

SCIENTIFIC METHOD

*Leading-edge technology spurs
biomanufacturing growth.*





NORTH CAROLINA'S EMERGING BIOMANUFACTURING SECTOR MOVES TO THE FUTURE WHILE tackling issues that include finding a talented workforce. *BUSINESS NORTH CAROLINA* magazine gathered a panel of nine industry leaders to discuss this and other topics.

The discussion, hosted by North Carolina Biosciences Organization, was moderated by Samuel M. Taylor. Sponsors were Biogen, FUJIFILM Diosynth Biotechnologies, Grifols Shared Services N.A. and Pfizer. The transcript was edited for brevity and clarity.

From top to bottom:

Bill Bullock, *senior vice president, statewide operations and economic development, North Carolina Biotech Center*

Bob Smith, *senior vice president, global gene therapy business, Pfizer*

Samuel M. Taylor, *president, North Carolina Biosciences Organization (moderator)*

Nelson Dollar, *N.C. House of Representatives*

Bob Kenyon, *vice president of North America manufacturing, Biogen*

Christine Vannais, *senior director of manufacturing, FUJIFILM Diosynth Biotechnologies*

Brandon Brega, *associate vice president, plant management, Merck*

Ted Lithgow, *chief operating officer, Humacyte*

Sergi Roura, *president, facilities North America, Grifols Shared Services N.A.*

This is a space that is not a 'dip-your-toe-in-the-water' activity. You just jump into the deep end of the pool.

BOB SMITH
Pfizer

WE'RE TALKING ABOUT BIOMANUFACTURING TODAY, FOCUSING ON BIOLOGICS. FOR A START, WHY DID YOUR COMPANY COME TO NORTH CAROLINA?

KENYON We came here because it's a great environment for our burgeoning business, which includes the educational system, support from the state and access to talent. We were one of the early players in the state, so we had a lot of support and were able to influence programs at universities to grow and expand and actually advance the talent pool. It's continued to explode from there. In 1995, it was the right place to build.

BREGA We had similar themes in terms of access to high-caliber education from

the major universities in this area. That was a big pull, as well as what we continue to see as a collaboration and cooperation with the local and state governments. We've had great relationships with Durham Technical Community College. Our original plant manager served on the board at Durham Tech, and since then, we've had a number of employees on the board, and those relationships over time have been beneficial to Merck. We're growing at our manufacturing facility. It does take time, but what employees in North Carolina can deliver is competitive with anywhere in the country.

ROURA The reason to come to North Carolina was really an acquisition of our competitor in 2011. However, we have invested and expanded in North Carolina.

We did an extensive site selection for our new wave of investments and expansion for the long range. We decided on Clayton because of access to workforce and education, along with land availability, infrastructure and efficiency in terms of energy and other costs.

VANNAIS North Carolina is one of the three major hubs for biologics in the U.S. — Boston, San Francisco and Research Triangle Park. To serve our clients, we have to be where they are and be accessible to them. As we're working with clients on clinical and commercial products, tying into that accessible, highly trained workforce is critical. We also have the ability to expand as the clients need us and have a flexible delivery method. We partnered with academia and get a lot of value out of that collaboration.

LITHGOW We located here for many of the reasons that everyone else mentioned. We also have connections in terms of intellectual property with some of the schools here, mainly Duke University. We work very closely with Duke in terms of pre-clinical development. Some of our medical and clinical personnel have been faculty in the past and have friends on the faculty, so there's a logical connection both from an intellectual-property point of view, but also from a pre-plan and even into trials and clinical studies.

BULLOCK The state has made an investment in this space for a long time — leadership and the legislature, Rep. Dollar in particular — to understand that this takes continuity and consistent investment over time. That creates a business climate and an ecosystem that I think is favorable for life science in general, but specific activities focused on manufacturing. It's an opportunity for me to sit down with a company and

say, we're really good at biomanufacturing in North Carolina. In fact, we're investing in and having very granular conversations around areas like gene therapy and plasma-based therapeutics and monoclonals. Talent is still our main currency in North Carolina for what allows people to come here. A lot of people in this room can invest their resources anywhere in the globe. Part of our challenge at the state [level] is to make sure those investments come here, and it's the right environment for them to continue to grow.

WE HAVE AN \$86 BILLION DOLLAR INDUSTRY, WITH 262,000 PEOPLE EMPLOYED DIRECTLY OR INDIRECTLY. WHAT OTHER COMPANIES, VENDORS, MARKETERS AND COLLABORATORS BRING MORE VALUE TO THE STATE'S ECONOMY?

