



The of **FUTURE** **Biotech**

FUELED BY GREATER MARKET CAPITALIZATION, combined with a maturing market, biotechnology companies are starting to **EXERT MORE CONTROL** over their product lines — a growing number of these entities, once dependent on big pharma for capital, are **BECOMING INTEGRATED COMPANIES** on their own.

Until fairly recently, top-tier pharmaceutical companies obtained license rights to a product developed by a biotechnology company, thereby infusing much needed capital for furtherance of clinical research. In return, the pharmaceutical company obtained outright or majority rights to marketing and manufacturing.

In 2000, biotech companies saw their bank accounts increase exponentially as venture capitalists poured money into the industry and biotech stocks soared in value. During that year, U.S. biotech companies raised \$33 billion on Wall Street, more than in the previous five years combined, according to a report from Ernst and Young — Focus on Fundamentals: The Biotechnology Report. While financing slowed in 2001, a year that was considered the worst financing environment in a long time, the biotech industry raised about \$13.4 billion — its second-biggest financing year ever.

All of this means the biotech industry is relatively flush, with more than 50% of publicly traded companies having at least three years of cash on hand. That cash injection has enabled biotech companies to develop their products to a later stage before seeking a partnership, and to begin to realize the goal of greater autonomy through their own commercialization efforts.

ON THE CUTTING EDGE ...

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FARIBA GHODSIAN, PH.D. Managing director/director, healthcare research, Roth

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LONNIE MOULDER. Executive VP, responsible for operations, commercialization strategy, and business development, MGI Pharma Inc.,

nology

The Genesis

MAC. Many biotech companies were started around core technologies that had either sequencing efforts or functional genomics efforts. In the past 12 to 18 months there has been a shift in business models for a lot of these companies. Instead of relying on collaborations for their technology, biotech companies are realizing that to better serve investors and shareholders, they need to have a recurring source of revenue, which isn't found on the content side.

POSTLE. Biotech companies with tool kits such as genomics, proteomics, monoclonal antibody technologies had leads over anybody else. They had unique intellectual property. But a lot of this intellectual property is being eroded, and now it's not so much how good the intellectual property is, but how good is the company at applying that intellectual property in a way that leads to products in

development. Many biotech companies started with a business model that was based on their platform technology and they created a sustainable business. The trouble is these various tool kits quickly become commodities and so the opportunity to develop a sustained business just by being a platform technology company diminishes.

MAC. Companies that provide gene sequence, gene expression, and SNP data are seeing erosion of pricing power, as more efforts are undertaken in the public domain. They have a problem with depreciation of that asset base, and to drive the organization they have to move downstream into drug discovery and development.

GHODSIAN. From the beginning there have been companies that have been moving toward the direction of full integration. The



MGI Pharma anticipates launching several products between now and 2005, and establishing them in the U.S. oncology marketplace.

LONNIE MOULDER

largest biotech company, Amgen, established the model of a fully integrated biopharmaceutical company and obviously that trend is continuing. A lot of companies seek a partnership with large pharma for their first product, but

Minneapolis, Minn.; MGI Pharma is an oncology-focused biopharmaceutical company that acquires, develops, and commercializes differentiated products that address the unmet needs of cancer patients

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for subsequent products they believe they could be in a better position to market products themselves.

BURRILL. The big test along the way always has been clinical milestones for integrated drug companies. But as we look to the platform and information companies that didn't have clinical milestones, it was difficult to evaluate them. For example, when companies began sequencing the genome, Wall Street's reaction was to ask, how does that translate into growth and earnings? Wall Street needed help to understand what that means. By and large the models that the information or technology providers began to offer to Wall Street didn't seem to have anything that Wall Street could really understand in terms of revenue and how the company could make money.

TANNER. Many biotech companies were started essentially with one discovery. There's the argument that through the discovery of something very important a company could be created around that discovery. But, the

question being raised is, does one discovery provide a track record for further discovery or was the company lucky once? The "renewability" of the pipeline is an issue. Merck, Pfizer, Bristol-Myers Squibb have a track record of always innovating and coming up with new drugs. But, with a scientist who started a biotech company because he or she cloned a gene or discovered a molecule — there's no real established track record. Establishing a biotech company as a fully-integrated pharmaceutical company in terms of sales and marketing based on one discovery might be putting the cart ahead of the horse.

BURRILL. Over the last 20 years, Wall Street has moved back and forth from being fully integrated company lovers to being lovers of companies that were able to extract tremendous value by being niched in a smaller area.

The Evolution

FELDBAUM. Within the ranks of biotech companies are future Pfizers, Mercks, Glaxo-

Financing — A Double-Strand Twist

BURRILL. Wall Street has honored predictability and consistency, and the enemy of Wall Street is unpredictability and uncertainty. The problem, by and large, is that the biotech industry has not met expectations, whether it's clinical expectations or revenue expectations or earnings expectations. Wall Street has had trouble trying to understand an industry that is not predictable, and that has led to a fair amount of complexity in trying to get Wall Street to follow it. So over the 20 years that Wall Street has had to deal with biotech it has tried to find surrogates for value and certainty. Corporate partnerships, head count, aggregate R&D spend, or quality boards all have been

surrogate vehicles in trying to give the unknowing Street some comfort that biotech companies are real and are going to do something.

POSTLE. There are too many biotech companies. And investors are becoming a lot more picky in terms of backing individual companies. I can remember when biotech was "in" and getting funds for any biotech company was relatively easy. But now, the biotech company's story has to be right.

ROSEN. The total amount of money raised in 2001, versus 2000, according to BioWorld (a major industry publication), was about \$13.4 billion versus \$36.5 billion. There is a bigger skew with IPOs. In 2000, there was about \$22.8 billion raised in IPOs or secondary offerings, and in 2001 it was only about \$4.2 billion.

FELDBAUM. In 2000, the biotechnology industry attracted more investment than in the previous five years combined — a record \$33 billion in the U.S. and \$6 billion in Europe. But what's almost even more amazing is that, despite a correction in valuations, the industry remains a magnet for investment. 2001 was second only to 2000 in terms of investment, with \$14.5 billion raised for the year. Moreover, the industry's market capitalization has

Over the last 20 years, Wall Street has moved back and forth from being fully integrated company lovers to being lovers of companies that were able to extract tremendous value by being niched in a smaller area.





SmithKlines, and Eli Lillys. Taking that initial leap into the marketplace is perhaps the most critical step. Already, this process is under way. Many of the dozen or so largest biotech companies have transitioned into launching and marketing products on their own. Indeed, these companies are now able to act much like large pharmaceutical companies

themselves — witness the Millennium-Cor acquisition, and the Amgen buyout of Immunex. Intra-biotech mergers of this size were simply unthinkable a few years ago.

