Cautious CAPITAL

BY LISA DRESS

The funding environment for biotech and start-up companies has improved considerably during the past few years. But venture capital investors are more cautious and more demanding than ever before.

SCOTT SALKA

The main challenge for earlier-stage biotech and pharma companies **IS TO PROVE TO INVESTORS THAT THEY HAVE A WELL-DEFINED PATH TO THE CLINIC AND THE REGULATORY EXPERTISE NECESSARY TO GET THERE.**

KAREN BOEZI

VENTURE CAPITAL INVESTORS WILL INCREASINGLY BE FOCUSED ON CAPITAL EFFICIENCY AND REDUCING RISK. We believe this focus will continue to favor product companies over platform technology companies.

GORDON RYERSON

INVESTMENT DOLLARS FLOW INTO MARKETS THAT ARE PERCEIVED TO BE FUTURE GROWTH AREAS. Areas that typically interest potential investors address the bottlenecks associated with getting new drugs to the marketplace.

Venture capital interest in the life-sciences industry, and specifically in biotech companies, is increasing. Yet while more venture capital has become available, investors are exercising caution. They are looking for a combination of a successful development track record in a company management team and technology with high therapeutic and commercial potential, as well as a short road to clinical development.

Health industry companies received a record share of venture capital investment dollars in 2004, leading all other industries and capturing 30.2% of all venture capital funds invested during the year, according to a recent MoneyTree Survey, conducted by PricewaterhouseCoopers, Thomson Venture Economics, and the National Venture Capital Association.

"Venture capital investment in the health sector has steadily increased, even through the post-Internet bubble hangover," says Tracy Lefteroff, global managing partner for life-sciences industry services at PricewaterhouseCoopers. "Investors have, on the one hand, sought to diversify their IT-heavy portfolios and, on the other, come to recognize the long-term potential of the sector. We believe the aging population in the developed world and recent commercial successes of life-sciences companies will continue to fuel investment in this sector to a point where investment in health-related industries will rival or surpass IT investments."

Reversing three consecutive years of declines, venture capital firms invested $6.33 billion in health industries during 2004, including companies in the biotechnology and pharmaceutical, medical device and equipment, and health services and information technology sectors, according to the survey.

Of the three sectors, biotechnology companies continue to attract the most substantial amount of venture capital funds among the health industries. Of the $6.33 billion invested in health industries in 2004, 61.1% of the dollars went to biotechnology companies. Medical devices and equipment received 28% of the total health industries dollars. Healthcare-services technology received 10.9% of the total health industries investments, according to the MoneyTree Survey. (For more information, see chart on page 25.)

"The early-stage investment environment has steadily improved since mid-2002 when the recovery began from the Internet bubble burst," says Raymond Thek, director and vice chairman of Lowenstein Sandler PC's tech group. "There has been a cleansing of portfolios. After dot.com businesses dwindled out, investors realized they still needed a well-thought out business plan and validation of concept and customer base to succeed. The early-stage investment environment is bouncing back, and there is renewed strength."

One reason for increasing venture capital interest in the life sciences is the changing demographics of the population, Mr. Lefteroff says.

"More and more people are tapping into the healthcare system, and there is more demand for products for diseases that don't have viable solutions," he says. "This is leading to an increased interest in products being developed by life-sciences companies."

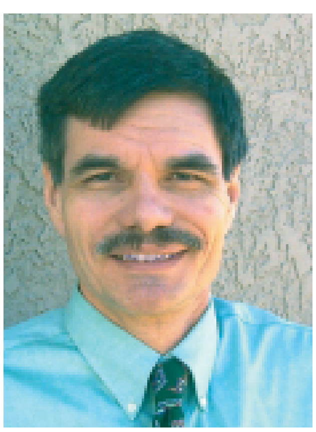
Investment dollars flow into markets that are perceived to be future growth areas, says Gordon L. Ryerson, managing director of Crosstree Capital Partners Inc.

DAN GIAMPUZZI

VENTURE CAPITAL IS CERTAINLY THE PRIMARY SOURCE OF FUNDING FOR MOST BIOTECHS, BUT THERE ARE WAYS TO SUPPLEMENT VC FUNDING. Gemin X has offices in the United States and Canada, which has allowed us to take advantage of the many tax benefits and government funding programs available in Canada.

P. SHERRILL NEFF

THE INVESTMENT ENVIRONMENT IS REASONABLY HEALTHY, BUT IT IS HIGHLY COMPETITIVE. Of 500 business plans we receive a year, we may make four to six investments. That is typical for the investment industry.



