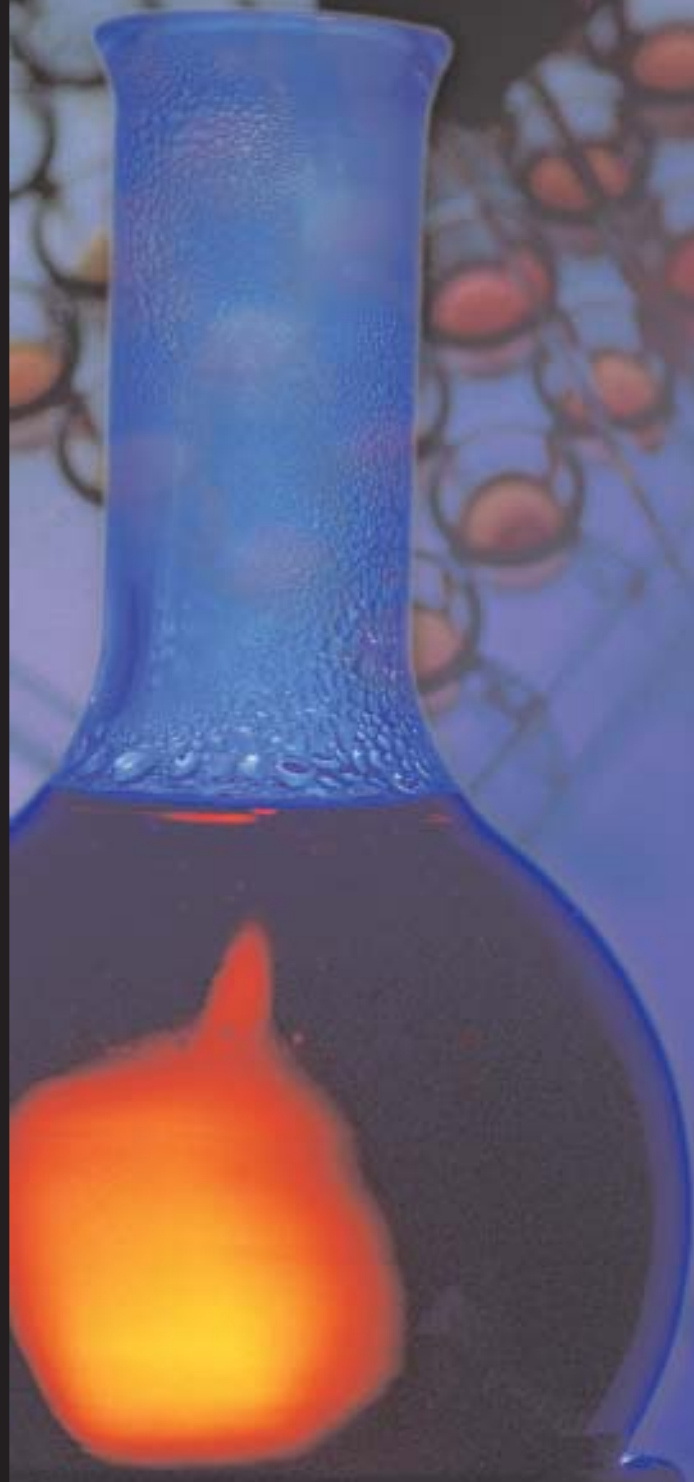


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A discussion of the state of the state



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As seen in the July 2006 issue of *BUSINESS NORTH CAROLINA*.

WHILE OTHERS STALL, LIFE SCIENCE GOES ON

Optimism about the state's future in creating and maintaining biotechnology jobs crosses a broad spectrum of experts.