POSTLE. Now is a nice time to be a biotech company. But there is one downside, and that is biotech is still a cash-burn industry, and

because it's a cash-burn industry it still relies on going back to the stock market for periodic injections of funds to keep its cash flow going. The stock market has shown over the last five years that it is very volatile — it's either open or it's closed. And if the market happens to be completely shut when a biotech company needs more funds, the company is dead. When the market is shut it's shut. If biotech is out of favor, then all biotech companies are out of favor.

BURRILL. The biotech industry is cash rich today relative to where it has been. The money companies have raised over the past three years puts the industry in substantially better financial shape than it's ever been in its history. Obviously, a better financial position allows biotech companies to partner from strength not weakness. The biotech industry has substantially more products in late-stage clinical development and a much stronger balance sheet — and therefore is able to partner with big pharma on much more favorable terms. In many cases, there's more risk sharing, more profitability ultimately accruing to the

remained high by historical standards, and is currently almost \$300 billion — off about 15% to 20% from the 2000 peak, but still more than three times the level of mid-1998 and double the industry's value in mid-1999.

BURRILL. The industry raised \$5 billion in 1996, 1997, 1998 and that was the industry norm for 20 years. In 1999, amidst the excitement around the human genome project the industry raised \$10 billion, then \$32 billion in 2000, and \$11 billion in 2001. Even in what is considered the worst financing environment in a long time, this industry had its second-largest financing year. The industry does have substantially more capital. The venture capital end of it in 2001 raised about \$5 billion in new money to invest, just in healthcare biotech. The industry's absolute market cap at the end of 2001 was \$366 billion. In December 2000, it was at \$422 billion, down by 13% from 2001. At mid-September 2001, the industry's market cap was \$305 billion. The industry went from \$422 billion at the end of 2000 to as low as \$305 billion after September 11, and then recovered to \$366 billion by the end of the year, so it had quite a ramp up in the fourth quarter.

ROSEN. What is happening in 2002, particularly after 2001, a year that was not as good for financing after a record year in 2000, is the continual movement toward building critical mass, which I define in three areas: product pipeline, financial stability, and product commercialization. These three things are driving the industry; and because it has been such a difficult year there are some relative bargains out there. Those companies that are in a good financial situation can pick up other companies and technologies relatively cheaply and enhance or increase their product line. The name of the game in the biotech industry is to secure a continuous product pipeline.

TANNER. One thing that has kept biotech companies from becoming fully integrated is a lack of capital, since it's an expensive proposition. It's only in the last year and a half that the window for capital has been opened. Companies such as Millennium or Human Genome Sciences went to the capital market several times in 2000. Most of these companies have historically high levels of cash and so their financial viability is greater in terms of their ability to take drugs further in development.

FELDBAUM. The market capitalization of Pfizer is \$247 billion; the entire biotech industry's market cap is just under \$300 billion. Why is one Pfizer worth almost as much as almost 300 biotech companies? Because Pfizer markets a vast array of products worldwide and has tremendous cash flow and substantial profits. The company's diversification across many established product lines ameliorates investor risk, even as a hefty portion of revenues are reinvested in R&D to create products for the future.

POSTLE. In Europe, there's a general nervousness about the market and the feeling I'm getting is that biotechs are almost turning their back on the market and finding that they have to get their funding elsewhere. There is far more of a focus on looking at significant up-front payments to fund the next stage of research. Companies aren't going to go for a rights issue, they are going to sell some of their family jewels and look to see if they can actually get the funds from a licensing deal. There's an acceptance that going back to the market right now is very difficult because the market has been closed for so long in Europe. Nobody is forecasting that it will open imminently.



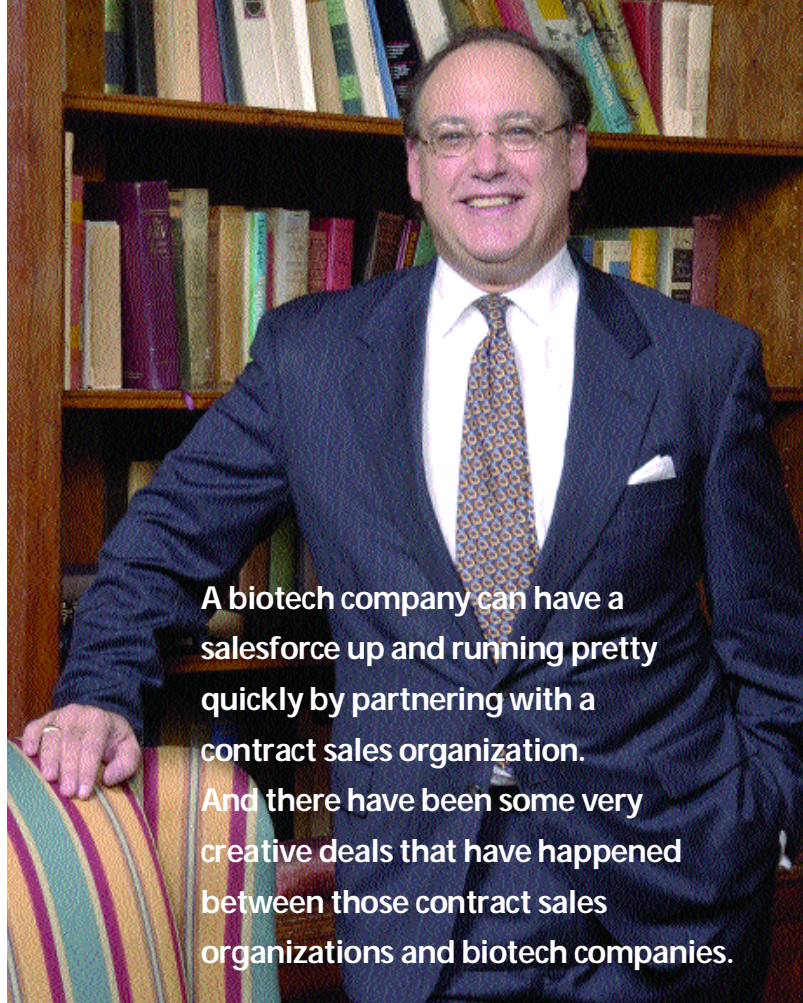
biotech partner, not just the pharma partner.

FELDBAUM. In general, there does seem to be a growing interest in moving to full integration. That trend now extends to R&D-stage companies, which are partnering aggressively and merging to combine technologies that will generate drug candidates. This means companies that can identify genetic targets are joining forces with those that can generate compounds to act on those targets — antibodies, antisense, and small molecules.

MAC. The industry is just coming to maturity. Much of the reason that it has taken time for biotech companies to become fully integrated has been access to capital in terms of being able to afford the downstream effort. The capital that was raised in 2000, when the financing window was opened, definitely helped. There's a cyclicity in the financing

window for biotech. As companies have been able to get a few years worth of cash on the balance sheet, they could then look to expand their capabilities. Downstream capabilities finally became areas that biotech companies realistically could support from a financial perspective.

