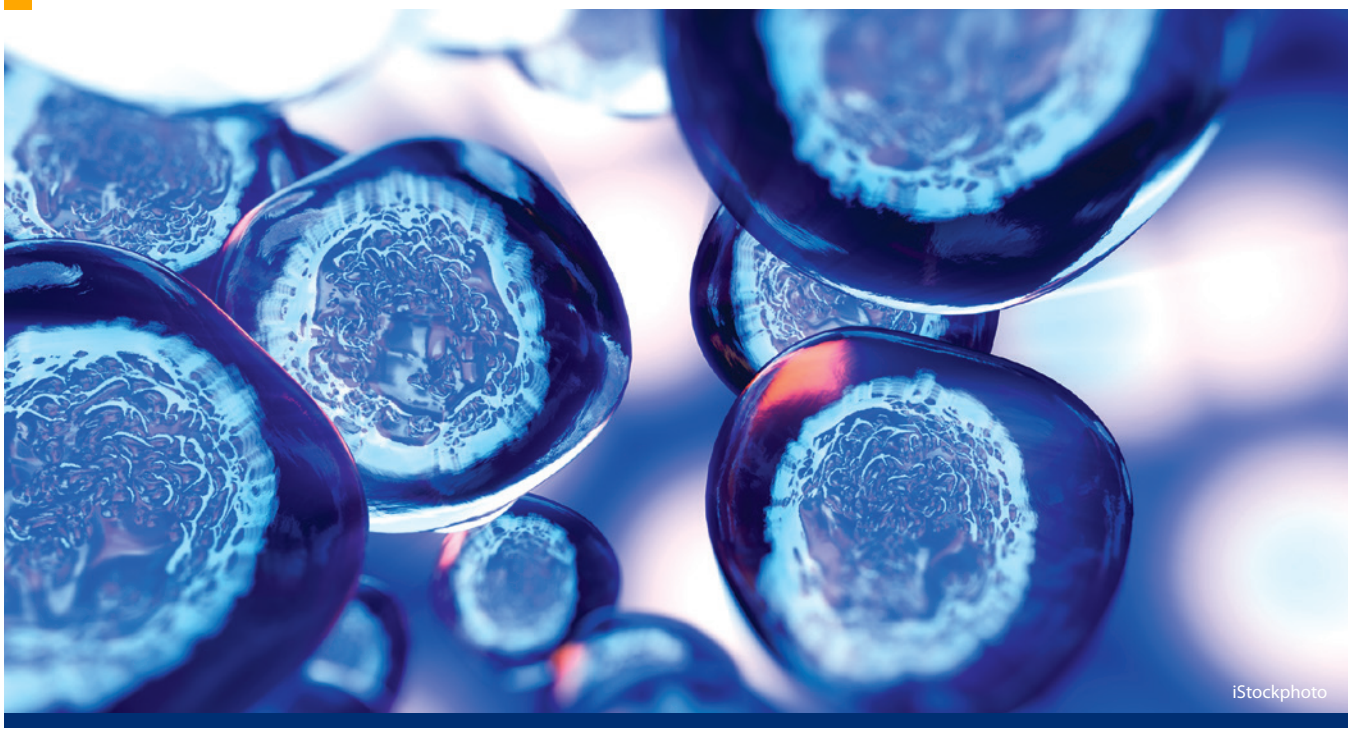
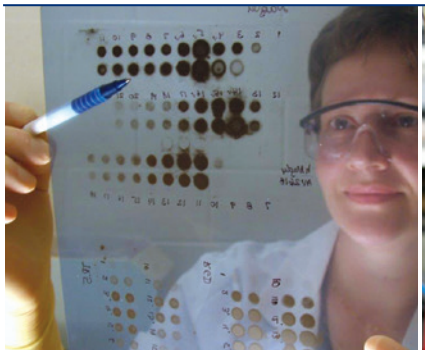
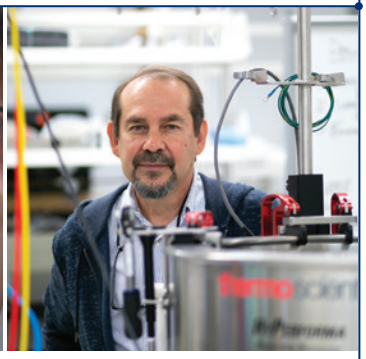
North Carolina: A Burgeoning Gene and Cell Therapy Hub



North Carolina has quickly established itself as a leading hub of gene and cell therapy activity. As curative therapies emerge and bring new hope to patients with rare diseases, North Carolina's established life science ecosystem is well-positioned to move these life-changing therapies from idea to market.

