

Biotech upstarts get injection of capital

By Jim Hopkins, USA TODAY

SAN FRANCISCO — Merck, the pharmaceutical giant racing to replenish its drug pipeline, hatched a \$100 million partnership in November with a tiny biotech start-up in Cambridge, Mass.

Eli Lilly, another drugmaking stalwart, is plunging into the sizzling anti-impotence market ruled by Viagra with help from a young biotech near Seattle. Bristol-Myers Squibb, struggling to replace a cancer drug, is betting on a \$2 billion deal with ImClone Systems — a biotech better known for its role in the Martha Stewart scandal.

More slow-growth pharmaceutical firms like these are partnering with fast-growth biotechs for a dose of new drugs battling cancer and other illnesses. Lilly, for one, has launched about 100 partnerships, mostly with biotechs, many in the last five years.

The trend underscores a power shift toward biotech in the drug and technology industries. Venture-capital investors are joining scientists in deciding what drugs get developed. Big pharmaceuticals are relying on biotechs to create new drugs for an aging population. And biotech is emerging as the next engine for innovation and jobs in the tech industry, long focused on computer chips and other traditional fare.

But there are risks. Venture capitalists are pickier about the biotechs they finance than they were 10 years ago during the last boom. That means discoveries with extra-high risk may get overlooked — and so won't reach patients. "There's no question that good ideas don't get funded," says Jim Tullis, CEO of Tullis-Dickerson, a biotech VC firm.

What's more, investors are betting on a highly regulated sector. The Food and Drug Administration slammed ImClone two years ago when it initially rejected its cancer drug. And the political debate over drug price controls makes VCs worry about paltry returns on start-up investments of \$50 million or more.

The industry has been an investors' roller coaster since the start. "Anyone who has tried to make projections has many times been wrong," says Alan Goldhammer, a regulatory official at the Pharmaceutical Research and Manufacturers of America trade group.

Boom in biotech

Yet there is powerful fuel for the shift to biotech: Big drug companies are slowing research to focus more on marketing other companies' discoveries. Years of work in biotech labs are yielding drugs proven to tackle cancer and other elusive targets.

Even well-heeled investors such as Microsoft's Bill Gates are seizing on biotech as the tech industry's future.

Venture-capital investors, who invest on behalf of institutions and rich individuals, poured more money into biotech in the third and fourth quarters than into any other industry — including software, the perennial

favorite. The share of venture capital going to biotech surged from 14% in 2002 to 19% last year, higher than in the last financing boom.

Biotech uses computer-powered genetic engineering to treat illnesses, create foods and improve manufacturing. Its high-tech promise is luring pharmaceuticals because of:

•**Dry pipelines.** The number of new drugs approved annually by the FDA has tumbled 45% since 1996 — the last peak year.

Ten years ago, traditional drugmakers were punching out 60 newly approved drugs a year. Biotech eked out just two to four, says Jim Broderick, a partner with Morgenthaler Ventures in Silicon Valley's Menlo Park.

By last year, the two sectors were about even, at 20 each. "Big pharma has fallen dramatically, and the biotech industry has grown dramatically," Broderick says.

That's caught pharmaceuticals' attention. For example, Lilly, running behind in developing an anti-impotence drug, formed a partnership in 1998 with Icos, the Seattle-area biotech, to develop and market Cialis.

Icos, whose early investors include Microsoft's Gates, started work on Cialis in the early 1990s. The FDA approved Cialis in November — pitting Lilly against Pfizer's blockbuster Viagra.

Experts debate why pharmaceuticals struggle to create new drugs. Their mammoth size may mean they've become too bureaucratic, so they chase only less-risky innovations more likely to produce a payoff, Broderick says. Also, they struggle to attract talent among biotech scientists who may think cutting-edge work can be better done at entrepreneurial start-ups.

