Bridging the Gaps

A Strategic Plan to Accelerate the Commercialization of Life Science Technologies in North Carolina

January 2011 | The North Carolina Biotechnology Center

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Executive Summary

A coordinated strategic plan is presented here for accelerating the commercialization of life science technologies and discoveries in North Carolina. It first describes the industry opportunity available to North Carolina and the key challenges that could jeopardize the state's ability to seize that opportunity. The plan then details several strategies designed to surmount these challenges, thereby providing a clearer path to companies seeking to commercialize life science products.

Background

North Carolina's longstanding commitment to biotechnology has played a key role in establishing a large and growing life science industry in the state. While job creation has been in decline for many of the state's traditionally strong industries, jobs in North Carolina's life science industry increased 29% from 2001 to 2008 with an average pay in 2008 of $74,829, which is 90% higher than the state's average private sector wages. With statewide biotechnology industry-related employment of 226,000 and an economic impact of $64 billion, the life science industry has become central to North Carolina's overall economy.

North Carolina benefits from a life science industry that is diverse and statewide. Throughout this report, the terms "life science industry" and "bioscience industry" are used interchangeably and incorporate: pharmaceuticals and diagnostics (including biotechnology-derived products), medical devices and equipment, industrial and environmental biotechnology, and agricultural biotechnology (including biofuels). North Carolina is unusual as a life science hub in that it has a significant industry base in each of these subsectors, with more than 500 biotechnology companies, a growing medical device cluster and an established agricultural biotechnology presence, including major biotechnology research operations for four of the nation's top five agricultural companies. Additionally, the life science industry is vibrant in all parts of the state, from natural products-focused businesses concentrated in the western part of the state, to biotechnology centers in the Research Triangle and Triad areas, to marine biotechnology opportunities on the coast. In fact, the North Carolina Biotechnology Center has regional offices in all parts of the state and active loans to biotechnology companies in each region.

The expansion of the state's life science industry has resulted from the combination of rapid growth in the size and number of emerging biotechnology companies and increased employment resulting from large biopharmaceutical companies locating large divisions here. Much of this growth can be traced to North Carolina's emergence as a center for the production and manufacture of therapeutics and vaccines. Overall, the industry's growth in the state has been buoyed by an infrastructure of universities, non-profit organizations and service providers adept at launching, attracting and supporting life science businesses. This support is exemplified by workforce development programs that have played a key role in attracting life science companies to locate here.

Request from the North Carolina General Assembly

Various dynamics suggest that the global life science industry will continue to grow rapidly, including: 1) the many highly prevalent diseases that remain poorly addressed by current treatments; 2) the aging of the population and other trends resulting in rapid growth in highly prevalent diseases; 3) the availability of new technologies enabling researchers to directly address more disease targets; 4) global population growth requiring new approaches to maximize food availability; and 5) an expected sharp increase in demand for biofuels. The projected long-term expansion of the global life science industry suggests that regions that are well-positioned to attract and grow promising companies will benefit greatly. However, the industry is highly dynamic and highly competitive. North Carolina's life science-focused companies and institutions must work together with state government to develop a clearer path to product commercialization in order to continue to grow a thriving industry. The state's life science companies face critical challenges along the path toward the commercialization of their products, as evidenced by:

- The low number of established (i.e., revenue-generating or public) biotechnology companies headquartered here
- The frequency with which North Carolina-based life science companies are acquired when on the cusp of success
- The mixed commercial results generated by the state's strong academic bioscience research institutions

North Carolina's state government is highly cognizant of the economic opportunity associated with the sustained growth of its life science industry and the need to continue to nurture it. As such, the North Carolina General Assembly requested that:

> **"The North Carolina Biotechnology Center shall prepare a strategic plan to accelerate the commercialization of promising life science technologies and discoveries being developed in universities and private companies in North Carolina and the related development and production of new commercial products."** (General Assembly of North Carolina, Session 2009, Session Law 2010-31, Senate Bill 897)

This plan presents a series of strategies to accelerate commercialization efforts by identifying and addressing the key challenges faced by North Carolina companies bringing life science products to market.