FELDBAUM. There is no single template as to which types of biotech companies are most likely to go it alone in the marketplace and when might be the right time to take such steps. Generally, a company doesn't launch a product on its own until it's reasonably established and on a solid financial footing. Often, a company takes that plunge with a second or third product after initially pursuing the traditional model of outlicensing. But again, much depends on the specifics of each company — its corporate vision, the status and size of its pipeline, and the size of markets its products address. Some companies pursue vertical integra-



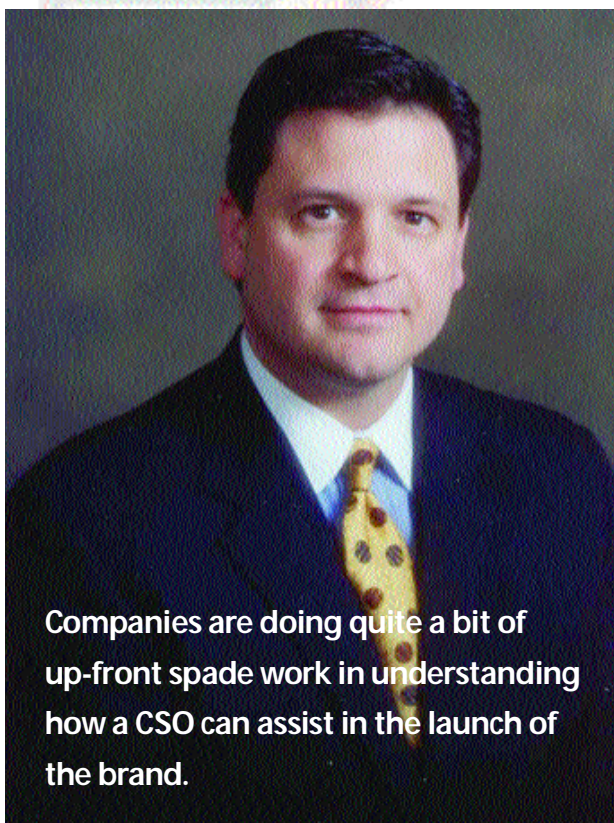
A biotech company can have a salesforce up and running pretty quickly by partnering with a contract sales organization. And there have been some very creative deals that have happened between those contract sales organizations and biotech companies.

MICHAEL ROSEN

tion by developing a product all the way through — from preclinical testing to marketing. Others leapfrog into the marketplace by acquiring rights to a late-stage or commercialized product. The permutations, quite simply, are as varied as the companies themselves.

BERNITZ. Organogenesis' move towards full integration has been a very purposeful and planned transition. It's to the company's credit that it's been able to integrate very quickly. From mid-2000 to where we are right now, we've made tremendous progress. It has involved some re-focusing of resources. We've added people in marketing and sales, we've reduced some people in our basic research areas. We really looked at what skills we needed and made the hard choices necessary to get there. Integration is certainly possible if the process is well-thought out and done well. But it's certainly something that can be done badly. A company needs to have people in place who have broad enough experience to be able to recognize the pitfalls and be able to react quickly to them.

FELDBAUM. These days, the largest biotech companies are opting to market products independently, and they're even licensing in promising or approved compounds from smaller biotechnology companies. These



Companies are doing quite a bit of up-front spade work in understanding how a CSO can assist in the launch of the brand.

STEVE COTTRELL

biotech companies structure their efforts around specific disease franchises, for example in cancer or cardiovascular products, and are developing and in-licensing products to expand those core franchises. This strategy maximizes a specialty salesforce.

BERNITZ. I come from the biotech industry, and before that big pharma, so I've seen many different types of companies go along the integration path. One thing I felt was highly risky, and I saw several companies have trouble with, is when a company invests large sums of money in infrastructure in advance of having sales to support it. When we set up our technology venture division to develop our near-term products, we started with an aggressive outsourcing strategy. We outsourced manufacturing and most of our preclinical development. During the development stage, we kept our internal fixed costs pretty low so that we could adjust our expenses as timelines changed and as our strategy evolved.

PRATT. As the biotech industry has matured, companies realize they don't necessarily have to partner with the big pharmaceutical companies for their drugs, they can take a compound all the way through development themselves. That is often where the highest economic return is, so to realize that return the company needs to be fully integrated.

ROCHE. Cephalon, in the past five years, has evolved from a pure discovery/research organization to an integrated company. Cephalon has gone through the various stages of maturation, growth, and development that followed the initial product paths through the drug evolution and development process 13 years ago. From bench research and discovery through early drug development, through pre-clinical development in non-human models, through early-stage clinical development in healthy volunteers into patients. And then through Phase I, II, III, and ultimately Phase IV research that a product follows in its life cycle. When I joined Cephalon in December 1994, we were just at the stage of embarking on our own commercialization exercise. We had drugs in development, and we had been successful in in-licensing compounds, such as Provigil at a relatively early stage in its development. So we were depending not only on our own discovery-research programs but also aggressively pursuing product prospects through business development means. We completed, at that point, the integration process, which included research, development, clinical activity, manufacturing, and selling and marketing. We built our own salesforce to co-promote a product with Bristol-Myers Squibb back in December 1994 (Stadol NS, a potent opioid analgesic marketed for the relief of moderate-to-severe migraine headaches). That really got us started

as an entity in the commercial arena. It allowed us to develop relationships that we continue to nurture today. We grew from a sales organization of 23 or 24 sales people to about 250 people today in the U.S. alone. And every portion of the business has grown significantly since those days. The decision to become fully integrated was a strategic one made by Frank Baldino, our CEO, years ago to ensure that Cephalon was able to fully benefit from its own research and development and from the revenue and profitability that comes from being able to sell and market its products, whether they are developed in-house or in-licensed from a third party.

POSTLE. We are seeing a model evolving of the in-licensing biotech company, which is quite novel. A biotech company might have some products, which have big commercial potential that it has to out-license, it has other products that it develops that can be commercialized itself, but it also tries to in-license products that already are on the market that it can commercialize. This allows the biotech company to wean itself away from relying on funding from the stock market to relying on funding from a cash flow from its own small revenue products.

BURRILL. Historically companies that have been larger and more integrated are companies that Wall Street is more comfortable with — the big drug companies, big electronics companies, auto companies, those that are fully integrated and less binary. In the late 1990s, Wall Street fell in love with genomics and believed that the sequencing of the human genome was real and was going to give rise to “a whole new industry,” in which we were magically going to be able to take all this information from genes and convert it into drugs. Wall Street had an enormous appetite and there were large amounts of money thrown at any company that had a technology that was going to be able to extract some information and “build value.” There was a tremendous ramp up that ended in March 2000 when Bill Clinton and Tony Blair made some errant comments and the industry lost \$100 billion in one week. That ramp up, which put expectations way ahead of reality, enabled 67 companies to go public in 2000 and enabled the industry to raise \$32 billion in 2000. The expectations by Wall Street were

that all these companies would be able to produce very large and growing revenue streams and high earnings and extract a lot of value from the information that they now had. As Wall Street began to sharpen its pencil, the reality versus the dream began to set in. Wall Street began to struggle with how all these companies were going to make money and who their customers were; how big the spend was going to be. Would these companies be able to really make big money or were they a job shop, a research shop, or an information provider? It was very clear that Wall Street understood the value of drug and biotech companies that came up with drugs, whether the company was ImClone, Human Genome Sciences, Genentech, or Amgen. Companies

DR. FARIBA GHODSIAN



A lot of companies seek a partnership with large pharma for their first product, but for subsequent products they believe they could be in a position to market products themselves.



that were drug companies as opposed to technology and information companies generally accrued higher values. There was a dramatic difference in how Wall Street perceived the value of an integrated drug company compared with an information provider.