•**Patent problems.** Pharmaceuticals are losing exclusive blockbuster drugs — those generating annual revenue of \$1 billion or more — as patents expire. That lets competitors swoop in to make generic versions, cutting into revenue.

For example, Merck's top drug, the cholesterol-fighter Zocor, lost patent protection last year in Canada and some European nations. Since then, Zocor sales are down. Its USA patent expires in 2006. Zocor generated \$5 billion, or about 23% of Merck's annual revenue, last year.

•**Merger mania.** A wave of big pharmaceutical mergers and acquisitions in the past five years has left fewer competitors to gobble up, depleting a quick source of revenue growth.

At least 20 deals have been announced or completed since 1999, including the record \$115 billion combination in 2000 of Pfizer and Warner-Lambert.

One of the rare deals more recently, still developing, is the \$58 billion hostile bid announced in January by Sanofi-Synthelabo for its French rival, Aventis.

•**Big risk.** Drug-development costs have soared as disease targets get more complex — and regulatory reviews grow longer.

Development costs for all drugs, from lab to FDA approval, average \$802 million per drug — more than double the cost in 1987, says the Pharmaceutical Research and Manufacturers of America. New drugs take as long as 15 years to reach FDA approval.

That means big pharmaceuticals, under pressure from Wall Street to boost profits, are more skittish about investing in new drugs. That's another reason to cut risk by linking with biotech start-ups.

Still, alliances have risks, too. That was the story at Bristol-Myers soon after it signed a marketing agreement for ImClone's cancer drug, Erbitux. The FDA, citing poor research data, rejected Erbitux in December 2001 — sending ImClone stock tumbling and threatening Bristol-Myers' \$2 billion marketing deal with the biotech.

Last month, acting on new data, the FDA finally approved Erbitux — boosting ImClone stock 29% in one day and winning Bristol-Myers a return on its gambit. It will get 61% of Erbitux revenue. The ImClone partnership is one of more than 190 that Bristol-Myers has signed with biotech and other firms.

A higher bar

Risks, amid higher investment costs, are one reason VCs are now choosier about biotechs. Last year, they invested an average \$11.2 million per biotech deal, nearly three times the average 10 years ago.

More VCs are looking for biotechs with drugs deeper in development. The best candidates are those close to, or already in, the first phase of human testing, says James Golden, research vice president at Life Science Insights, an industry tracker.

A recent example: GenPath Pharmaceuticals — Merck's new biotech partner. Founded by two Harvard University scientists, GenPath hopes to begin Phase 1 testing next year, says CEO Tuan Ha-Ngoc. That timetable attracted eight VCs and several private investors. They pumped \$42.7 million into the Cambridge company in October. The Merck partnership came the following month.

Merck has ramped up the number of such partnerships in the last year. It has more than 80, mostly with biotechs; 47 were formed last year.

Ha-Ngoc says GenPath is talking to other pharmaceuticals about deals. GenPath's workforce is growing, underlining biotech's job-building potential. The company, with 65 employees, expects to add 35 by the end of the year.

Certainly, these partnerships aren't a one-way street. Biotechs gain pharmaceuticals' expertise in guiding drugs through the labyrinth of human testing, which can account for half of development time. "It's very difficult to clear all the hurdles," says Icos CEO Paul Clark.

Moreover, Lilly and other pharmaceuticals are skilled at marketing and distribution. Icos has 165 newly hired sales representatives. Lilly will assist with its own sales force.

The growing number of partnerships is luring more investors. New Enterprise Associates, an influential VC firm in Silicon Valley, just raised \$1.1 billion partly for health investments. Venrock Associates, the Rockefeller family's investment arm, raised \$550 million in January. About 30% will go to biotech and other health start-ups.

Traditional tech is still profitable, but product life cycles are shorter, reducing investor returns.

Yet a biotech with a successful drug can generate \$500 million in annual revenue — with 95% gross profit margins for years, says Bryan Roberts, Venrock general partner in Menlo Park.

"Like getting a winning lottery ticket," he says.