DR. BRUCE SELIGMANN

FINANCING WILL REMAIN VC DOMINATED, but focusing on collaborating with pharma partners not only validates and supports programs but may provide a potential exit strategy route though acquisition.

"Services that are in demand and are anticipated to grow are the ones that will get the most attention from venture investors," he says. "Investors obviously want to jump into a market before the growth in sales dollars is actually realized because that is when they can typically get their highest investment returns."

Angel and seed investors may be motivated for reasons other than that of financial gain, especially in the biotech arena, Mr. Thek says.

"There are people who are interested in changing the way the world works, the way we think about and react to health questions, and our understanding of what life is all about and how the body functions," he says. "These are interesting and exciting areas of opportunity."

The hottest areas of venture capital funding in 2004, per the MoneyTree survey, were cancer drug development, new types of stents, pain management therapies, insulin-delivery systems, respiratory disease therapies, eldercare services, and physician-owned specialty hospitals.

"Areas that typically interest potential investors address the bottlenecks that are associated with getting new drugs identified, developed, and into the marketplace," Mr. Ryerson says. "Everyone is trying to find a way to get drugs to the marketplace faster and cheaper, and so the whole pharmaceutical outsourcing space is very active. Over the last few years anything related to the cardiovascular therapeutic area has received investors' attention and still remains one of the primary investment areas. The new therapeutic areas on the horizon are diabetes, oncology, and central nervous system."

CAREFUL CONSIDERATIONS

Industry experts say compared with a few years ago, venture capitalists are being more careful about where their investment dollars go.

"There is much more due diligence before making an investment," Mr. Ryerson says. "Investors are much more willing to walk away from a deal because of the number of people who got into trouble a couple of years ago."

There is a lot of venture capital available, but it's "cautious capital," says Scott Salka, CEO of Ambit Biosciences Corp.

"Venture capital groups are looking at companies that have a solid path to liquidity," he says. "Back in 1999, liquidity wasn't as big an issue; the funding environment was more like 'if you build it, they will come.' But now companies have to build it and prove it works."

Less venture capital money is going to basic science, says P. Sherrill Neff, managing partner of Quaker BioVentures.

"There is still money going to earlier-stage companies but these are companies that have an enormous potential to bring products to market," Mr. Neff says.

Overall, the funding environment has improved, says Dan Giampuzzi, president and CEO of Gemin X Biotechnologies Inc.

"Early-stage companies can secure funding but valuations for these companies may remain low for the foreseeable future," he says. "As always, a company must continue to demonstrate it has a unique and 'unfair advantage' in a high-potential segment of the market, as well as the right team to execute the

Venture Capital Financing in Life Sciences

HEALTH INDUSTRIES INVESTMENTS PEAKED IN 2000, BUT RECENT TRENDS SHOW AN INCREASE IN VENTURE CAPITAL INVESTMENT ACROSS THE HEALTH-RELATED SECTORS. VENTURE CAPITAL INVESTMENTS IN HEALTH AND MEDICAL COMPANIES INCREASED BY 13.5% FROM $5.58 BILLION TO $6.33 BILLION BETWEEN 2003 AND 2004 WITH 30 MORE DEALS OCCURRING IN 2004.

Of the three sectors, biotechnology companies continued to attract the biggest share of venture capital funds. Of the $6.3 billion invested in health industries, 61.1% of investments went to biotechnology companies. But health services and technology companies experienced the biggest increase in venture capital investments. Medical devices and equipment received $1.77 billion, or 28% of the total health industries dollars. Healthcare services and technology received $687 million, or 10.9% of the total health industries investments.

As a percentage of venture capital dollars, investments in health industries are at the highest level ever in the 10-year history of the MoneyTree Survey. Hot areas of investment included cancer drug development, new types of stents, pain management therapies, insulin delivery systems, respiratory disease therapies, eldercare services, and physician-owned specialty hospitals.

Investments in Health Industries as a Percentage of Venture Capital Dollars

Industry	% of total venture capital dollars in 2003	% of total venture capital dollars in 2004
Biotechnology	18.6%	18.5%
Medical Devices and Equipment	8.3%	8.4%
Healthcare Services and Technology	2.5%	3.3%
Total Health Industries	**29.4%**	**30.2%**

Source: The MoneyTree Survey, conducted by PricewaterhouseCoopers, Thomson Venture Economics, and the National Venture Capital Association. For more information, visit pwcmoneytree.com, ventureeconomics.com, or nvca.org.

plan, if it wants to be successful in raising venture capital funds. Today, the biggest challenge for early-stage companies is advancing one or two key projects to within striking distance of the clinic, using minimal funding so as to have a mature story to present when it solicits venture capital funds for investments."

