



## An eye toward affordability

*Cheaper option / Bothell startup makes antibodies in inexpensive yeast and could someday provide sought-after drugs at half of current costs.*

Saturday, 2006-07-08

by Luke Timmerman / Seattle Times business reporter

If Alder BioPharmaceuticals is successful over the coming decade, its technologies could cut prices in half for some of the most expensive drugs in modern medicine.

The startup company from Bothell is a long way from putting a drug on the market, but it has moved toward that goal by raising \$16 million in its second round of venture capital. Alder raised the cash after proving to investors over the past year that it can make antibody drugs in yeast that are equivalent to antibodies made in standard mammalian cells.

Simple economics explain why that matters. Yeast is an inexpensive raw material, meaning that Alder can produce antibodies for \$20 to \$40 a gram, roughly 1/10 of the \$300 a gram for the mammalian cell-based methods used to make hit antibody drugs like Rituxan and Avastin.

Yeast cells naturally divide much more quickly than cells from mammals, so Alder believes it can run commercial-sized tanks that churn out

antibodies in three to five days, instead of three to five weeks.

"If you can make your product at one-tenth the cost, do it faster, and get out of the supply logjam, suddenly you can make drugs at a lower price and still make a profit," said Randy Schatzman, Alder's chief executive and former senior vice president of research at Celltech R&D.

So far, Alder's tests have all been done in the tightly controlled worlds of petri dishes and animal experiments. It will spend the new cash trying to clear a higher bar, testing its drugs in people.

The first clinical trial in healthy volunteers is scheduled for the second quarter of 2007. A few months later, the company plans to begin testing its antibodies in patients with rheumatoid arthritis, cancer and lupus. It intends to hire 10 to 15 people with expertise in clinical drug development, regulatory affairs and manufacturing.

Antibodies as drugs have become a booming business since the first was approved by the FDA in 1997. By 2005, there

were 17 on the global market, generating \$11.2 billion in sales, according to Dublin-based Research & Markets.

The new so-called targeted drugs are especially in demand by patients with cancer and autoimmune diseases because of the drugs' ability to zero in and attack diseased cells while mostly sparing healthy tissue. Market research from Business Communications Corp. shows 80 more antibody drugs in clinical trials.

One catch is they are much more difficult and expensive to make than conventional pills and often come with stratospheric price tags. Genentech's hit cancer antibody, Avastin, costs the health-insurance system \$100,000 a year for each patient.

Schatzman, 52, doesn't want Alder to just make generic versions of antibody drugs. Instead, he says his company will be a "fast-follower" in the antibody world, making less expensive drugs similar to blockbusters, but made from a patented recipe with advantages of its own.

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Besides being cheaper and faster to make, Alder's antibodies may be better, chief business officer Mark Litton said, because the company can select ones that bind more tightly with diseased cells. That means the antibodies could be effective at lower doses, causing patients fewer side effects.

Making such potent antibody drugs in yeast has been scientifically difficult.

Smaller, simpler molecules like insulin have been made in yeast, but partly because antibodies are about 15 times the size of the molecules and have complex 3-D folding patterns that must be consistent, drug companies have only been able to make fragments of antibodies in yeast.

Alder's method works around that problem by inserting DNA fragments of the desired antibody into individual yeast cells. Alder then coaxes the yeast cells to mate and fuse together, where the DNA fragments transform into antibody fragments, which can then assemble into a full antibody.

Jim Cregg, a professor of molecular biology at the Keck Graduate Institute in Claremont, Calif., and an inventor of the yeast technology licensed to Alder, said the biotech industry tried conventional baker's yeast to make drugs in the 1970s and '80s. Those efforts were scrapped because baker's yeast ferments and produces ethanol, which was toxic to the drugs they were trying to produce.

Cregg's research developed a second-generation strain of yeast — *Pichia pastoris*, genetically altered so it doesn't ferment — so it can produce large protein molecules in high densities.

Cregg, a consultant to Alder, said Alder isn't the only one interested in the *Pichia* yeast strain. Biotechnology's two biggest companies, Amgen and Genentech, are aware of it and are trying it themselves, he said.

Other biotech companies have looked into turning plants and animals into biotech drug factories as an alternative to the standard methods, but the work remains controversial.

One direct competitor making drugs from yeast, GlycoFi of Lebanon, N.H., recently was bought by Merck for \$400 million.

Alder's vote of confidence from investors came from HIG Ventures, and its earlier crew of backers, Sevin Rosen Funds, Ventures West and WRF Capital, the venture investment arm of the Washington Research Foundation.

Besides the investors, Alder has gotten support from partnerships with Seattle Genetics and pharmaceutical company Schering Plough. Clay Siegall, the chief executive of Seattle Genetics who recently joined Alder's board, said his company may consider using the Alder technology to make its antibodies.

"They are an up-and-comer here in Seattle," Siegall said.

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### **Alder BioPharmaceuticals**

**Founded:** Jan. 2004

**Located:** Bothell

**CEO:** Randy Schatzman

**Employees:** 15

**How it started:** The four founders had worked together at the Celltech R&D center in Bothell until its parent company closed it down in 2003. Soon after, they founded Alder.

**Investors:** HIG Ventures, Sevin Rosen Funds, Ventures West and WRF Capital, the Seattle-based venture investment arm of the Washington Research Foundation.

**What it does:** Developed a patented method for mass-producing antibody drugs more quickly and at lower cost using yeast cells. It is using the yeast-based system to discover and manufacture new antibodies for rheumatoid arthritis, cancer and lupus.

**Source:** *Alder BioPharmaceuticals*