BERNITZ. As part of our strategy of becoming more commercially focused we've done two things. The first thing we did was develop the Technology Ventures Division, which was operationally separate from the rest of the company. That allowed the division to develop products rapidly without having to pull people off Apligraf, our primary product. Once the new products were ready to be commercialized, we reintegrated them into the company under the Worldwide Commercial Operations department. That worked very well. We formed the Technology Ventures division in August of 2000, and we launched the first product the following October, and the second one was approved in January 2002. Those products were FortaPerm and FortaGen. We started the division with three people — myself as general manager; a head of product development, who planned and oversaw most of our outsourced activities; and a head of business development. We then brought in a very experienced director of sales and marketing after we decided to integrate into commercial operations.

ROCHE. Cephalon has used a number of very innovative and highly productive means of selling and marketing. What we have done, at least as well if not better than any other niche pharmaceutical company, is to build our own sales organization and to train, prepare, direct, motivate and incentivize that sales organization in a fashion that has caused it to become extremely effective and highly productive in terms of generating revenue.

TORMEY. Our research has led us to conclude that biotech is a very exciting and emergent marketplace. There have been 117 biotechnology drug products and vaccines approved by the FDA. Of the biotech medicines on the market, 75% were approved in the last six years. There are more than 350 biotech drug products and vaccines currently in clinical trials targeting more than 200 diseases. According to Ernst & Young, there are more than 1,200 biotechnology companies in the U.S., of which 300 are publicly held. Our experience



Smaller biotech companies will look to merger and acquisition activities to build a greater infrastructure, whether it's on the R&D side for more pipeline and more clinical development support or on the sales and marketing side.

SUSAN C. SHAKE

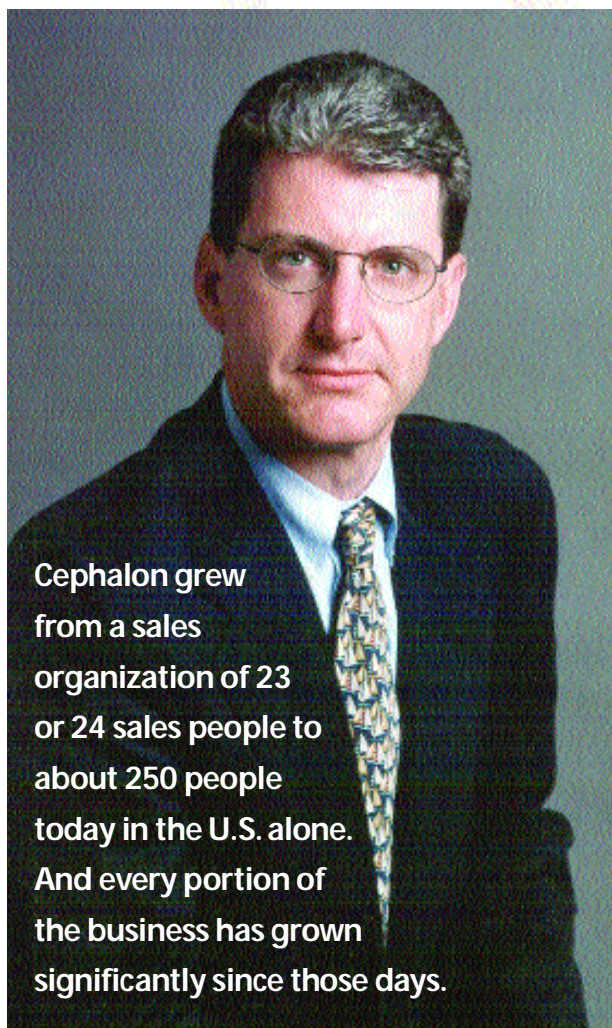
at Nelson Professional Sales is there is a tremendous interest in outsourcing the selling functions with these biotech companies. The biotech companies requesting our assistance in commercializing their product vary. Inquires typically start with market research, then a request for marketing assistance. The biotech company's need for sales support is usually the next topic. Their needs range from contracted field sales to telemarketing to lead generation to peer events to salesforce training and recruiting.

HEATH. Our intention at NPS Pharmaceuticals is to commercialize through our own organization two of the products that we have in development. The first of these products, Preos, human parathyroid hormone, is under study for the treatment of osteoporosis. We are currently conducting a large Phase III clinical program with Preos that we project will lead to our first NDA filing in 2004. The second proprietary product we have in clinical development is a novel therapy for short bowel syndrome, a condition that prevents adequate absorption of nutrients. This product, ALX-0600, has been granted orphan drug status in the U.S. and Europe. We also have retained co-



At Millennium, having a commercial infrastructure opens a host of new doors and opportunities for us that were further away before having an integrated infrastructure.

MARSHA FANUCCI



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BOB ROCHE

promotion rights to selected products that we have licensed to other companies for development. In addition, we are looking for products that could complement our own product line and be a strategic fit in a new sales organization.

GHODSIAN. If biotech companies are targeting a niche market, and they understand that market, going to a smaller number of physicians may be very effective. Amgen took on the dialysis anemia market 20 years ago and built it into a \$2 billion market. At the time, many pharma companies thought the market was too small.

MOULDER. We have put in place a well-balanced and unique pipeline. With Salagen tablets and Hexalen capsules on the market followed by palonosetron and irifolven in Phase III and MG98 in Phase II trials, we believe that our commercial organization is well-positioned to launch oncology products over the next several years. We anticipate launching several products between now and 2005 and establishing them in the U.S. oncology marketplace. Also, we will be executing on our business development and licensing strategy, which is to obtain currently marketed products and selectively pursue oncology product candidates that have demonstrated activity in human clinical trials, in-license those products, and then fully develop them with our in-house development group. When MGI first launched Salagen in 1994 it had less than 20 people in its sales and marketing team. In the spring of 2000, we really grew the salesforce and the internal marketing group.

GHODSIAN. A good strategy for biotech companies looking to become fully integrated is to collaborate with a large pharma on one of the indications for their first one or two drugs through a co-promotion arrangement rather than a license arrangement. Through a co-promotion agreement, companies can gain experience and learn how to promote their drug. They can establish a smaller salesforce and learn the marketing game, and apply that knowledge more effectively to their later drugs.