Mr. Salka says the main challenge for early-stage biotech and pharmaceutical companies is to prove to investors that they have a well-defined path to the clinic and the regulatory expertise necessary to get there.

"Venture capital groups have been very interested in how we will advance our lead program for stroke into clinical trials this year and how we will follow this project up by moving our lead program for cancer into clinical trials next year," he says.

According to Mr. Giampuzzi, his company recently initiated Phase I and Phase I/II clinical trials for its lead product for the treatment of cancer and was soliciting most of the money while the product was still in preclinical development.

"Investors wanted to make sure we had a solid plan not only for getting our products into the clinic, but also the right team and approach for advancing them through the clinic," he says.

Another challenge for a company is the ability to distinguish itself from all the others and address the unique reasons why it will succeed, says Bruce E. Seligmann, Ph.D., founder, chairman, and chief scientific officer of High Throughput Genomics (HTG).

"Our company easily distinguishes itself from the competition, but faces the challenge of being a tools company versus a products company," he says. "For tools companies attracting investors is difficult today, though I believe the tide is changing since the FDA has called for new tools. The pharma industry recognizes it needs new tools to help increase productivity and success."

SECURING FINANCING

Attracting and receiving venture capital funding is highly competitive, Mr. Neff says.

"We receive business plans from about 500 companies a year and screen those opportunities," he says. "About 1 of 10 companies is invited to a meeting to discuss the opportunity. From those, we seriously evaluate about half. So of the 500, we may make four or six investments, and that is typical for the investment industry."

To raise venture funding, a company must present a credible and fundable business plan, have an experienced management team, have a product that can be protected against competition that addresses a large, measurable, underserved market with differentiating characteristics, and be clear about the risks and opportunities, says Robert A. Ashley, chairman, CEO, and president of AmpliMed Corp.

Often what drives venture capital funds is how quickly start-up and biotechnology companies can establish the connection to their future revenue stream, says Douglas M. Tucker, Ph.D., CEO of Neurognostics Inc.

"Venture capitalists, however, may make a leap of faith since companies may not have anything tangible at the early-investment stage," he says. "In this case, it's about trust. Do investors trust the company? Is the company credible? Does management have experience that will lead investors to think they know what they are talking about? Early on, some of a company's best contacts are people who work in the field and understand the technology and concept being pushed forward. Later on, investors look at revenue streams."

One of the biggest mistakes a company can make is to unnecessarily complicate its capital structure and corporate governance, Mr. Ryerson says.

"For example, some companies may have dozens of private investors, which could be given different classes of shares," he says. "This would convolute the capital structure of the company and how it is governed, which in turn may impact the company's valuation and attractiveness to a venture capital firm. I think companies need to keep their capital structures as simple and as clean as possible because this would allow for an easier transaction with an institutional investor in the future. All things equal between two similar deals, venture capital groups have a greater likelihood of walking away from a deal with an excessively convoluted capital structure rather than trying to work through it."

According to Karen Boezi, cofounder and managing partner, Thomas, McNerney & Partners, venture capital investors will increasingly be focused on capital efficiency and reducing risk.

"We believe investors will continue to favor product companies over platform technology companies; creative financing strategies that include milestone-based funding; alternative operational strategies, including virtual company approaches and offshore divisions; as well as companies focused on reformulations/improvements of existing compounds," she says.

Ms. Boezi says to obtain venture funding, it is advantageous if companies focus on large, rapidly growing, and underserved market segments.

"If there is not a big market opportunity, it takes more to build a significant business, leading to less value creation for investors," she says. "The ability to achieve a market leadership position is also very important. A market may be large but if there are a significant number of competitors and the company is the fifth to market with a 'me-too' product, value realization for investors is also difficult."

Additionally, a convincing business model with the potential to achieve significant, sustainable value with reasonable risk, and strong leadership are important pieces of the venture funding puzzle.

Sound Bites from the Field

PHARMAVOICE ASKED INDUSTRY EXPERTS TO DISCUSS THE BIOTECH INVESTMENT ENVIRONMENT, AS WELL AS FUTURE TRENDS.

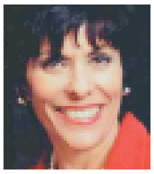
CAMILLE D. SAMUELS
Managing Director of Versant Ventures, Menlo Park, Calif., a venture capital firm devoted to healthcare; the company manages more than $650 million in committed capital. For more information, visit versantventures.com.