The state's gene and cell therapy sector is supported by world-class research, a foundation in manufacturing, numerous resources, top talent, and an exceptional business climate. All of these elements work together to create the optimal destination for gene therapy companies and researchers to flourish.





(left) AskBio uses tiny genetic "trucks" to deliver DNA fixes for specific diseases. (right) Jude Samulski, Ph.D. Photos courtesy of AskBio.

In 1993, The University of North Carolina School of Medicine, with grant help from the North Carolina Biotechnology Center, recruited gene therapy visionary Jude Samulski, Ph.D. Samulski pioneered the use of the harmless recombinant adeno-associated virus (AAV) as the premier delivery mechanism for gene therapy. This AAV technology is the foundation used by more than two-thirds of the gene therapy industry world-wide, was brought to life in a North Carolina university, and to commercial reality by Asklepios BioPharmaceutical (AskBio), a Research Triangle Park company cofounded by Samulski.

An Established Hub

From large pharmaceuticals to university spinouts, gene therapy activity in North Carolina is broad and diverse. These companies are leaning on North Carolina's deep expertise in life science to transform research into commercially viable products that can be manufactured on a large scale. Below are just a handful of companies in North Carolina that are making significant progress in the development of gene and cell therapy technologies.

- **Asklepios BioPharmaceutical, Inc.**, a premiere gene therapy platform company whose founders pioneered AAV therapies, has spun out four companies and received $235 million in investments to develop its gene therapy capabilities.
- **bluebird bio's** 125,000-square-foot facility in Durham, which will manufacture lentiviral vector for use as gene therapies targeting rare diseases and certain cancers.
- A new RTP facility is under construction for **AveXis**, a Novartis company. AveXis will manufacture its AAV gene therapy treatment for spinal muscular atrophy here.
- Also using AAV vector technologies, UNC spinout **StrideBio** recently closed a $15.7 million investment to continue development of its therapies for rare diseases.
- **Pfizer** has invested more than $1 billion in acquisitions and expansions in North Carolina specific to its gene therapy capabilities, including AskBio spinout **Bamboo Therapeutics**.
- **Locus Biosciences**, based on the research of North Carolina State University's Rodolphe Barrangou, Ph.D., has opened enrollment for a Phase 1b trial of a potential treatment for urinary tract infections caused by Escherichia coli (E. coli) bacteria. The study will evaluate LBP-EC01, a bacteriophage "cocktail" that has been engineered with the gene editing technology CRISPR Cas3 to target the E. coli genome.
- In Durham, Duke spinout **Precision BioSciences** raised $126 million in its initial public offering in early 2019, and recently gained approval from the FDA to advance its second genome-edited cancer therapy to clinical trials.
- Clinical-stage biopharma company **Cellectis** announced it will invest $70 million and create 200 jobs in its first North American manufacturing facility in Raleigh. Paris-based Cellectis is developing a new generation of cancer therapies.

Since 2016, Pfizer has invested more than $1.2 billion in expansions and acquisitions in North Carolina. It stems from a major shift in focus to expanding its end-to-end capabilities in gene therapy including research, development and manufacturing.

Pfizer

August 2016 — *Pfizer acquires Bamboo Therapeutics with an upfront payment of $150 million and eligible payments up to $495 million if milestones are met*

February 2017 — *Pfizer provides $4 million in funding for a multiyear gene therapy academic fellowship program managed by NCBiotech*

August 2017 — *Pfizer announces a $100 million investment in its Sanford gene therapy manufacturing operations*

March 2019 — *The Duchenne muscular dystrophy therapy developed by Pfizer-acquired Bamboo Therapeutics is administered at Duke University to its first human patient with successful results*

August 2019 — *Pfizer announces an additional investment of $500 million and 300 more jobs for its gene therapy site in Sanford*

October 2019 — *Pfizer purchases a 60,000-square-foot building in Durham to be renovated into an Advanced Therapy Medicinal Facility for an additional investment of $19 million*

Foundation to Support Growth

North Carolina's foundation in biological and pharmaceutical manufacturing has laid the groundwork for a promising future in gene therapy manufacturing. Pharma giants such as Pfizer, Novo Nordisk, Biogen, Novartis, Grifols, Eli Lilly and Company, Merck, Seqirus and GSK set up shop in North Carolina because they were confident in the network of specialized resources that work to grow manufacturing capabilities across the state. From **industry-driven training programs** to funding opportunities and abundant physical infrastructure, North Carolina is well-positioned to support continued growth in this highly specialized manufacturing.

