Church. "But now it seems very vibrant." ■

BIOTECHNOLOGY

Bankruptcy of nanomedicine firm worries drug developers

Financial troubles of leading biotech firm highlight challenges of making innovative drugs.

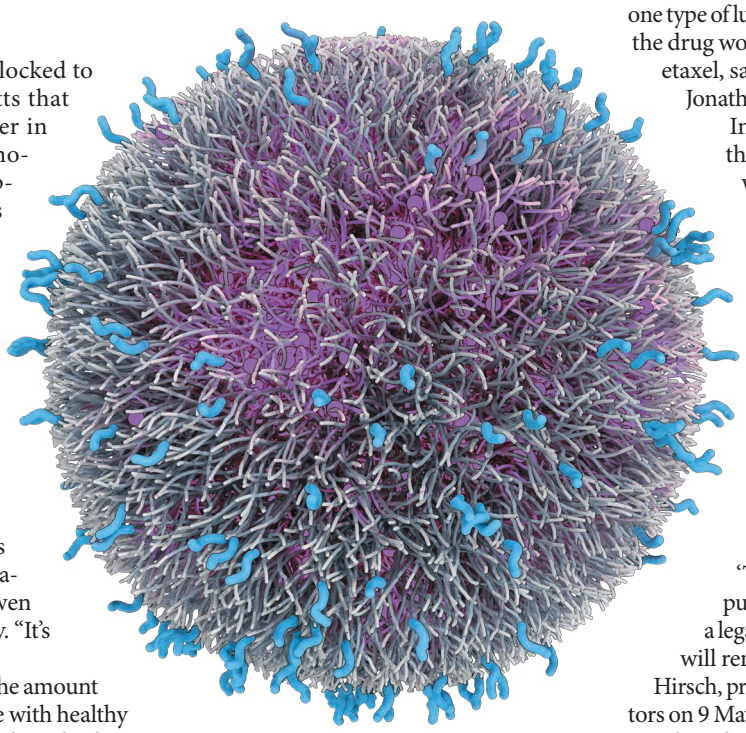
BY HEIDI LEDFORD

Not long ago, investors flocked to a firm in Massachusetts that was hailed as the leader in a wave of next-generation nanotechnology companies developing ways to ferry cancer drugs to tumours. But on 2 May, the company — BIND Therapeutics — declared bankruptcy.

Researchers in the field of nanomedicine are waiting anxiously to see whether the Cambridge-based firm will pull through its financial crisis — and whether its troubles will taint the swiftly evolving field of nanoparticle drug delivery. "It's been a rapid rise and fall," says Eric Schmidt, a biotechnology analyst at the investment bank Cowen and Company in New York City. "It's all unravelled pretty quickly."

Because nanoparticles lessen the amount of contact that cancer drugs have with healthy tissue, they offer a chance to deliver higher doses with fewer side effects. In 1995, the US Food and Drug Administration approved the first such treatment, Doxil, which packages a chemotherapy drug called doxorubicin in a lipid nanoparticle. The particles are too large to escape from normal blood vessels — and so are less toxic to the heart than naked doxorubicin — but they can seep out of the leaky blood vessels often found in tumours.

BIND's nanoparticles were designed to target tumours more precisely than liposome particles can. The company's lead product, BIND-014, involves a polymer particle coated with a molecule that steers the particle to a protein found in many tumours. The particle releases the chemotherapy drug it carries, called docetaxel, inside the tumour.



COURTESY BIND THERAPEUTICS

BIND Therapeutics' nanoparticle is coated in molecules that target it to tumours.

Early tests in animals and small clinical trials showed that the approach was safer than docetaxel alone — and fuelled BIND's US$70.5-million initial public offering in 2013. But later clinical trials disappointed. BIND-014 failed against cervical and head-and-neck cancers. Although it was somewhat effective against one type of lung cancer, it was not clear whether the drug worked any better than regular docetaxel, says BIND's chief scientific officer Jonathan Yingling.

In April, the company announced that it would cut back on its work with BIND-014, and Yingling says that the firm will now explore new targets. It cut the number of employees by 38% and aims to trim its expenses to $6 million per quarter — a dramatic decrease for a company that spent $11 million on research and development alone in the first quarter of 2016.