To assess the nature of these challenges, the North Carolina Biotechnology Center gathered input from more than 50 key life science industry stakeholders. These stakeholders included technology transfer officers, life science company executives (from small, mid-sized and large companies), investors, bankers, service providers, and executives representing the state's life science-focused non-profit organizations. These discussions revealed that the major challenges to commercialization of life science technologies are the limited availability of funding required by companies at critical junctures in their evolution and the shortage of highly experienced life science executives in North Carolina.

Key Challenges

According to most of the stakeholders surveyed, North Carolina's primary challenge in commercializing life science technologies is funding. While a shortage of early-stage funding was frequently noted as an obstacle, the limited availability of later-stage funding to build facilities and production lines was also deemed to be a key challenge for the state's industry.

Most North Carolina life science companies report that the ***early-stage funding gap*** is the most daunting obstacle preventing them from converting a promising research discovery into a commercial product. This gap occurs for life science technology-based companies when they have progressed beyond the stage where very early-stage funding vehicles (such as federal grants and North Carolina Biotechnology Center loans) are appropriate. These companies have typically not yet progressed to the point where they are able to attract venture capital funding or strategic partners. This funding gap has widened over the past decade as venture capital funding has declined and has been increasingly directed toward later-stage companies. The issue is exacerbated in North Carolina because relatively few life science-focused venture capital groups are active in the state.

Later-stage companies face a ***debt funding gap*** that is as challenging as the early-stage funding gap. Companies caught in this gap typically have a product on the market or soon-to-be on the market. At this point, such companies often require a significant cash infusion to finally capture their commercial opportunities. For a life science company, debt funding is often employed to initiate or expand the company's manufacturing capabilities and sometimes to build sales and marketing efforts or complete late-stage product development. The shortage of debt financing available for these companies stems from the limited number of banks willing to make loans to companies that are not yet profitable. Importantly, receipt of debt funding often represents an inflection point in hiring new employees who might play a role in manufacturing or commercializing a new product. As such, a new approach to bridging the debt funding gap would be expected to greatly increase the number of life science jobs in North Carolina.

In addition to early-stage and debt funding challenges, the state's limited number of experienced life science executives with product development, commercialization and financing experience was viewed by many stakeholders (especially those in the investment community) as a significant impediment to bringing products to market successfully. There are far more promising, innovation-driven companies at all stages of maturity in North Carolina than there are accomplished executives to drive them, creating a ***management gap***. The limited size of this talent pool appears to constitute a rate-limiting step that prevents more promising North Carolina-based life science companies from reaching a commercial plateau that reaps economic benefit to the state in the form of jobs and tax revenue.

Strategies to Bridge the Gaps

The core of this report focuses on several strategies to bridge these funding and management gaps and thereby accelerate the commercialization of life science technologies in North Carolina. Some of these recommendations describe new programs while others are focused on altering or expanding programs currently in place. It is highly recommended that the strategies to bridge the funding gaps be undertaken in parallel with the strategies to bridge the management gap—a coordinated approach will both drive an increase in the local availability of funding required to attract top-tier executives and build a stronger base of life science executives that will be able to attract additional funding. Table ES-1 lists these programs and the gaps they would help to bridge.

Table ES-1: Strategies Recommended to Accelerate Life Science Technology Commercialization