"Because there is a lot of money in life-sciences ventures capital firms, good start-up companies are able to raise venture financing relatively easily and at good valuations. I would describe the financing environment for early-stage companies as positive.

For later-stage companies, there is capital available, but not necessarily at the valuations that management is looking for. Late-stage valuations are constrained by the low prices being garnered by biotech companies at the IPO stage.

Venture capitalists are generally positive about the long-term fundamentals of biotech investing, but worry about the increased caution at the FDA, the low valuations seen in 2004 IPOs (again, constrained upside), and a decreased emphasis on operational efficiency among entrepreneurs and venture investors.

Venture capitalists are still interested in "specialty pharma" or NRDO (no research development only) companies. These companies in-license clinical-stage drugs from pharmaceutical or academic sources. There are many companies in this area already, especially in oncology and increasingly in CNS and pain."



MARILYN NYMAN, M.ED., CCC/SP
President and Founder of The Nyman Group, Fort Washington, Pa., a strategic consulting firm that provides innovative, client-focused services, involving strategic planning, project facilitation, and communications initiatives to foster leadership development at all organizational levels. For more information visit nymangroup.com.

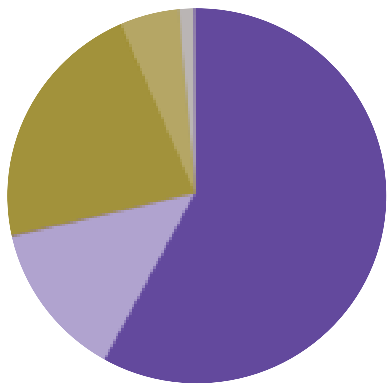
"Venture capital firms want to hear the "elevator speech" from executives at start-up and biotechnology companies. Venture capital firms want a quick executive summary of the plan and how they will achieve their goals. Executives need to know their story and must be able to tell it well. They only have a few minutes to convey competence, confidence, and credibility.

They need to use language that appeals to investors' logic and sense of imagination, and they need to create a picture in their heads."

PharmaVOICE Reader Survey: Venture Capital

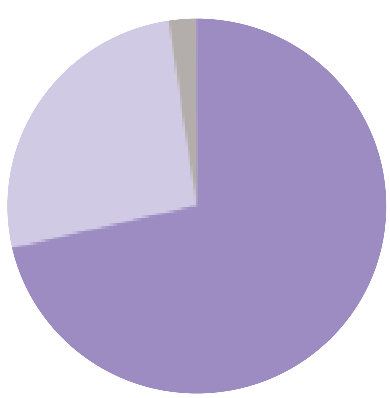
Growth Strategies

HOW DO YOU INTEND TO GROW YOUR COMPANY IN 2005?



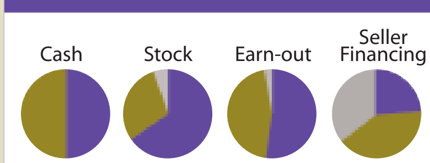
- **55.9%** Organic growth (no acquisitions), no financing required
- **14.4%** Organic growth (no acquisitions), financing required
- **21.6%** Organic growth and acquisitions, no financing required
- **5.4%** Organic growth and acquisitions, financing required
- **2.7%** Other

HOW DOES YOUR COMPANY CONSIDER ACQUISITIONS?



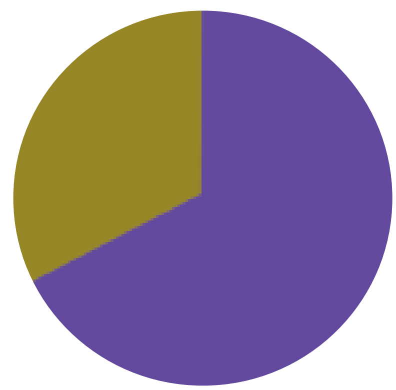
- **55.2%** Review acquisitions opportunistically
- **41.4%** Formal acquisition search program (tactical acquisition plan)
- **3.4%** Other

WHAT FORMS OF FINANCING WOULD YOUR COMPANY CONSIDER WHEN MAKING AN ACQUISITION?



Very Likely | Somewhat Likely | Not Likely

WILL YOUR COMPANY USE THE SERVICES OF AN INTERMEDIARY/INVESTMENT BANKER TO MAKE ACQUISITIONS?



