Daphne Zohar

Playing a contrarian card, Zohar's firm, PureTech Ventures, sees opportunity in forming companies around early-stage assets.

There are some early signs that investments in biotech companies whose products are in the early stages of development could be on the rise again—in contrast to financiers' recent appetite for companies with lower-risk product candidates closer to market approval. But that's always been the philosophy at Boston-based PureTech Ventures, founded in 2001 by youthful entrepreneur Daphne Zohar.

A born company-builder, Zohar started her first enterprise when she was sixteen. "I like the creativity of starting a company," she says. "The challenge is to bring together different elements—people, technology and money. The three elements attract each other, so an entrepreneur's job is to overcome the initial inertia and draw them in." During her college years, she went to Israel as the youngest participant in a program started by Israeli industrialist and philanthropist Stef Wertheimer to bring entrepreneurs together to start companies that would help the Israeli economy. While there, Zohar was part of the group that devised a business plan to apply modern production methods to olive oil production—the only proposal Wertheimer ultimately invested in himself.

Zohar, whose father is a researcher at Massachusetts General Hospital in Boston, eventually began talking to people there about licensing, technology transfer and building companies in the life sciences. "Every time I talked to someone they said 'That's what Bob Langer does,'" referring to the Cambridge-based Massachusetts Institute of Technology professor who has founded life sciences companies in areas ranging from biomaterials to drug delivery.

Zohar sought out Langer, who cofounded PureTech, as well as former top industry executives John Zabriskie (CEO of Pharmacia & Upjohn and also a PureTech cofounder), Bennett Shapiro (executive vice president at Merck), and Ron Cape (cofounder of biotech original Cetus). All are current venture partners at the firm, as is former Aventis chief scientific officer Frank Douglas, who joined PureTech this year.

PureTech's perspective on how to build a company differs from that of many venture capitalists. "We do it a bit backwards," says Zohar. "We start with the problem rather than the technology." Take its aesthetics start-up, Follica: "We didn't know what we were going to have before we formed the company, but we knew the hair follicle was involved in regulating so many things: hair loss, hair removal, acne. So we said 'If we could put together a group of people who really understood the biology, and could do anything to manipulate it—someone would pay for that resulting therapy.'

"The underlying principles we're interested in are novelty and the scope of the opportunity, so that you have the technical risk of whether something will work, but not market risk," Zohar goes on—"and that you have the ability to address the technical risk without too much time and money." PureTech has applied the same first principles in forming its other portfolio companies, among them the pain therapy start-up Solace Pharmaceuticals and the predictive tools firm Enlight Biosciences, which is already being funded primarily through contracts with pharma companies.

As companies move downstream into human clinical trials, costs increase dramatically. Thus, it should be easier to increase the value of preclinical assets, she believes—and in so doing make them attractive to pharma company collaborators, which can be an alternative funding source for a company. "If a product represents a novel approach in an important therapeutic area, it will be attractive [to buyers] if you can demonstrate preclinical proof of concept," she says. For an oral drug aimed at a large market, for example, that inflection point could be demonstrating that it is orally bioavailable. "These are currently undervalued assets in the area—venture capital—that traditionally moves them forward. And it doesn't cost that much in time or money to get to those answers."

That's counter to the thinking currently prevalent in the venture capital world. "There's been a big demand for later-stage products, partly driven by the state of the pipelines in pharma and biotech," comments Zohar. That's led to a significant pipeline issue for venture capital that has been "largely avoided to date by creative strategies to extract value from older science," she declares. But those assets are fairly picked over by now. "By being focused on one space, the price [of those assets] has gone up and the quality has gone down," she explains.

Also, VCs that are trying to exit many of their existing investments are doing so at a time when the public markets are unappealing. Recent data from Windhover Information, for example, show that from January 2004 to August 2006, the 'step-up' in valuation of companies going public was significantly less than two times the total private money invested in those companies—a notoriously poor rate of return. "Later-stage assets are being priced more reasonably" by the public markets, notes Ed Hurwitz of Alta Partners. "Therefore, late-stage investors [those who finance the most recent rounds] can't make money."

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PureTech Ventures

Norm Selby, senior managing director at the well-known private equity firm Perseus, agrees that the pressure to exit, coupled with a risk-averse mentality driven by recent poor returns on venture capitalists' investments, has left other assets undervalued—the same reasoning Zohar puts forward. Similarly inspired by the void left by the venture industry in life sciences, Perseus, which for years co-managed a biotech portfolio with the Soros Fund but has not made a new investment on its own behalf in seven years, recently announced its return to the biotech investment arena.

Selby expects Perseus to remain in its investments for a much longer time than Zohar envisions for the more merger-and-acquisition–oriented PureTech portfolio. But both know they will have to dedicate considerable resources to managing their portfolio companies as they progress.

Indeed, points out managing director Noubar Afeyan of Flagship Ventures, it's always been harder for venture capitalists to raise money for early-stage concepts because of the time required to manage them—an issue exacerbated by the current size of their portfolios: "As portfolios grow and as innovations are few and far between, the sheer capacity of time, much more than money, become a limitation."

Mark Ratner, Cambridge, Massachusetts