Strategy	Gap Bridged	Potential Benefits
Establish an Early-Stage Life Science Investment Fund (Chapter 4)	Early-Stage Funding Gap	Progression of the most promising life science companies to later-stage product development when venture capital and partner funding is available
Expand the Biotechnology Center Loan Program by $3 Million/Year (Chapter 5)	Early-Stage Funding Gap	$3 million in additional funding expected to result in $300 million in external follow-on funding over time to these loan portfolio companies
Expand the Annual Cap on SBIR/STTR Matching Program Funding to $5 Million/Year (Chapter 5)	Early-Stage Funding Gap	Potential creation of more than 50 additional jobs annually; encourages companies to access federal funding to develop and mature their technologies
Increase the Cap on the QBV Tax Credit Program and Include Institutional Investors (Chapter 5)	Early-Stage Funding Gap	Increased funding for emerging life science companies and attraction of investments from new class of investors; resulting larger funding rounds could help companies advance through early-stage funding gap
Establish the Life Science Development Corporation (LSDC), a $70 Million Loan Fund (Chapter 6)	Debt Funding Gap	Retention of high growth life science companies in North Carolina and attraction of out-of-state companies; potential for 100-250 jobs to be created immediately from LSDC funding
Implement New Programs To Attract Successful Out-of-State Life Science Executives (Chapter 7)	Management Gap	Growth in number of experienced life science executives in North Carolina, stimulating increased investment and driving more products to commercialization
Implement New Programs To Support Homegrown North Carolina-Based Entrepreneurs (Chapter 7)	Management Gap	Growth in number of experienced life science executives in North Carolina, stimulating increased investment and driving more products to commercialization

Overall Benefits

Despite the state's success in the life science industry to date, maintaining the status quo is not an option if North Carolina expects to continue to compete successfully on a global basis. Other states also see the opportunity available from the aggressive pursuit of growth in the bioscience industry. All 50 state governors highlighted bioscience in their most recent state-of-the-state addresses. As such, it will be important to address the funding and management gaps described in this report to allow for continued growth in the economic benefits currently enjoyed by North Carolina as a leading life science industry center.

The implementation of the seven strategies detailed in this report would allow for these gaps to be bridged, thereby accelerating the commercialization of life science technologies in North Carolina.

Key benefits would include:

- An increased number of high-paying life science jobs
- Continued growth of the sector's direct and indirect economic impact from biotechnology, already $64 billion for the state
- Retention of high growth companies in North Carolina
- Recruitment of promising life science companies from outside the state
- Attraction of additional investment to the state from internal and external sources

Overall, by surmounting the three major challenges described in this report, North Carolina's life science companies will have a clearer path to commercialization through expanded funding options and a deeper base of executives with a proven ability to bring products to market. This clearer path will enhance North Carolina's ability to obtain an outsized share of the expected rapid expansion of the global life science industry.

CHAPTER 1:

Life Science Market Opportunity

The social and economic impacts of the life science industry cannot be overstated. While the human health impacts of the life science industry may be well understood, the industry's current and potential impacts on industrial processes and food and fuel production are not as obvious. This chapter describes how the life science industry has grown in importance, especially since the launch of the biotechnology industry in the early 1980s. It also highlights the tremendous opportunity that lies ahead for companies and localities that are prepared to be at the forefront of the development and commercialization of new products and technologies.

North Carolina was early in recognizing this opportunity with the opening of the North Carolina Biotechnology Center in 1984—the Biotechnology Center was the first of its kind. The life science industry's overall impact on jobs and the state's economy has exceeded expectations, and North Carolina's life science infrastructure is one of the strongest in the country, as detailed in Chapter 2.

Factors such as the aging of the population and need for additional food and fuel sources result in a promising outlook for the life science industry. However, the high cost of life science product development has led to funding challenges for companies seeking to develop and commercialize such products. These challenges are discussed generally in this chapter and are more fully delineated as it relates to North Carolina in Chapters 2 and 3.

Throughout this report, the life science industry definition incorporates pharmaceuticals and diagnostics (including biotechnology-derived products), medical devices and equipment, industrial and environmental biotechnology, and agricultural biotechnology (including biofuels). While definitions of the life science and bioscience industry vary depending on the source, the nomenclature is used interchangeably in this report.

Life Science Definition

Throughout this report, the life science industry definition incorporates pharmaceuticals and diagnostics (including biotechnology-derived products), medical devices and equipment, industrial and environmental biotechnology, and agricultural biotechnology (including biofuels).