- **34.5%** Yes
- **65.5%** No

WHAT TOTAL PRICE WOULD YOUR COMPANY CONSIDER IN MAKING AN ACQUISITION?

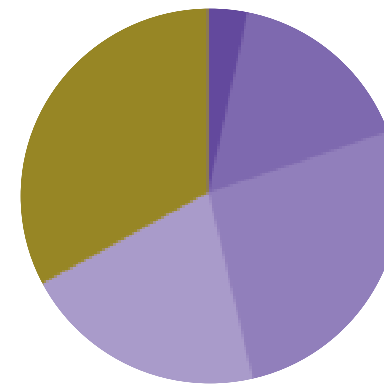
- $5 million or less **57.1%**
- $5 million to $50 million **78.6%**
- $50 million to $250 million **17.9%**
- More than $250 million **3.6%**

WHAT GEOGRAPHIC AREA(S) WOULD YOUR COMPANY CONSIDER WHEN MAKING AN ACQUISITION?

- United States **92.9%**
- Europe **67.9%**
- India **32.1%**
- South America **28.6%**
- Canada **25%**
- China **25%**
- Other **17.9%**

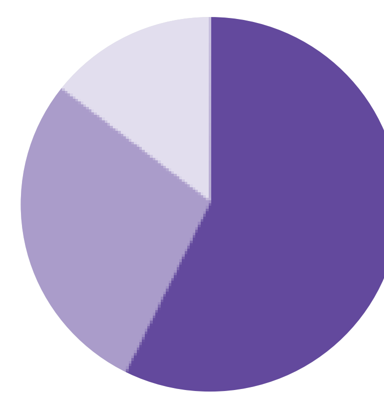
Exit/Liquidity Strategies

WHEN DO YOU PLAN ON EXITING/OBTAINING LIQUIDITY FROM THE COMPANY?



- **3.2%** Within a year
- **15.1%** 1 to 2 years
- **24.7%** 3 to 5 years
- **23.7%** More than 5 years
- **33.3%** No exit plan

HOW WILL YOU EXIT THE BUSINESS OR OBTAIN LIQUIDITY?



- **59.5%** Sell the entire company
- **26.6%** Partial sale of the company
- **13.9%** Initial public offering

WHAT FACTORS WILL INFLUENCE THE TIMING OF A POTENTIAL EXIT OR LIQUIDITY EVENT?

- Market timing **50%**
- An unsolicited offer **47.4%**
- Retirement/estate planning **46.4%**
- Asset diversification **13.6%**
- Other **8%**

Source: PharmaVOICE, Titusville, N.J. For more information, visit pharmavoice.com.

Note: Survey analysis is based on 117 responses: 53% from companies with revenue less than $10 million; 30.1% from companies with revenue of $10 million to $100 million; 8% from companies with revenue of $100 million to $500 million; 2.7% from companies with revenue greater than $500 million.

RAYMOND THEK

THE EARLY-STAGE INVESTMENT ENVIRONMENT HAS STEADILY IMPROVED SINCE THE RECOVERY FROM THE BURSTING OF THE INTERNET BUBBLE BEGAN IN MID 2002. There has been a cleansing of portfolios. The investment environment is bouncing back.

ROBERT ASHLEY

There is a lot of venture capital money around **BUT THERE ALSO IS A RELUCTANCE TO INVEST SEED CAPITAL OR TAKE PRECLINICAL RISK.**

"An investor would love to have the perfect management team on day one of funding but that rarely occurs," Ms. Boezi says. "In early-stage companies, we believe strong technical managers with a sense for business are the most important to a company's success. But the needs of a company change over time, and as the company develops, business leadership becomes more important."

Ms. Boezi says investors also seek companies that have products with reasonable regulatory timelines and well-defined clinical-trial endpoints.

"The longer a clinical trial will take to get to the relevant endpoint and the more patients that are required, the more capital a company needs to raise, which results in dilution," she says. "We look for opportunities with well-defined endpoints, where huge amounts of patients don't need to be involved for regulatory risk. The best financial stability insurance for a start-up or biotech company would be to raise capital from several venture firms that have deep pockets and have a history of supporting their portfolio companies over multiple rounds of financing and during hiccup periods."

Industry experts say companies shouldn't wait until they need capital to start raising money.

"Raising money while a company is still financially stable puts it in a position where managers can take their time and identify the investors that understand and support their business," Mr. Giampuzzi says. "Companies should remain focused on core, product-building activities rather than elegant science so as to streamline the development process. Every time a risk factor in a project is eliminated, the chances of securing additional financing improve."✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

Experts on this topic

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