Photography by Steve Exum

Can biotechnology be the savior of North Carolina jobs? That's the question put to a panel of life-sciences experts assembled by Womble Carlyle Sandridge & Rice PLLC, a Winston-Salem-based law firm: Don deBethizy, CEO of Targacept Inc., a Winston-Salem company developing treatments for central-nervous-system disorders; Jan Turek, CEO of Biolex Therapeutics Inc., a Pittsboro drug maker; Jeff Clark, managing general partner of The Aurora Funds, a Durham venture-capital company; Robert McMahan, Gov. Mike Easley's science adviser; and Sam Taylor, president of the North Carolina Biosciences Organization, a trade group based in Research Triangle Park. The discussion — moderated by Jeff Howland, group leader of Womble Carlyle's corporate and securities practice, and Arthur O. Murray, BUSINESS NORTH

CAROLINA managing editor for special projects — was held at the firm's RTP office.

What is the state of biomanufacturing in North Carolina?

McMahan: Clearly biomanufacturing is a

“Let's think about the new initiatives that can be put in place.”

newer area of emphasis and investment for the state. But it holds great promise because it also is the way in which we can leverage the innovation that we have in our research to the benefit of some of the more traditional manufacturing regions in the state.

Turek: If you look at North Carolina and the industries that exist today, you have Bayer, with the largest biomanufacturing factory for plasma products; you have Wyeth, with one of the largest vaccine-manufacturing factories in the world; Baxter, with an intravenous-solutions factory; Novozymes, with large-enzyme manufacturing. So there is a huge infrastructure of large multinational companies here that do biomanufacturing.

Some of these companies are in places you would not necessarily expect to find them.

Turek: For established technologies, which most of those large companies are, there are benefits to being in communities or in counties that provide economic benefits to build your infrastructure. For companies such as ours, where technologies are a little bit more nascent, it's important to be in areas where you have access to universities as well as scientists.

deBethizy: You're talking about large-molecule biomanufacturing. Companies like ours, which are working on small molecules, don't look to North Carolina for that capability. Small-molecule manufacturing developed in New Jersey and in Switzerland, for the most part. We have our compound synthesized in Switzerland.

Why not North Carolina?

deBethizy: Nobody wants to build a capital-intensive plant right now. I've talked at length to the CEO of the company that makes our product in Switzerland to get him to build a plant in North Carolina, and he said, “You know, Don, it



Jeff Clark



would be better for you if I built my next plant in China.' But there is so much momentum that eventually someone will locate a small-molecule plant here.

Is Asia a threat to drug manufacturing?

deBethizy: There's a movement in India, which is changing its patent structure and laws so that people would be more comfortable. But there's still a fear of losing control of our intellectual property. We have a novel molecule at the mid-stage of development. The last thing we want to do is take the risk that you would have somebody manufacturing it in China or in India and start selling it ahead of approval. We would go there for steps along the way but not for the final product.

Turek: While one of the drivers of lowering cost of goods is through labor, the majority of the cost is the huge capital outlay. Building a factory using traditional methods, whether you do it in China or North Carolina, would cost \$300 million to \$400 million to make one protein. Our technol-

ogy at Biolex offers the ability to build that same factory for one-quarter or one-third as much. So we're able to have the benefits of low capital without having to go offshore.

Clark: We've done a very good job of bringing in lots of companies with sizable plants. Several of us just got back from the BIO meeting in Chicago, and the exhibit hall is now filled with state after state, country after country extolling the virtues of why you need to build your plant there.

Can North Carolina compete?

Clark: We have a very innovative hub in RTP and a developing hub in Winston-Salem. These are companies that are developing next-generation therapies. They will need initial manufacturing efforts. At the hub, you will have the core research and development, but in the more rural areas, you can actually go build the plants to have proximity to those efforts. One of our companies is Argos, which is developing a vaccine for cancer and infectious disease. The pilot plant is in Durham County.



Sam Taylor

“We had a large number of workers who needed retraining.”

We’re going to be able to do all of the trials up through Phase II, but then we’re going to have to build a much larger facility. I think serious consideration will be in North Carolina in close proximity to our existing efforts.