North Carolina at the Forefront of Regenerative Medicine

Recent breakthroughs in our understanding of the complex mechanisms controlling organ growth and tissue repair allow researchers to begin to create replacement organs and cellular therapies. Important regenerative medicine research ongoing in North Carolina includes:

- Individual cells in culture are organized into pulsing tissue that beats like the heart that produced them.
- Bladders grow on scaffolds, "seeded" with cells derived from the patient.
- Doctors collect cells from umbilical cords donated by parents of newborns and transform them into therapies for children with cerebral palsy and other disorders.

High-profile practitioners of this "tissue-building" approach include Anthony Atala, M.D., director of the Wake Forest Institute for Regenerative Medicine, and Duke cord-blood pioneer Joanne Kurtzberg, M.D. The Pentagon has put more than $42 million into a multi-campus consortium involving Atala and others, seeking to develop battle-wound treatments.

Healing, Fueling, Feeding

Many have dubbed this century as the "Bio Century"[1] as a result of the vital contributions the life science industry has delivered to tackle many of the world's greatest challenges.

Global competition is intensifying as more countries, regions, states and local governments look to participate in the growth of the life science industry. Continuing to build this bio-based economy here in the United States is a clear economic imperative that is expected to lead to job creation and wide-ranging economic impacts. In fact, according to Peter Pellerito, Senior Policy Consultant for the Biotechnology Industry Organization (BIO), all 50 governors emphasized the importance of the bioscience industry in their last state of the state address.[2]

BIO, the bioscience/biotechnology industry association and advocacy group, describes bioscience as, "helping us live longer and healthier lives, have a more abundant and sustainable food supply, use safer and more efficient industrial manufacturing, and reduce our greenhouse gas footprint."[3] BIO's annual report examines how bioscience has and will impact our lives in three broad categories: healing, fueling and feeding the world. The next three sections describe the bioscience industry's impact in these three areas, including statistics from the BIO report and other sources.

Healing

The life science industry is best known for its development of drugs, devices and diagnostics to extend and improve quality of life. The industry continues to be successful in these pursuits:

- Life expectancy for cancer patients has increased, on average, by three years since 1980; 83% of these gains are due to new treatments, including medicines.[4]
- According to AdvaMed, a medical technology industry association, from 1980 to 2000, rapid technological progress resulted in: 1) a 25% decline in disability rates, 2) a 56% reduction in hospital days, and 3) a 3.2-year life expectancy increase.[5]

1 *Growing the Nation's Bioscience Sector: State Bioscience Initiatives 2006*, Battelle Technology Partnership Practice and SSTI for Biotechnology Industry Organization, page vii.

2 Personal communication, November 9, 2010.

3 *Healing, Fueling, Feeding: How Biotechnology is Enriching Your Life*, BIO (Biotechnology Industry Organization), June 2010, page 3. *http://www.valueofbiotech.com/sites/default/files/pdfs/ValueofBiotechFINAL.pdf* (accessed December 21, 2010).

4 Sun, E., et al., "The Determinants of Recent Gains in Cancer Survival: An Analysis of the Surveillance, Epidemiology, and End Results (SEER) Database", *Journal of Clinical Oncology* 26, suppl. 15 (2008): Abstract 6616. *http://meeting.ascopubs.org/cgi/content/abstract/26/15_suppl/6616* (accessed December 21, 2010).

5 "About Our Industry", AdvaMed. *http://www.advamed.org/MemberPortal/About/Industry* (accessed on December 21, 2010).