After one of its creditors demanded that BIND repay a loan ahead of schedule, the company filed for bankruptcy (see 'Troubled times'). It plans to dispute the need for early repayment at a legal hearing on 18 May. "BIND is and will remain open for business," Andrew Hirsch, president of the company, told investors on 9 May.

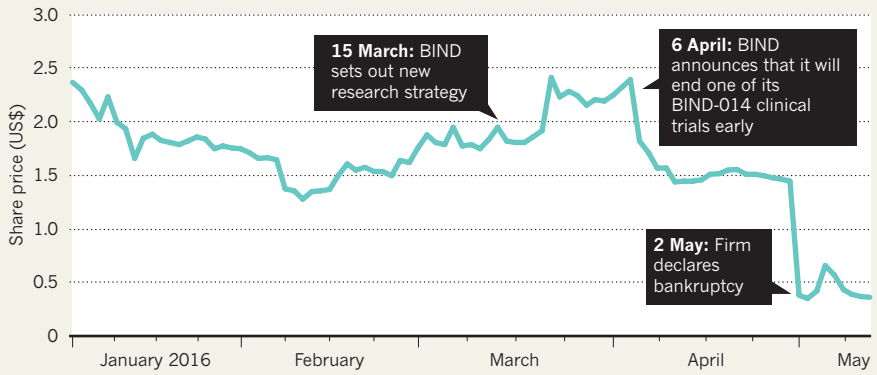
Schmidt says that BIND remains at the technological forefront of nanoparticle drug delivery, but waited too long to move away from BIND-014. By then, the investor enthusiasm for biotechnology that had driven BIND's initial public offering had cooled. "People are not interested in funding technology right now," Schmidt says. "They're interested in funding later-stage projects. And the one at this company didn't have what it takes."

In the time since BIND-014 was developed, researchers have also realized that differences between tumours — such as size, density and leakiness of the blood vessels that lace through

SOURCE: YAHOO FINANCE

TROUBLED TIMES

BIND Therapeutics raised US$70.5 million in an initial public offering of stock in September 2013. But the company's stock price has fallen in response to its recent financial woes.



them — can affect how well nanoparticles penetrate them, says Warren Chan, a biomedical engineer at the University of Toronto in Canada. "You should eventually be able to personalize the nanoparticles to the need," he says. "It's just that we're not even close to there yet."

PERSONAL APPROACH

Omid Farokhzad, who studies nanomedicine at Brigham and Women's Hospital in Boston, Massachusetts, and is a co-founder of BIND, thinks that companies should determine whether a nanoparticle would penetrate a patient's tumour before administering the therapy. Farokhzad points to Merrimack Pharmaceuticals, also in Cambridge, which used an imaging agent called ferumoxytol to assess the effects of its liposome-encased chemotherapy in a clinical trial last year. Early results suggested that tumours that took up ferumoxytol were more likely to respond to the nanoparticle-encased drug.

Meanwhile, a third generation of nanoparticles is in the works: particles that shuttle larger molecules such as RNAs, says Pieter Cullis, who studies nanomedicine at the University of British Columbia in Vancouver, Canada. Cullis has been working with Alnylam, a biotechnology firm also in Cambridge, to develop nanoparticles that deliver therapeutic RNA molecules to the liver. The excitement over gene-editing techniques such as CRISPR–Cas9, which could one day be used to correct disease-causing genes, is also fuelling interest in using nanoparticles to shuttle in the RNAs and proteins needed for the method, he says.

But some are worried that BIND's struggles could frighten investors away from the field. Mark Davis, a chemical engineer at the California Institute of Technology in Pasadena, is quick to note that other nanoparticles are showing promise. Last month, Celator Pharmaceuticals of Ewing, New Jersey, announced that its liposome-wrapped chemotherapies are effective against a form of leukaemia. And Cerulean Pharma of Waltham, Massachusetts — a company that Davis co-founded — is making a polymer-based, targeted nanoparticle that has shown promising results in early trials when combined with other chemotherapies.

"I personally would be shocked if 20 years from now, we're not seeing a lot of nanotechnologies helping a lot of people," says Robert Langer, a bioengineer at the Massachusetts Institute of Technology and a co-founder of BIND. "It will happen." ■