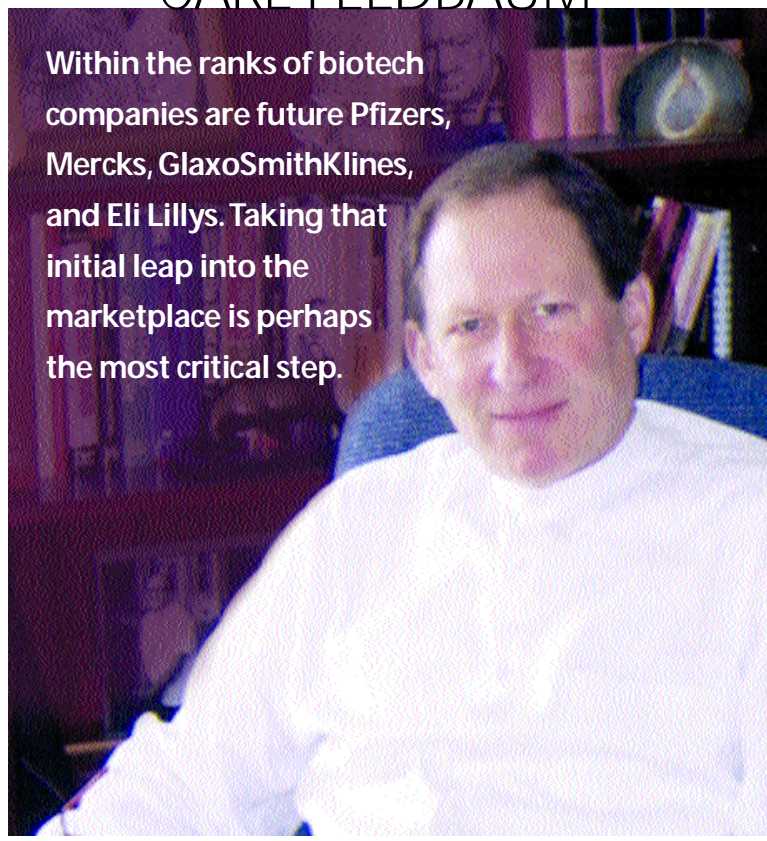
FANUCCI. We have been very focused on the strategic milestones for the company, ensuring that we are building a company that's durable in the long

term and prepared to weather market downturns. Our focus is on continuing to build on that vision, with the understanding that the capital markets will reward that strategy in the long term. We have a very ambitious objective for the company, and in charting that path forward our perspective has always been very oriented toward the future and looking at what we believe is required to succeed against the model. And while we certainly look at more defined areas to see what we can learn about success, we try not to constrain ourselves by the historic approaches to building a company. There has not been a successful leading small molecule company that has been founded in the last 100 years. We're operating in uncharted territory.

MOULDER. With the commercialization of our own products generating sales revenue of \$30 million, we have a product contribution that actually funds a good portion of the company business. So the financing needs of MGI have been less than most other companies in our sector because of this revenue and the resulting product contribution generated by the sales and marketing organization.

BERNITZ. Integration will lead us into a much stronger financial position. Once a company has a commercialization capability that can be demonstrated it enables the company

CARL FELDBAUM



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STEVEN BERNITZ

to bring in potential products from other companies that are more research based. It also allows us more control over our own destiny. Integration will allow us to enter into worldwide markets faster than if we were dependent on another company. The sentiment in the investment community is those companies that can commercialize products successfully probably will fare better in the future. The key for a small company like ours was to find within our portfolio products that were cost effective to develop and get to market, and that could be targeted to groups of physicians whom a small salesforce could adequately cover.

Splicing Techniques

BURRILL. In the last year, the biotechs did a better job in partnering with big pharma. I don't believe, though most people do, that there will be as much consolidation in biotech as is expected. Partnerships are a great alternative and biotech traditionally has been a heavily partnered industry. Big pharma has been able to acquire a lot of what it wants through partnering, it hasn't had to do it through acquisition.

POSTLE. Biotech-biotech mergers work, but usually that's only a preliminary phase. If the

biotech-biotech merger can result in a company that then can become a pharmaceutical company and have its own cash flow, that's great. When big pharma acquires a biotech company, there's a tendency of big pharma "ruining" what it just bought. Suits and the sandals don't often mix that well. There's another model that we're seeing evolve, and that's where big pharma acquires a majority shareholding, and in exchange they put into the biotech company a small product stream that will allow the company to be self-sustaining.

ROSEN. Recently, there have been a number of mergers announced, including our own. There always has been consolidation within the biotech industry. MedImmune bought Aviron for \$1.3 billion and there was Millennium and Cor, and more recently Amgen and Immunex. In our case, it was by comparison a smaller deal, but we completed our own \$12 million to \$15 million acquisition of a small company. The reason for our merger is that we faced the same issues as other larger biotech companies. The key question was how to build further critical mass. The foremost issue was a product pipeline. The difference between what happened last year and this year in the marketplace is that the investment community basically believed that if a company's product wasn't in Phase III or Phase II, it really wasn't a product. From an investment community perspective, when a drug is in a pre-clinical or even Phase I stage there's too much development risk, so it doesn't "feel" like a product. Any company that had a technology that was Phase I or earlier has been heavily discounted and that is reflected in stock prices. One of the strategic missions for us was to acquire a product portfolio that was closer to the marketplace as well as build our intellectual property base.

SHAKE. Smaller biotech companies will look to merger and acquisition activities to build a greater infrastructure, whether it's on the R&D side for more pipeline and more clinical development support or on the sales and marketing side.

BURRILL. A large number of companies are moving to full integration through acquisition. Millennium and others are using a strong balance sheet and a strong equity value to acquire companies that have candidates or technologies that are very synergistic and for whom the opportunity to build a capital base off the boomlet in Wall Street didn't happen. Now in more difficult financing times, it's much easier for the richer biotechnology companies to use their cash and currency for acquisitions that add to integration. And since integration is perceived by Wall Street to be important, they oftentimes get more value in the post-acquisition valuation that

actually pays for the acquisition by an increased market cap. A lot of biotechnology companies are looking at other biotechnology companies as a vehicle to increase integration from outside.