Taylor: It’s an industry that requires as much as nine months for a worker to get enough training to be able to work unsupervised. What North Carolina has tried to do through investments in the Biomanufacturing Training and Education Center at N.C. State, the Biomanufacturing Research Institute and Technology Enterprise program at North Carolina Central and our community-college system is to shorten that time by at least three months. When you’re talking about building a \$300 million factory, that’s a lot of capital. We may not ever catch California or Massachusetts in research and development, but I think we have a really serious opportunity to leapfrog those states in terms of our biotech-manufacturing employment.

deBethizy: We have a student who became an employee at Targacept. Her name is Regina Whitaker, and she’s a graduate of Forsyth Technical Community College’s first biotech program. She worked at Unifi running a darning machine, and her whole family had worked in textiles. She saw that those jobs were going away, then saw the biotech program and got in. She interned in our company and became a full-time employee, and she is an outstanding laboratory technician. It has turned out to be a real success story for that transition from textiles into the biotech industry.

Turek: Our manufacturing facility in Pittsboro used to be a hosiery mill that we retrofitted into a

biomanufacturing factory as well as research-and-development offices. So it can be done.

Taylor: That was exactly the theory that we offered to Golden LEAF when we proposed this training initiative — that we had a large number of skilled workers in our manufacturing economy who needed retraining for the industries of the future. We’re looking forward to getting that fully operational and to providing the kind of skilled labor to companies like Jan’s and Don’s and companies like Bio-gen Idec, Diosynth, Talecris, the companies that are here and that are coming, Merck and United Therapeutics.

What else needs to be done?

Taylor: You can’t get FDA approval of a biologic product or a biomanufactured product without demonstrating that you can manufacture it at scale the same way every time, which essentially means you’ve got to build your factory before you can get your drug approved. So you go to the bank and say, ‘I need \$5 million, \$10 million, \$20 million to build out this manufacturing center,’ and the bank says, ‘We need collateral. We need revenue. We need at least some receivables to set that against.’ So we have to find a way to help those companies bridge that gap.

Any ideas?

Taylor: We’re looking at a debt-service reserve fund that the state might set up to guarantee a portion of the cost of those facilities or a tax credit for institutional investors who make guarantees and then have to pay out on those guarantees.

Turek: Our company has both aspects as a core of what we do. One is developing therapeutic proteins clinically but also putting in place the core manufacturing. We have just leased a 40,000-square-foot factory in the Triangle. We now have to upfit that. It’s going to cost us millions. We are looking to obtain that financing, but you can imagine when you’re a venture-backed company that equity money is expensive to put into a facility. So you look for other methods. Anything that the state can do to make it easier for us is important. It brings up one of my bugaboos that I’ve always had in every business I’ve been in. States are always looking at ways of attracting new companies. They also need to find ways to ...

Clark: ... support them.

Turek: So that companies like mine can follow what Don has done, where he’s now a public company. The more public companies we have

here, the more the image and the strength of North Carolina are enhanced.

deBethizy: Most of the incentives now are hard to find. That's the reason that I've gotten involved with NCBIO, because it's so important to get people to realize that we've created this incredible, bubbling cauldron of opportunity. People are still judging this industry by saying, 'Is it really going to have the impact that people are saying?' The answer is, clearly, yes. It will have that impact, and it's just a matter of investing now so that this energy that we've been able to create over the last five or eight years gets realized.

McMahan: All these are fundamentally a recognition of the importance of growth of entrepreneurship. It's widely recognized that the growth of small business is the primary source of jobs in our economy. I've been an entrepreneur, trying to make my numbers, trying to not use my American Express card again. You're not focused on kind of the larger public-policy environment in which business is flourishing. That is changing in North Carolina. Members of the General Assembly and the administration are very eager to understand the particular requirements of growth entrepreneurship. But unless the growth entrepreneurship community tells them, they don't know.

Clark: About three years ago, we came out of an emerging-issues forum. Everybody was touting all the new initiatives in other states and in other countries. There was a group of us that thought North Carolina wasn't being innovative enough. Like the proverbial ostrich, we would like to stick our head in the sand and just say, 'It's all going to be OK.' But, unfortunately, when you do that, another piece of the anatomy ends up being high in the air and can be shot off. We decided that was probably not the best tactic.