Currently in North Carolina, there are 131 production and manufacturing companies that employ more than 27,000 people. These skilled workers are manufacturing pharmaceuticals, monoclonal antibodies, cell and gene therapies, industrial enzymes, and vaccines. More than a third of N.C.'s life science jobs are dedicated to our **thriving manufacturing sector**.[1] Compared to other US life science hubs, North Carolina has the most biological product manufacturing employees.[2]

Production and Manufacturing in North Carolina

131
companies

27,000
employed

In addition to a myriad of manufacturing capabilities, North Carolina has expertise in trial design, patient recruitment, data management, and regulatory requirements. N.C. is home to more than 150 **contract service organizations**. Industry founders IQVIA, PPD and LabCorp call North Carolina home as do innovative leaders Rho and Syneos Health.

Pharma giants in North Carolina


Grifols

Biogen

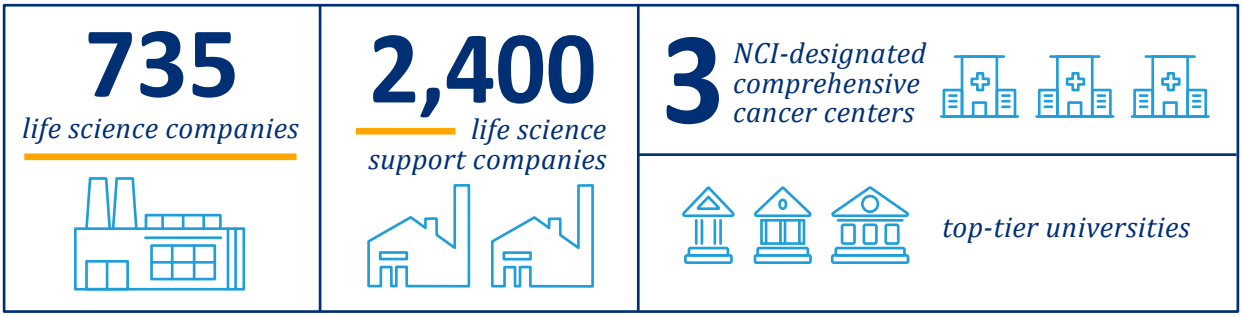
Pfizer


NovoNordisk

[1]NCBiotech Life Science Intelligence Unit, 2020.
[2]US Bureau of Labor Statistics, Quarterly Census of Employment and Wages, 2018.

Resources to Nurture Innovation

North Carolina's life science ecosystem includes 735 life science companies and 2,400 supporting businesses. The connectivity between specialized organizations that bring partners together, a network of top-tier universities, and statewide medical expertise supports the development of gene and cell therapy technologies.



Unlike any other state, North Carolina has a resource solely dedicated to the health of its life science sector. Since 1984, the **North Carolina Biotechnology Center** (NCBiotech) has taken a unique approach to statewide life science economic development and houses the capabilities to guide companies through the challenges encountered at all stages of growth. With headquarters in the Research Triangle Park, NCBiotech has funding programs, focused efforts in emerging sectors, and an in-house team of analysts among many other avenues of expertise.

To help develop North Carolina's full potential in the growing areas of human therapeutics such as gene and cell therapies and precision health, **The North Carolina Precision Health Collaborative** (NCPHC) was formed. The NCPHC, facilitated by NCBiotech, is a strong and diverse group of leaders in research, healthcare, insurance, investment, policy and information technology who have partnered to accelerate initiatives to nurture research, equip providers, and engage industry in this sector.

In the academic space, the University of North Carolina at Chapel Hill created a dedicated **Gene Therapy Center** in 1993 to foster discovery and development in gene therapy research. Scientists have access to resources through two core facilities—the UNC Vector Core and Human Applications Laboratories—that ensure availability of gene therapy vectors needed for preclinical or clinical studies. The Gene Therapy Center was created to facilitate the progression and translation of gene therapy research from the laboratory bench into Phase 1 clinical trials to treat human disease.[3] So far, the Gene Therapy Center has initiated and completed a number of Phase 1 gene transfers including:

- Completion of first AAV gene delivery study for neurological disorder (Canavan Sic Trans-2012)
- Completion of the first AAV gene delivery study for Duchenne muscular dystrophy (NEJM 2010)
- Completion of first Limb Infusion Safety Study for DMD (Mol Ther 2012)
- Initiation of AAV gene transfer Phase 1 study for Hemophilia B patients using UNC modified FIX transgene

North Carolina has three **NCI-designated Comprehensive Cancer Centers**: Duke Cancer Institute, Wake Forest Baptist Comprehensive Cancer Center and UNC Lineberger Comprehensive Cancer Center. More than 700 clinicians and researchers focus on cancer genetics and genomics, cellular therapies, clinical research, and cancer prevention and control, among others.

[3]Gene Therapy Center, med.unc.edu/genetherapy, November 2019.