Expanding the Chain

MAC. The evolution started with Human Genome Sciences, and then we saw companies such as Millennium become fully integrated by acquiring downstream capabilities through the acquisition of Cor Therapeutics. A lot of these companies are moving from just discovering and validating novel drug targets to actually internally taking those compounds

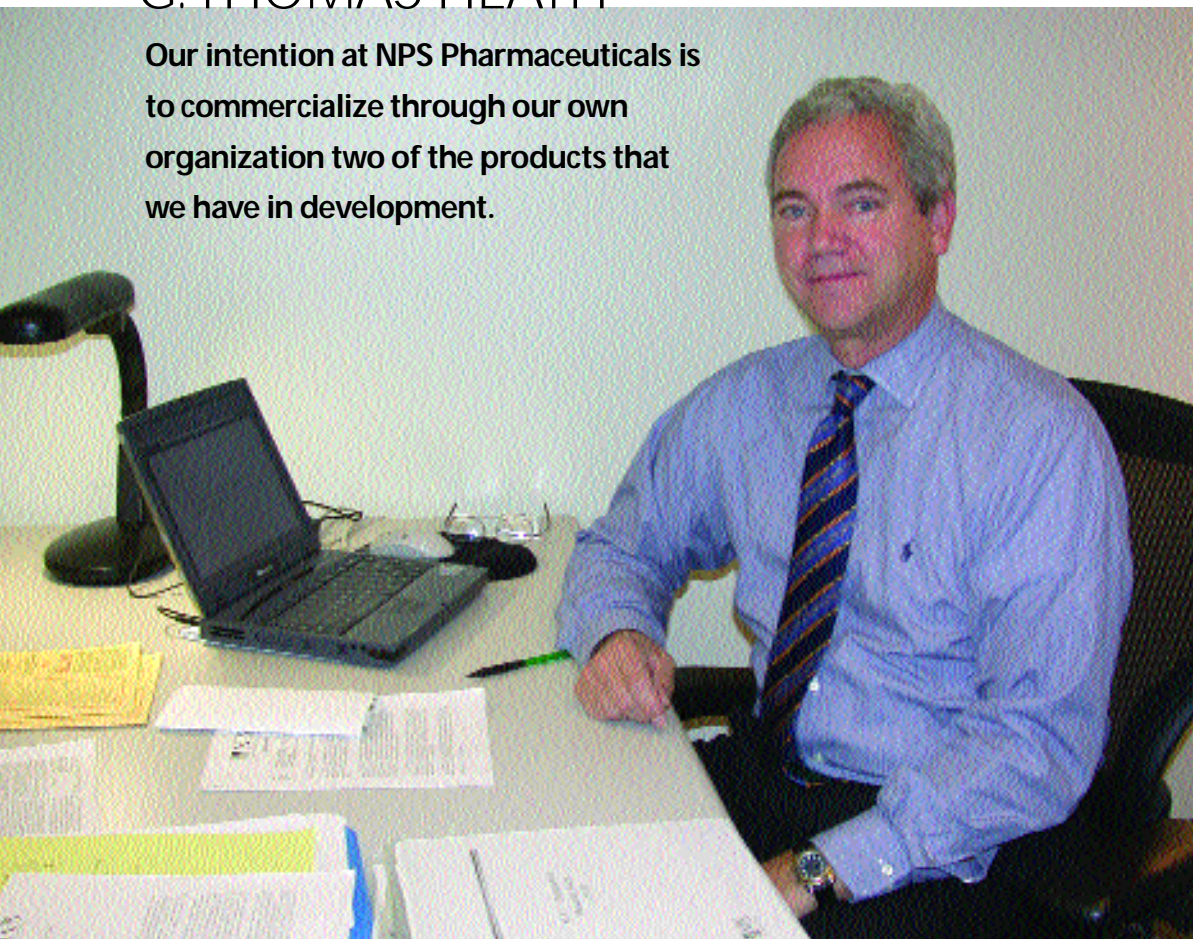
tures, which is up significantly from the 9% royalties the company received only two to three years ago.

POSTLE. As more and more database companies enter the arena, and as more and more of the human genome becomes public data, what these companies have to offer is really not worth that much. So they need to evolve up the value chain. They need to move from being database companies to being companies that specialize in targets coming from the genomic database. If they don't become fully integrated pharmaceutical companies, at least they need to get into a product development mode.

integrated like Merck — biotechs can acquire many of those resources through partnering. They don't have to build their own sales and marketing forces, although a lot of companies are. Biotech companies have to look at the reality of managed care and specialty practices to understand markets. In specialty markets, a few people can get a lot of leverage and cover a lot of space, compared with having to call on family doctors in 42,000 cities. A lot of biotech companies are focusing on markets where they can get both clinical approval and niche their way in by building a sales and distribution force in an area where they're not competing head-to-head with giant marketers.

G. THOMAS HEATH

Our intention at NPS Pharmaceuticals is to commercialize through our own organization two of the products that we have in development.



HEATH. In preparation for Preos, and anticipating future product launches, we have started building a marketing organization. We are studying our options for developing our own sales force and evaluating the experiences of other companies that have commercialized their first product. Over the next couple of years we will determine the optimal size and configuration of our own sales organization. We aim to be in a position to generate greater return on our product investments, a greater return than license and royalty revenues. This requires that we take the greater risk of selling our own products. Our best path to profitability is to capitalize on our product development investment by selling our own products.

COTTRELL. The biotech companies are developing unique, specialty markets. To gain presence in those markets, one practice is to in-license older brands within that target market that are either line extensions or have different delivery options. Another option is to launch medical science liaisons for educational purposes before a new product introduction to gain a market presence and properly introduce the new treatment. The biotech companies are now looking to the outsourcing industry to help with these and other strategies.

through clinical development. It's a higher risk strategy, but the payoffs are much greater. When Millennium started out it formed collaborations for validating drug targets with pharmaceutical partners, getting about 9% royalties. Since Millennium has downstreamed its capabilities, the company is taking products through screening, through talks, into the clinic and is forming new partnerships with pharmaceutical companies for co-promotional activities — 50-50 joint ven-

BURRILL. It is easy for a company to become virtually integrated, and for that reason biotech companies have been able to use virtual integration as a vehicle to access specialty marketing forces or distribution capabilities, and/or partner in a limited area with big pharma companies or others that have sales or marketing forces in particular therapeutic categories. That gives biotech companies leverage that they don't have to build themselves. They don't all have to grow up and be fully

ROSEN. It's not as expensive as it used to be to market products. Major pharmaceutical companies are abandoning markets with product sales of less than \$500 million, so that opens the way for specialty pharmaceutical companies that have products with potential sales between \$20 million to \$100 million, or more. Most major pharmaceutical companies today measure how many drugs they have in the "billion-dollar" club. That means there are opportunities for biotechs to



If biotech companies are to build a salesforce it should be for a product that targets a smaller indication and a smaller group of physicians.

FELICIA REED

market to niche areas — markets where there is a much more select physician audience and patient population. A biotech company can have a salesforce up and running pretty quickly by partnering with a contract sales organization. And there have been some very creative deals that have happened between those contract sales organizations and biotech companies.

POSTLE. If a company has a product it has something that effectively no other company can take away from it, unless it sells it. The company also has something that biotech analysts understand and can believe and value. Biotech analysts are very bad at valuing platform technologies, but they can value products in development.

BURRILL. There are two types of companies. There are those companies with late-stage clinical products. And there are a large number of companies that are technology and platform providers. They don't all aspire to be the next Merck, but that doesn't mean they can't be very successful companies.