KENYON Biogen works with more than 350 suppliers in and around the area,

especially if you take things like capital investments in this facility. At one point, we had about 1,000 tradesmen on-site. And these aren't unskilled-labor jobs anymore. These are engineers and people who can do orbital welding. It's not just the plumbers and the electricians. They're important, too, but there's a huge volume of engineering and automation that goes into it. The whole industry is growing those types of jobs all around us.

VANNAIS IT infrastructure, along with IT software and systems are vital as we move into paperless systems that make us more efficient across multiple sites. We have the IT partners to help us do our day-to-day work and then help us get to the next level, some of them local.

SMITH You have the benefit here of an end-to-end capability, very basic early discovery research through clinical development, all the activity related to manufacturing — regulatory and even



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Founded in 1978, Biogen is one of the world's oldest independent biotechnology companies and has been part of the North Carolina biomanufacturing community since 1995.
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We have several clinical candidates for neurological disorders, everything from ALS to Parkinson’s disease.

BOB KENYON
Biogen

commercialization. When you have that full spectrum in a concentrated area, you have a natural synergy and connectedness. We’ve combined our basic research scientists with process development scientists as well as engineers. And we’re building that so it’s a cohesive team from one end of the spectrum to the other.

CAN YOU TALK A LITTLE BIT ABOUT THE TALENT IN NORTH CAROLINA AS A DRIVER OF GROWTH?

BREGA We do internships every summer with well over 20 engineering students from N.C. State, and we probably hire the majority of those interns.

Certainly on the topic of the high-skilled labor perspective, North Carolina does a

nice job in that arena, and we’ve always had an ample workforce. I think. One of the things we struggle with is how do we supply the amount of skilled labor we need in terms of things like HVAC mechanics?

There is a high desire for those types of skill sets — mechanics in all trades and crafts — that we need to support this industry. We focus on the high end, and North Carolina does as well as anyone. Every state struggles with those types of trade skills, and if North Carolina can help these companies solve that problem and attract more of the potential employees in that direction, we’ll be even more successful.

KENYON Finding craft workers has been much harder as we get into projects and it’s hard to get qualified people.

There’s so much growth in the area that trying to find people skilled in automation specifically seems to be a real challenge. There’s a tremendous ex-military community here. We have an opportunity to do much more with the veteran community, really make an investment in those folks as they’re rolling out and help with short-term programs — six-month programs, 12-month programs — to really get them more actively engaged in the business. We have been doing a lot to try to hire those folks. There’s a tremendous amount of internal training that we have to do, which is fine. It’s still the right thing to do. If we can create an ecosystem that’s more engaged in going after that population and retraining

them, it's a largely untapped population of people that are very skilled nowadays. It's not the military position of old.

VANNAIS There's a culture in the training and the human error prevention that military brings to [Good Manufacturing Practice] aspects of following procedures and executing records. Our staff from the nuclear industry and our Navy people have helped implement a call-out technique that has reduced errors in the plant. These methods are built into the way ex-military people work.

I'M TOLD THAT CHILDREN DECIDE PRETTY EARLY WHETHER THEY WILL PURSUE A STEM PROGRAM. SERGI, DESCRIBE YOUR COMPANY'S PROGRAM.

ROURA Discover the Plasma. This is something we decided to do three, four

years ago. There was some money coming from a grant at the state for training, so our head of the training group came to me and suggested that we create a program to further the education of children in the school system in Johnston County. We got corporate involved and then we created a pilot program with eighth-graders. We partnered with Johnston Community College and the school system in Johnston County. We started with three schools and we are now delivering the program to all Johnston County eighth-graders. It's a two-week program that is web-based. It has been a great success.

HOW DOES THE LEGISLATURE PARSE DECISIONS OUT WHEN YOU'RE THINKING ABOUT BIOTECH AND THE STATE BUDGET?

DOLLAR We're working on a number of fronts. The investment in biomanufacturing

over the years is some \$70 million, and I think that will continue to grow. We're helping with lab classrooms at N.C. Central and also working with the community colleges, contributing money to them where they can be more flexible. They can set up training that fits in whatever industry space or industry clusters they're trying to grow or support in a given area. In the Triangle, life sciences and biotechnology are important industry clusters. We are trying to support that, whether it's Durham Tech or Wake Tech or the folks down in Sanford.

HOW DO ACADEMIC MEDICAL CENTERS PLAY INTO BIOTECH?