Talent to Drive Creativity and Commercialization

Perhaps its biggest advantage, the **talent infrastructure** in North Carolina is robust, ever-evolving and industry-driven. With more than 4,600 biological and biomedical sciences degrees awarded in the 2017-2018 school year, many North Carolina graduates are prepared for careers in the life sciences. Almost half of those degrees were awarded at colleges and universities within the Research Triangle, a centrally located region named for the geographic relationship of world-renowned universities UNC Chapel Hill, Duke University and North Carolina State University.

In addition to North Carolina's **globally recognized universities**, there are 58 **community colleges** across the state. The life science training initiative of the N.C. Community College System, NC BioNetwork, provides support for students looking to advance their career. NC BioNetwork also develops custom training programs with companies who are looking to grow their talent pipeline. Companies such as AveXis and Merck lean on N.C.'s community colleges for customized training solutions.

University-level training is available at NC State's Biomanufacturing Training and Education Center (BTEC). Undergraduates, graduate students, and working professionals train at BTEC for hands-on learning with the latest biomanufacturing technologies. A cGMP pilot plant, including FDA inspectors, and facilities fitted with industry-standard equipment prepare students for on-the-job, real-world application of the technologies.

In Durham, North Carolina Central University's Biomanufacturing Research Institute and Technology Enterprise (BRITE) offers undergraduate and graduate degree training. Students move through curricula designed with industry input to ensure that graduates learn up-to-date training techniques. BRITE has a strong focus on research and drug discovery.

Unique to North Carolina and specific to gene therapy is the **Pfizer-NCBiotech Distinguished Postdoctoral Fellowship Program in Gene Therapy**. The program is a partnership between Pfizer Inc. and NCBiotech that supports the scientific and professional development of postdoctoral fellows interested in establishing careers in gene therapy. NCBiotech continues to work with industry partners to tailor programs that meet workforce development needs.

NC BioNetwork's flagship course BioWork *gives prospective professionals the opportunity to learn foundational skills needed to enter the biomanufacturing workforce.*

Ten community colleges across the state offer the BioWork certificate program, a 136-hour course that teaches bioprocessing techniques required for entry-level positions in biopharma manufacturing. Designed for people with a wide range of educational backgrounds, the course provides thorough comprehension of Current Good Manufacturing Practices (cGMP), chemistry for process manufacturing, process flows, fermentation, cell growth and more. Students are ready for entry-level processing positions after completion of the program.


NC State/BTEC


NC BioNetwork

Climate to Live Comfortably

North Carolina has an advantageous business climate and offers an **exceptional quality of life** to its residents.

Compared to other life science hubs, the **cost of doing business is low** in North Carolina. N.C. boasts the lowest corporate income tax rate at 2.5%. In biomanufacturing specifically, labor and operating costs in North Carolina are the lowest of all major U.S. hubs. In fact, it is 24% less expensive to operate in North Carolina than the Boston and San Francisco areas.[4]

The North Carolina Department of Commerce (NDOC) works with economic development and industry-specific partners across the state to create an environment where businesses can thrive. **North Carolina's targeted, performance-based incentive programs** help companies that are relocating or expanding their business in North Carolina by limiting the tax burden and overall costs. NCDOC awards individual incentives based on a variety of metrics, including project location, jobs created, investment level and economic impact.

North Carolina's **prime mid-Atlantic location** provides easy access to millions of people. The state's infrastructure includes four major international airports, the largest consolidated railroad system in the country, and the second-largest highway system with more than 90,000 miles of road.

As a **family friendly and culturally rich state**, North Carolina has something for everyone. Iconic mountains. Hundreds of miles of coastline. Bustling cities. The moderate climate includes mild winters, warm summers and enjoyable spring and autumn seasons. Arts and culture, professional and nationally ranked sports teams and a welcoming cost of living round out a first-rate business climate, making North Carolina the optimal destination for businesses to thrive.

Learn more about how North Carolina's life science ecosystem can support your company. Contact us today.

ncbiotech.org/genetherapy

#1
North Carolina ranked #1 economic growth potential
Business Facilities 2019, "Business Facilities' 15th Annual Rankings Report: State Rankings"

#1
North Carolina named best state for business
Forbes 2019, "Best State for Business"

#1
Durham-Chapel Hill Area named Top NIH Per-Capita Funding
2019, "Useful Stats: NIH Awards by Metro, 2014-2018"

#2
Raleigh named 2nd best place to live
Liveability 2019, "These are the Top 100 Best Places to Live in America"

[4]The Boyd Company Inc. "Comparative Biomanufacturing Industry Operating Costs." 2019.

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North Carolina Biotechnology Center

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The North Carolina Biotechnology Center is a private, nonprofit corporation that transforms North Carolina's life science opportunities into economic prosperity through innovation, commercialization, education and business growth.