What did you do?

Clark: Steve Nelson and I started the North Carolina Entrepreneurial Association. The idea is, let's be on the offensive. Let's think about what are the new initiatives that can be put in place to empower entrepreneurs. You have lots of hurdles, and we need to make it as easy as possible.

deBethizy: It's starting to happen. Wake Forest just moved up to the top tier of entrepreneurial universities. The Triad has seized on this as a way to grow. We have a great example. Her name is Sara Yocum. She started a diagnostic company for aquaculture, diagnosing diseases in fish. She did this as an under-

graduate at Wake Forest and is now in a master's program, working part-time at Targacept, and she's CEO of her little company. When I met her, she handed me a business card and her résumé. She did an elevator pitch, and I was dumbfounded at how skillful she was.

McMahan: One of the best entrepreneurial programs in the United States is at Western Carolina in Cullowhee. It's one of the few universities in the nation that offers a master's in entrepreneurship. But we're not going to be the entrepreneurial state just because we say we are. We're going to be the entrepreneurial state because of what we do to support entrepreneurship.

Taylor: This is a difficult nut to crack because the data is very soft. We need to show that these small companies can, for the risk and the cost involved, produce just as many jobs as the big companies that we recruit to North Carolina.

You're proposing a change in state strategy?

Taylor: I'm not knocking industrial recruitment. We've been very successful. But when you're recruiting companies like Merck or United Therapeutics, you're recruiting companies that can go anywhere. And so you usually provide some sort of financial incentive. You're paying top dollar because you're competing in a world marketplace where your only advantage is not unskilled labor or low-wage labor or natural resources anymore. Compare that with how much you have to spend to get a small company started. The founder is here. His scientist is here. His work force is here. He hasn't got time to move it. We need

**"Investors
are going to
play where
their return is
greatest."**



Robert McMahan



Don deBethizy

“Most of the entrepreneurial incentives offered now are hard to find.”

to do a better job of convincing legislators that there's a major payoff to investing in them.

Turek: We have three major pharmaceutical companies that we collaborate with: Johnson & Johnson, one of the largest health-

care companies in the world; MedImmune, one of the world's largest biotech companies; and Medarex, an up-and-coming biotech. We'll work with their programs that we'll be producing here in North Carolina. That ripple effect can cause them to say, 'If we're looking to build biomanufacturing or research and development, these people know what they're able to do.' That can bring more jobs outside of just what that small entrepreneurial company has done specifically for itself.

Taylor: We've got to sell ideas, the new thing that we discovered, that we commercialized, that we manufactured and then that we sold to somebody else in another part of the world who wished they had thought of it first.

You mentioned western North Carolina. Businesses out there are having a tough time getting venture capital. What can they do?

Clark: If you look at the number of venture capitalists in the state that could lead a life-science deal, it's sub-10. The number of firms in North Carolina focused on life-science industries is three. You've got a classic chicken-or-egg problem. The venture capitalists will tell you that, 'What you need is successes. If you have successes, we'll come and invest more money.' The entrepreneurs will tell you, 'We need the money to build the successes.' Probably the real answer is, you need both.

But how do you do that?

Clark: In North Carolina, our hub is RTP. Would I say we truly have critical mass in terms of world-class management teams, entrepreneurs that have done it before, the service providers that really know how to structure deals, how to bring in proper talent in terms of executive recruitment, financial folks that have been down the roads from starting companies to exits? But if you think about exits — which are what investors care about — we really haven't had multibillion-dollar life-science companies built here. There have been several companies that have kind of moved up from the mid-\$200 million to probably \$500 million: the Trimerises, the Inspires, the

Pozens of the world. But to get a lot of interest, we're going to have to have bigger exits. Even that's a bit of a conundrum because as you build companies and things go well, you have opportunities to sell companies earlier. And on a risk-adjusted basis, sometimes it's very hard to let the bird in the hand go.

McMahan: What companies are actually saying is not that they need venture capital ...

Turek: They need capital.