LITHGOW It's been a key to success for Humacyte in that our organization is founded by women and primarily led by women, and that grew out of the relationship with Laura Niklason who met a number of her clinicians and fellow



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clinicians at Duke University, but she is now teaching at Yale University. She still spends two or three days a week here in the Triangle, and we work very closely with both MIT and Yale, together with Duke and UNC Chapel Hill. Most of the folks at Humacyte are biomedical engineers, Ph.D.s, M.D.s. We're going through a transition now. We're moving from medical discovery and clinical research. Even for a small biotech without a commercializable product yet, we have eight major clinical trials in the field with 100 people in the company.

WHAT DOES YOUR FUTURE LOOK LIKE IN TERMS OF NEW PRODUCTS AND NEW PATIENT POPULATION?

SMITH We're really excited about this phase. It's highly innovative technology,

and the science behind it is what's really driving our investment. We're translating some of those science concepts into exciting clinical programs, and hopefully they'll continue to advance well in the clinic and will progress through the regulatory approval process and onto commercialization. This is a space that is not a "dip-your-toe-in-the-water" activity. You just jump into the deep end of the pool. We're here to stay and excited about what we've done in a relatively short period of time.

DESCRIBE GENE THERAPY.

SMITH There are a number of diseases, roughly about 6,000 or so, that are called monogenic diseases. They're caused by a single gene defect.

Either the gene is missing, or it produces a dysfunctional protein or too much of a protein that then causes a disease. We're using modified engineered viruses called vectors that will deliver to an appropriate cell within a tissue, or that will deliver a correct copy of that gene, or that will knock down or silence a defective over-expressive gene. So it's a way that you can address directly the cause of disease where it's a genetic mutation or a missing gene.

KENYON We have an active gene-therapy program and some collaborations with universities not here in state, but hopefully at some point we will involve N.C. universities. We have an active program in oligonucleotides. We just built a manufacturing facility down the



“*As we're working with clients on clinical and commercial products, tying into that accessible, highly trained workforce is critical.*”

CHRISTINE VANNAÏS
FUJIFILM Diosynth Biotechnologies

street, quite small, but with hopes of expanding it. We have several clinical candidates for different neurological disorders that are using this [antisense oligonucleotide] technology, everything from ALS to Parkinson's disease and a few others. We recently launched the first treatment for a disease called spinal muscular atrophy last year, and that was an ASO and one of only a very small number that have ever been launched, so that's an emerging area, much like gene therapy. There are very few people in it, but it certainly has tremendous promise.

VANNAIS As we serve our clients and they bring clinical programs to us, we must have a workforce that is not only well-trained but knowledgeable. Those are two fundamentally different things sometimes, because if you're not making the same product all the time, you need to understand the science

behind what is happening. We built a certification program for our technicians; as they learn the unit operations, they improve their proficiency through testing and training beyond the GMP qualification.

SOME OF US THINK WE'RE ENTERING A NEW WAVE OF BIOTECHNOLOGY. CAN YOU DESCRIBE THAT?

BULLOCK The state has done a phenomenal job of being ahead of the curve in this space — walking the walk and not just talking the talk. It's important to realize that the pace of technology changes much faster than the ability of companies to realize it — and probably the ability of state and local governments to keep up with it as an economic developer. We have a good infrastructure, arguably — I

would say — best in class globally around training, but the technologies are changing: gene therapy, cell therapy, oligo-based products and disposable manufacturing. All of these are moving forward, and we need to keep investing so that our trained workforce is keeping up with those technology changes.