SHAKE. A biotechnology company may have a product for a small targeted audience, but unless the product has a broad market potential, it's still not worth building a marketing structure. If the biotech company is coming into a market for hairy cell leukemia, for example, it's not going to have a \$500 million drug. Until the company has greater potential to generate revenue through its clinical development plan, which includes additional indications, building an infrastructure is not viable. I think biotech companies acknowledge that as long as they can get a partner that believes in their drug as much they do, then they are better off partnering until they have enough revenue to support the infrastructure themselves.

REED. If biotech companies are to build a salesforce it should be for a product that targets a smaller indication and a smaller group of physicians. That doesn't mean that at some point a company couldn't look at some of its products for indications that target a larger group of physicians where it believes it could be competitive.

FANUCCI. In the broadest context, what we have set out to do is to identify candidates that accelerate the objective of building a fully integrated company that positions us for leadership in the industry. Our 10-year vision is to be among the the top 10 biotech companies. We have gone through, and continue to have, a process of identifying companies that are aligned well with that Millennium vision, with our culture, and in areas that we believe we can leverage.



The question being raised is, does one discovery provide a track record for further discovery or was the company lucky once? The "renewability" of the pipeline is an issue.

DR. WILLIAM TANNER

TANNER. For biotech companies to become fully integrated they need first to develop a drug successfully. They're going to have to find a market that is targetable, such as oncology. Then biotech companies have to take a good hard look at themselves and ensure that if they do establish a sales and marketing effort they have something with which to follow.

POSTLE. We advise companies that want to go up the value chain to think very carefully. First of all, as they go up the value chain it takes a lot more funds, especially as the product goes into development. It takes much more money for development than if the company continues just to invest in its tool kit. And, the competitive position it enters as a company is very different. For example, Millennium now has its own products on the market, so it is competing with companies that at one time were its customers for its technology. The more a company invests megabucks in product development the greater the risk. The company is capturing more value, but it is also accepting that it is running with a higher degree of risk. As the biotechnology industry evolves, and as com-

panies mature, they move into a position in which they can accept more of that risk. We think that all biotech companies will eventually have to go along that route. They can't stay as self-sustaining tool kit companies.

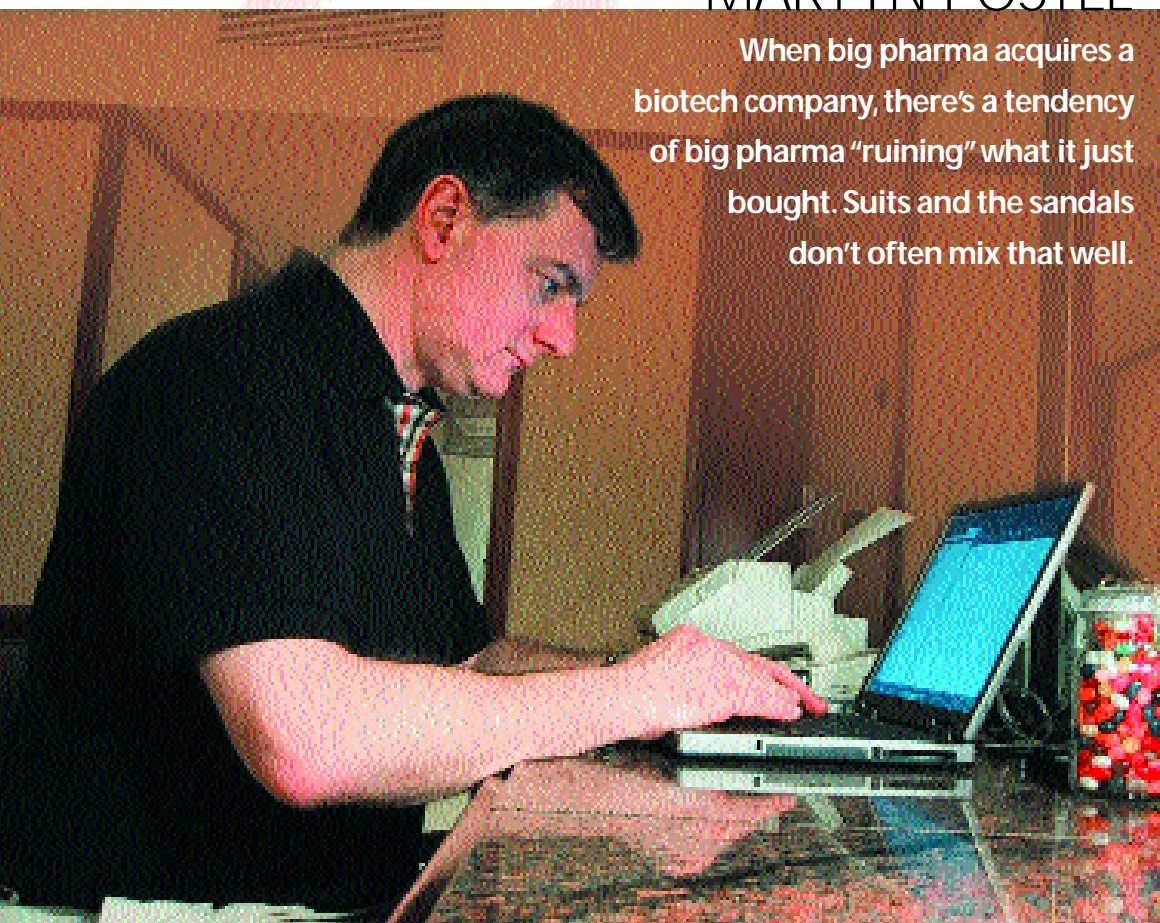
Finding the Right Link

COTTRELL. We have seen an increased interest within the biotech arena. It's been developing over the last 12 months to 18 months. Companies are doing quite a bit of upfront spade work in understanding how a contract sales organization can assist in the launch of the brand. Companies are looking at traditional CSO services as well as market development services such as target analysis and forecasting. Additionally, biotech companies are looking for national accounts and managed-care expertise.

POSTLE. Markets for exploration are any niche market. Biotech companies need to understand whose behaviors they will have to change to make their product a commercial success. Then they have start to think of what is the most cost-effective way to change those behaviors. Going head-to-head with Pfizer or Merck in selling antirheumatic drugs probably is not the most cost-effective model to adopt.

MARTYN POSTLE

When big pharma acquires a biotech company, there's a tendency of big pharma "ruining" what it just bought. Suits and the sandals don't often mix that well.



