THE MARKETECH GROUP MINUTE

INTERVIEW

Biotech Update - Two Continents, Two Venture Capitalists

Interview with Fred Dotzler
Managing Director, De Novo Ventures

Interviewer: Christian Renaudin, TMTG

CR: Fred, could you please provide us with a little background on your partnership?

FD: De Novo Ventures invests in two different sectors, medical device and biotech/pharma. In the year 2000, we raised a $100 million fund, and in 2004 we raised a $250 million fund.

We have six managing directors: Rich Ferrari, Joe Mandato, David Mauney, MD, John Simpson, PhD, MD, Jay Watkins and me. Each has either extensive venture, entrepreneurial, operating, and/or clinical experience. We believe we add significant value to the companies we fund. We view ourselves as partners with the entrepreneurs.

Recently one of our portfolio companies, Renovis, went public. Favrille is currently in registration to go public. We have four medical device companies with extremely steep sales ramps. Fox Hollow Technologies, which has developed a device to remove plaque from peripheral arteries, is growing rapidly. Many of the patients treated with the Fox Hollow device have been spared lower limb amputations. MicroVention, which has developed the next generation of coils for treating aneurysms in the brain, is growing rapidly. Sales are growing rapidly for CryoVascular and Senorx.

CR: Tell us about your background and how it prepared you to become a venture capitalist, and about some of your previous investments in biotechnology and pharmaceutical companies?

FD: I worked in product management for the pharmaceutical division of Searle, and was promoted to be Director of Marketing. Next I was recruited to be Director of Marketing for Millipore where I learned about the tools and applications of biotechnology. Then I became VP of Marketing and Sales for Merrimack Laboratories, a company that developed and sold lasers for surgery. Previously I worked in acquisitions and manufacturing, and I sold computers for IBM.

I've invested in biotech companies such as Anergen, Anesta, Biosite, Inhale (now Nektar), Tularik, and Vitaphore. At De Novo I've made investments in Favrille, Point Biomedical and Renovis, and medical device companies Microvention and Senorx.

CR: We have had numerous cycles in the biotech industry. In the '80s it was companies like Amgen, and in the late '80s and early '90s, everyone, including investors, was going crazy about biotech. In the end, growth wasn't as fast as originally thought. Investors did not foresee the slow FDA approval process and how it would significantly slow the growth of the industry. Do you agree with this overview, and if so, what would you say is responsible for the renewed interest in investments in biotech companies by venture capitalists?

FD: Yes, I do agree that the interest in biotech companies of the late '80s and early to mid '90s tapered off, and that there is a renewed interest in investing in this sector. As far as the drivers for renewed interest in biotech, we can look at multiple factors.

The most important driver for this renewed interest is the number of drugs that have successfully moved through clinical trials. In addition, many

of the companies financed in the '80s and '90s, including Gilead, Cephalon, Idec, have reported significant increases in sales, earnings, and share prices. Genentech and others have generated tremendous returns for investors. The approval of additional drugs and increases in product sales have driven their significant increases in valuation.

Another driver for the renewed interest in investing in biotech companies involves acquisitions. Large biotech companies, as well as large pharmaceutical companies, have acquired several of the smaller biotech companies. For example, Amgen acquired Tularik and J&J acquired Scios. Millennium acquired Cor Therapeutics. Pfizer recently acquire Esperion.

CR: What event or phenomenon destroyed or slowed investment in biotech startups at the end of the 1980s and the beginning of the 1990s?

FD: I will answer this question more as a summary of what we look for when investing in biotech companies. Many companies started 10 to 15 years ago that still struggle today due to a variety of factors, including a narrow technology base (not usable across applications), the lack of strong teams (science, clinical, regulatory) capable or reaching the finish line , and the lack of strong investor syndicates that were prepared to fund the company through several financing rounds.

When investing in a biotechnology firm, we look for the following:

- A large potential market
- A platform technology that will create biologics or small molecule pharmaceuticals with a high probability of producing meaningful clinical results
- A management team with experience
- The ability to raise sufficient capital to bring the product through clinical trials.

Taking these factors into consideration will certainly increase the probability of success for an investment in an early stage bio/pharmaceutical company.

No key indicators exist to predict the ability of a company to go public and raise large amounts of capital. The willingness of investors to buy stock of a company that does not yet have approved products in the market in an initial public offering (IPO) is difficult to predict. IPOs are usually viewed as financing events, and not exit strategies for investors.

CR: Is there the same interest in biotechnology today as in the 1980s?

FD: In the 1980s, a promising technology could get funded without fulfilling all of the investment criteria I mentioned. To raise initial capital today, a startup needs a strong technology, but more than that, needs proof that the products being developed and tested will produce a clinical benefit in patients. The company needs a strong management team and a strong scientific team.

CR: What about orphan diseases?

FD: The Orphan Drug Act was passed in 1983 to abet investment in diseases with low prevalence, those affecting fewer than 200,000 patients. Companies developing drugs targeted at these diseases receive marketing exclusivity for 7 years, they receive tax incentives, and those targeting serious diseases benefit from expedited approval by the FDA.

We view these incentives very favorably, but we do not have a particular focus or emphasis on companies working in these areas.

CR: What criteria do you evaluate when assessing an investment opportunity? Is it platform technology or disease focus?

FD: We will invest in companies with either a disease or platform approach, providing the markets are large and the company can convince us that the products being developed will yield significant therapeutic clinical benefit.