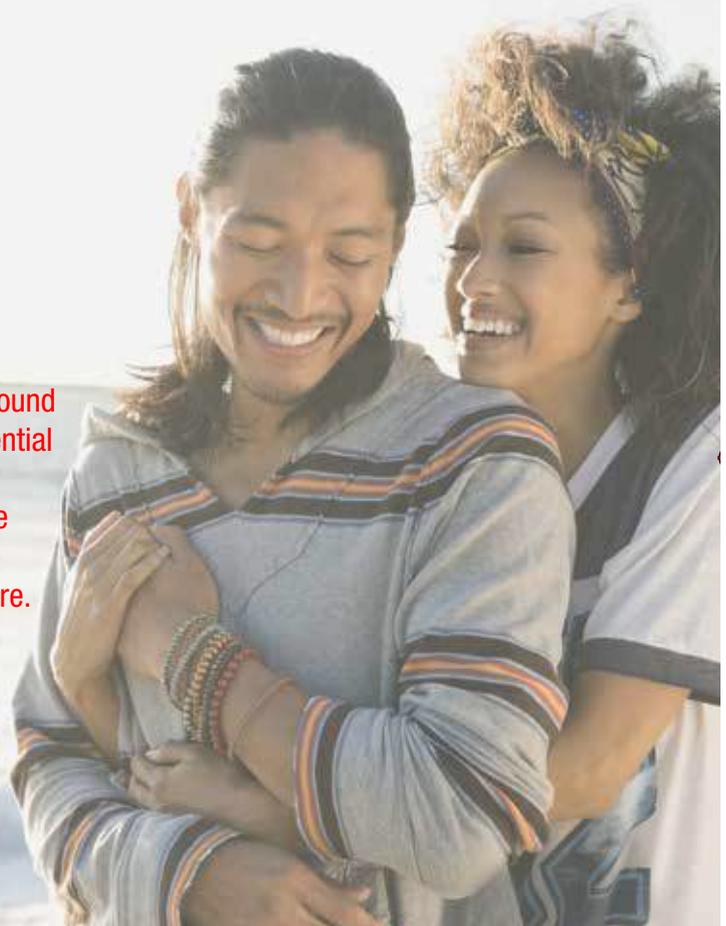
WHAT ARE THE CHALLENGES FOR NORTH CAROLINA, ESPECIALLY FOR EXISTING COMPANIES YOU'RE GROWING AND MAKING BIG INVESTMENTS. WHAT ARE THE LIMITING FACTORS IN YOUR FUTURE GROWTH?

ROURA I find that the environment changes very quickly, and sometimes we don't even realize that the environment has changed. We've already invested in a new wave of long-range

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expansion of resources. This was taken three years ago after one year of analysis from different sites across the world. We landed here, but today the environment is very different than three years ago. Employment rates are running as low as they can be. All the companies represented here are heavily invested in the area, so we have put a lot of pressure on the

workforce and the talent. We are doing a lot to take care of the connection between the schools and the colleges, and I think we are doing a great job. But in the future, I wonder if this is going to be enough. Maybe we have to really look at this, maybe we have to attract people from other states or other countries, because it's not enough.

KENYON What you're seeing is waves of new discovery, and it happens from time to time in the industry. What's different, at least from what I'm seeing, [is that] companies are making significant pre-investments. We're investing ahead of what we've typically done in the past, which means as companies, we're taking more and more risks. If there are ways that state or local governments can think about how to best help companies make that more palatable, whether from a tax perspective, those are important discussions to have. There's no guarantee that some of these pre-investments may be in phase one, phase two. If it doesn't turn out, you have an idle facility. I know, having worked in other states, there are creative ways that state and local governments can work with companies to build upon what is already a very attractive place from an employment perspective.

I HEARD THE "T" WORD, THE TAX WORD. REP. DOLLAR, I THINK THAT'S YOUR CUE.

DOLLAR We have been very pleased over the last several years in North Carolina to engage in tax reform. We want to have a pro-growth policy, a pro-investment policy in North Carolina. We want to make it worth your while to make these investments in North Carolina, so that when you're successful, you can enjoy the fruits of that success, because that's how you're able to grow and that's how our citizens are able to have the kind of jobs that they want, not just for themselves but for their children and grandchildren. We certainly have more tax reductions that'll be coming online in 2019.

We have strong bipartisan support for a number of these issues. We want biomanufacturing and the life-sciences industry on a larger scale to continue to grow and to continue to have a space where you can prosper. ■

Meet Ray
Quality Control Scientist, Sanford, NC

As a mom, it's her instinct to protect her children and her job to protect others worldwide.

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\$93K+ average salary for NC
biotech job

\$55K+ for early career salary
in biomanufacturing

\$86 BILLION in annual
economic activity

260,000 jobs

\$3.7 BILLION in new
facilities since development
of biomanufacturing training
programs

3000-5000 new
biomanufacturing jobs
expected in next 3-5 years

From 2012 to 2014, life science
employment in North Carolina
grew 6.6 percent, 3 times the
national growth rate.

**ROBERT
KENYON**
Vice President,
North America
Manufacturing,
Biogen

In the early 1990s Biogen sought to expand its biomanufacturing capabilities as the company's drug development pipeline grew. As part of a global search, North Carolina rose to the top of the list thanks to the state's skilled workforce, attractive business climate, ability to meet our infrastructure needs and a demonstrated commitment from state leaders to make North Carolina a great place for biotech to grow.