FELDBAUM. For younger companies, co-promotion is an increasingly popular option. The increasing frequency of such deals reflects the stronger cash position of biotechnology companies in recent years — because big pharma and, increasingly, big biotech are all chasing the low-hanging fruit of late-stage products, a company with such a product is usually in the driver's seat these days and able to secure co-promotion rights. With such a deal, the company secures financial support, but also the prospect of market presence. For smaller companies with highly specialized or small-market products, direct marketing on their own may be a viable option, even for a first product. Often, by the time a product is launched, the key "thought leaders" in the relevant medical specialty already have worked with the product in clinical trials and reported formally and informally to their peers. Frankly, if a product serves a previously unmet, or poorly met, medical need, the physicians will be there from day one. Yet another model is to outsource marketing. These deals allow companies to tap into ready-made marketing expertise on a commission basis and for relatively short terms (often under five years).

GHODSIAN. Amgen has been one of the best models for full integration. For its first product, Epogen, the company needed the money/validation from big pharma, so it out-licensed partial rights to Epogen in some markets, but at the same time kept one market for itself. Through that strategy the company developed its salesforce and grew the dialysis anemia market very successfully. This allowed the company to establish itself as a fully integrated biopharmaceutical company with an established salesforce. Therefore when their second drug was available, it did not have to share it or co-promote.

MAC. One of the major shifts in the industry has been in the area of biotech to pharma partnering. Biotechs are now in a much stronger negotiating position. Pharma companies desperately need to bolster their pipelines as they face major patent expirations. They are increasingly reliant on the biotech industry. The problem is big pharma is going to have to pay more for those products now that the biotech industry is more established.

FELDBAUM. Pharmaceutical companies have enjoyed stellar earnings gains in recent years, and they are under tremendous pressure from investors to keep posting double-digit growth. To do that as products go off patent, they must refill the pipeline with patent-protected products. That's good news for biotechnology companies with Phase III or NDA/BLA-stage products, because these are the optimum replacements for off-patent

drugs — they are novel and just on the cusp of entering their patent-protected period on the market. Hence we've seen a spate of \$100 million-plus deals in recent years.

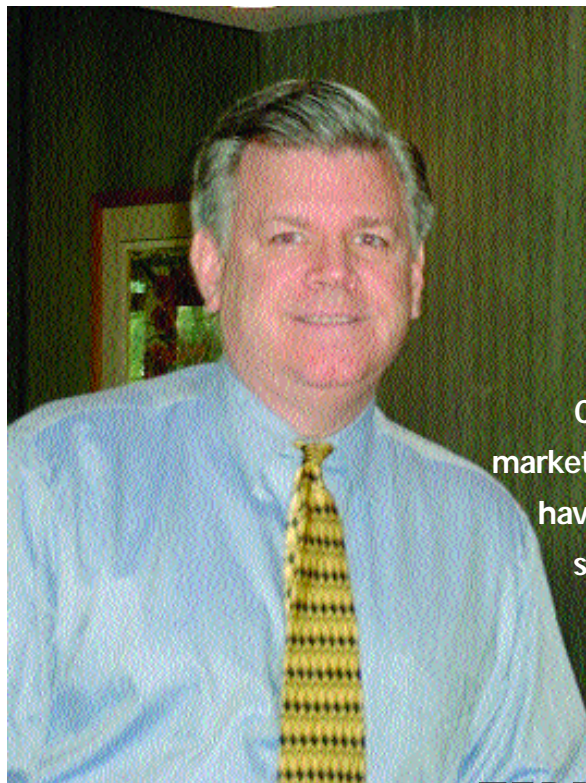
GHODSIAN. In general, biotech companies that have a broad platform are better able to pursue an integration strategy because they can share a portion of the revenue, but at the same time they keep enough to be able to go forward independently. Partnering with big pharma brings in cash as well as validation to a biotech company's technology platform, making it easier to pursue the rest of its product pipeline on its own.

MOULDER. Clearly the way for a company to capture the most value from a biopharmaceutical product is to retain rights in key markets, such as the U.S., and to commercialize the product on its own, or to collaborate with a partner in its commercialization. MGI Pharma has elected to follow this business model, retain the rights and commercialize our products alone or in combination with a partner. The greatest economic value flows to the company that has a sales and marketing capability and can actually commercialize its own products.

BERNITZ. It's almost universal that a product is never as important to the big pharma company as it is to the company for whom it's that company's livelihood. Apligraf is an important product to Novartis, but it's our life. That philosophy exists in pretty much 100% of these types of collaborations. The other issue is a lack of control over the decisions that are made on commercializing and marketing. A biotechnology company may believe that it knows the technology better, but is not in a position to make all the decisions on its own.

TANNER. Maintaining more control over the product might allow biotechs to evolve at a more rapid rate than in the past. In addition, control positions them as an attractive acquisition target. Companies that have given away the crown jewels are not attractive acquisition candidates.

FANUCCI. Our corporate vision is transcending the limits of medicine. The whole idea is to apply the combination of productivity enhancement — and that is changing the algorithm for successful drug development — and to apply personalized medicine to be able to address the right drug to the right patient at the right point. We're trying to merge some unique concepts with some of the more traditional requirements in building a company to get to a leadership position within our 10-year strategy. Having a commercial infrastructure opens a host of new doors and opportunities



Companies looking to do their own marketing and sales recognize they don't have the internal resources necessary, so they're going to outsource those functions — everything from the marketing, to the selling, to the ancillary services.

TERRENCE TORMEY

for us that were further away before having an integrated infrastructure.

ROCHE. Before we had our own products to commercialize, sell, promote and support, we worked with several other pharmaceutical companies, Bristol-Myers Squibb, Abbott Laboratories, and a device company called Medtronic, and co-promoted their products for them. This was about three years before we launched our own products. We established a salesforce and a marketing team to build a reputation, a market presence, and relationships with key customers who would be critically important when we were ready to launch our own products. And it was through the relationships and strategic alliances that we developed with Bristol-Myers Squibb and Abbott that we were able to achieve our strategic objectives as well as establish our commercial organization as a self-funding entity within the company. We launched Provigil, our first product in the U.S. in February 1999, and were able to experience tremendous initial success in the marketplace because of the excellent relationships that we had been nurturing and supporting over an extended period of time.

COTTRELL. The basic tasks of biotech sales teams are not largely different than big pharma. A sales person must have sales ability. The difference lies in the execution of the strategy, the positioning of the brand, and the technical/educational requirements needed to

launch/support the product. The biotech industry is now seeing outsourcing as a viable alternative given the kind of quality services that are now available.

TORMEY. Companies looking to do their own marketing and sales recognize they don't have the internal resources necessary, so they're going to outsource those functions — everything from the marketing, to the selling, to the ancillary services. As the biotech company matures, and as its products are brought online, the company begins to pick and choose the components it wants to bring in-house.

SHAKE. The greatest difference between pharmaceutical companies and biotechnology companies is a lack of infrastructure, in particular the lack of sales and marketing. Because biotech companies don't have the infrastructure or established relationships with a lot of vendors, they are much more receptive to a comprehensive integrated solution for their sales and marketing commercialization needs. It's an alternative to out-licensing or co-promoting with big pharma, and allows them to keep more control of their product, as well as hold onto better downstream rights. ♦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmalinx.com.