McMahan: The Kauffman Foundation last year came out with assessments of entrepreneurial activity in the U.S. Last year, 627,000 companies were created every month. Most were single-person businesses. For the year, professional money managers and venture-capital firms made 175 early-stage investments. This is like getting struck by lightning. When you talk about western Carolina, they don't necessarily need equity capital. They need subordinated debt. Venture capitalists are going to play in the space of need where their return is greatest. That creates holes. The question then becomes, what are appropriate public-policy responses to fill those holes? Probably the best solutions are incenting the private sector.

Taylor: We're going to have \$5 billion in tobacco-quota-buyout money coming into the state over the next 10 years. We ought to find a way to get that money into innovation-based small businesses that are going to grow and add value and create wealth. If we can't — to borrow a phrase from Ross Perot — the sucking sound that you hear is going to be that money leaving North Carolina and going into investments nationally.

Any ideas?

Taylor: We're pushing very hard to get a capital-gains-tax exclusion for founder's stock. The

only tax hit that you take from that is the capital-gains tax that you would have gotten, so you only pay if the company succeeds. It'll be three to five years before you have any gains mature that will cause any tax impact. The exclusion for founder's stock in innovation companies could bring a lot of future value back into the present, leverage that tobacco-trust-fund money and get started in a big way in some of these innovation companies.

Clark: It's all upside. This is not out of current income. We think it would have a huge impact in terms of people starting things.

What about the North Carolina Research Campus in Kannapolis?

deBethizy: It's fairly close to the Triad, and there was a lot of concern that it was going to draw resources away from us. But UNC Greensboro recognized right away there was an opportunity to leverage its research capabilities. So I see it as an opportunity. It's a lot of money, if it actually materializes as it's been envisioned, and it's only going to raise the visibility of the state.

Turek: One of the smartest things they are doing is focusing in a certain area: nutrition. That allows them to really build an expertise. The entrepreneurs who can really build the business, with scientists with the access to the capital and the research facilities to build those businesses, can come from that.

Taylor: Kannapolis will present some challenges because we don't have a major life-science academic center near there. We're consolidating assets out of UNCG, UNC Chapel Hill, N.C. State University, Duke University and really working to build a core of scientific talent that creates the critical mass to succeed. But that's a heavy lift.

McMahan: It's the kind of big play that great states do. We're going to learn an awful lot about how one grows a technology-intensive cluster-research infrastructure in an area that isn't directly tied to a research university. Those lessons are going to serve us well in how we drive the technology economy across the state. It begs the bigger question. Biomanufacturing and biotechnology and the growth of these clusters are but one element of a larger phenomenon. The state has definitively put one foot in the bathtub. The other foot is a host of technologies synergistic with biotechnology.

Please explain.

McMahan: About two weeks ago, the Southern Growth Policies Board

released an analysis of nanotechnology resources within the Southeast. North Carolina comes out as being the best of class in terms of its research capacity, its basic innovation capacity in nanotechnology. I would argue that the states and the regions of the world that are going to be the most competitive in the future in biotechnology are those that are investing across all the disciplines that intersect it. Since most innovation is occurring at the boundaries of disciplines, it's the states and the regions that capitalize on broad-based competencies in information technologies, biotechnology and nanotechnologies that are going to be the ultimate winners.

deBethizy: I'm co-chairing a capital campaign to build a building in Piedmont Triad Research Park called the Center for Emerging Technologies, and it's focused on biotech, nanotech and high-performance computing. Five years ago, that would not have happened in this state.

McMahan: Bioinformatics is one of the hottest areas of biotechnology. It's the combination of high-performance computing technologies and biotechnology. Some of the most promising medical devices in the drug-delivery side come from the hybridization of nanotechnologies and nanoscale materials and pharmaceuticals. This is a competency that the state has. If we put these pieces together, what we have is not competing disciplines, it's not information technology or biotechnology or nanotechnology. It's technology. We are competing with Massachusetts, with California, with Singapore, with Korea. This is one of the ways we distinguish ourselves.

“Anything that the state can do to make it easier for us is important.”



Jan Turek

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