CR: With regard to cancer, hasn't approval traditionally taken a long time?

FD: The approval pathway for cancer therapies has changed in terms of the approval criteria. The FDA used to look at prolonging life as the key criteria for approval. Now the agency is willing to approve bio/pharmaceuticals for cancer based on prolongation of time to progression of the disease.

CR: Conversely, are there diseases for which it is difficult to raise capital because of time to gain FDA approval?

FD: Tough diseases for obtaining funds include diseases such as Alzheimer's disease. To gain FDA approval to market a pharmaceutical, companies need to prove efficacy. The time course of progression of this disease is highly variable, so the trials can take years. It is also difficult to define and measure clinical endpoints.

Some cancers (prostate, breast) often progress very slowly, so the time to prove significance benefit in clinical trials can be quite long.

CR: Are your institutional investors stringent on the rate of return?

FD: Our investors expect to make a rate of return significantly above the rate they can earn by investing in public companies. We perform modeling of each individual company prior to investing. It helps us determine rational pre-money valuations at which we are willing to invest.

CR: How do you define a successful biotech startup, one that starts out with an international outlook or one that prefers to maintain a regional strategy?

FD: As far as success is concerned, we look at a projected multiple of our investment. For example, if we invest $15 million over a 3 to 4 year cycle, we would like to return at least five times that amount within a 5 to 7 year time horizon.

The companies in which we have invested have focused almost exclusively on the U.S. market, primarily because it has the best reimbursement rates in the world. So, we usually invest in companies that are U.S. based and have a U.S. outlook initially. Most companies will eventually find partners to take them into international markets.

For example, Favrille is conducting clinical trials in the US. Renovis has a partnership with AstraZeneca for their pharmaceutical for stroke, and the phase III clinical trials are being conducted throughout the world.

CR: What advice do you have for someone with a desire to create a biotech startup who is coming directly from the academic arena, that is, how do you resolve, as an entrepreneur, the lack of a track record coming from academia?

FD: First, the person should plan to develop products with meaningful clinical benefits targeting large and growing markets. Second, it is important to secure strong patent protection for intellectual property as soon as possible. Third, it's essential for the founder to recruit the best scientists and other team members that one can find. It can be very helpful to find someone with industry and start-up experience to help guide one early on. Our team at De Novo Ventures will work with a scientific team to help recruit the rest of the executive team.

CR: What about a biotech startup that already has a corporate partner?

FD: This definitely represents a plus because it is an independent validation of the company's technology. A corporate partner can also serve as an alternative source of less dilutive financing.

CR: What are the next hot trends in biotechnology over the next five years, and in what areas of biotech will VCs invest?

FD: There will be significant investment opportunities for products aimed at diseases that have not historically had good therapy. There are major opportunities to have an impact on the treatment of diseases of all major organ systems. In the CNS it's diseases such as epilepsy and stroke. In cardiovascular there remains a major therapeutic gap in heart failure. Immune dysfunctions such as multiple sclerosis need much better therapies. Moreover, there are no good treatments for chronic obstructive pulmonary disease. Infectious diseases such as hepatitis C are not well treated with current therapies. In ophthalmology we are just at the beginning of promising biopharmaceuticals for macular degeneration. Effective treatments for irritable bowel disease are lacking.

We've made progress in treatments for some diseases during the past ten years. Rheumatoid arthritis was only marginally treatable five to ten years ago with steroids, which have serious side effects. Now new and better therapies exist, including biologics such as Enbril, Remicade, Humira and others. If one was diagnosed with AIDS 20 years ago, the prognosis was bleak. Now, HIV infections and AIDS have practically become chronic diseases for many who are infected. Despite the progress we've made, there is much more to be done.

We're bullish on personalized therapies for diseases which have high patient-to-patient variability. That's why we invested in Favrille, a company that is developing patient specific treatments for lymphomas.

In the absence of clinical data, we're not capable of predicting which technologies will work for a particular disease. Researchers in universities and

companies are pushing the envelope on all fronts – small molecule pharmaceuticals, proteins, carbohydrates, nucleic acids, lipids, etc.

The discovery tools are getting better, and companies have access to drug libraries that are more robust. The fruits of sequencing the human genome are beginning to ripen.

As you can see from my investing history, I like companies developing small molecule pharmaceuticals, and I like drug delivery companies.

CR: Are there technologies where you're more cautious?

FD: I'm still optimistic about the great potential for stem cell therapy, but I believe it will take awhile to perfect the technology and create winning business models. I'm also quite cautious about gene therapy. Successes to date have been limited, but they will come.

CR: Should investor be optimistic about investing in bio/pharmaceutical companies today?

FD: Investors need to be selective in determining what they will fund. They still have to ask the right questions and make sure that the companies they are evaluating have a proven team and enough cash available to get to the finish line. In the early '80s, biotechnology was so new that a basic discovery could get funded.

The opportunities to impact diseases which are unsatisfactorily treated with current therapies are almost limitless. With careful selection, investors can earn great rates of return while having a significant impact on large numbers of patients throughout the world.

CR: What is the exit strategy for investors? Is an IPO still valid?

FD: An IPO should be viewed as a financing strategy for a bio/pharmaceutical company that does not have FDA approved products. Liquidity for investors usually comes from either an acquisition of the portfolio company, or from an increase in valuation of the company's public security driven by a significant ramp in product sale.