- Worldwide, 10.5 million cases of infectious diseases and 2.5 million child deaths are prevented each year through immunization.[6]
- There are more than 1,200 bioscience diagnostic tests in clinical use.[7]
- More than 600 new biologic medicines are in development – including treatments for cancer, HIV/AIDS, Alzheimer's, and many other conditions.[8]
- According to a 2007 article in Health Affairs, "Over the past thirty-five years, U.S. age-adjusted mortality from cardiovascular disease declined 50 percent." The article emphasized that a combination of drugs, diagnostics and device-based treatments (all tools of the life science industry) contributed to this marked reduction in cardiovascular disease mortality.[9]

The impact of bioscience on North Carolina – from advances in regenerative medicine to the statewide growth of biomanufacturing and an emerging vaccine cluster – are explored in more detail in Chapter 2.

Fueling

The world's growing energy needs are staggering, and global energy consumption continues to rise rapidly. Industrial bioscience is providing solutions for energy conservation, climate stabilization and reducing our dependence on fossil fuels, while fueling economic growth and providing economic security.

- Economic development: Biofuels R&D promotes new business development, job creation and economic growth. Although in its infancy, the biofuels industry currently has 187 ethanol biorefineries operating in the U.S.,[10] already exceeding the 137 petroleum refineries in operation.[11]
- Bio Economic Research Associates projects that the economic impacts of building an advanced biofuels economy by 2022 (meeting the U.S. Renewable Fuel Standards requirement for 21 billion annual gallons of production by 2022) would be to create 29,000 direct jobs by 2012 and 190,000 by 2022; total job impacts in the economy (comprising direct and indirect employment via the employment multiplier effect) could reach 123,000 in 2012, and 807,000 by 2022. [12]

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6 "How to Save Millions of Lives", BIO (Biotechnology Industry Organization). *http://www.bio.org/about_biotech/global* (accessed on December 21, 2010).

7 Allingham-Hawkins, Diane. "Successful Genetic Tests Are Predicated on Clinical Utility", *Genetic Engineering and Biotechnology News*, 28:14, 2008.

8 "How to Save Millions of Lives", BIO (Biotechnology Industry Organization). *http://www.bio.org/about_biotech/global* (accessed on December 21, 2010).

9 Weisfeldt, M. and S. Zieman. "Advances in the Prevention and Treatment of Cardiovascular Disease." *Health Affairs* 26(1):25-37, 2007.

10 "Ethanol Industry Overview ", Renewable Fuels Association. January, 2010 *http://www.ethanolrfa.org/pages/statistics* (accessed on December 21, 2010).

11 "Number and Capacity of Petroleum Refineries", Petroleum Navigator: Refining and Processing. U.S. Energy Information Administration, 2010. *http://tonto.eia.doe.gov/dnav/pet/pet_pnp_cap1_dcu_nus_a.htm* (accessed on December 21, 2010).

12 *U.S. Economic Impact of Advanced Biofuels Production: Perspectives to 2030*, Bio Economic Research Associates. February 2009, page 1. *http://www.bio.org/ind/EconomicImpactAdvancedBiofuels.pdf* (accessed on December 21, 2010).

Fueling North Carolina

North Carolina buys 5.6 billion gallons of liquid fuels every year. Almost all comes from outside the state, and none of these imported gallons contributes to the state's agriculture, forestry, or manufacturing economy. The Biofuels Center of North Carolina is developing a statewide biofuels industry to reduce this dependence. By 2017, 10% of liquid fuels sold in North Carolina – or about 600 million gallons – are projected to come from biofuels locally grown and produced. Filling up with locally grown and manufactured biofuels blends will allow citizens to power not just their vehicles, but also the North Carolina economy.

- The associated cumulative reduction in petroleum imports over the period 2010-2022 is expected to exceed $350 billion.[13]
- Total (direct and indirect) economic output generated by the advanced biofuels industry could reach $20 billion by 2012 and $149 billion by 2022.[14]
- McKinsey & Company found that 60% of the bioscience industry sources surveyed believe that bio-substitutes for gas will be the dominant alternative by 2025, outpacing biodiesel and electric options.[15]
- From an environmental sustainability standpoint, businesses and governments are working to reduce the human impact on climate change through green manufacturing and new technologies that create process efficiencies, limiting waste production and reducing energy use.[16]

Feeding

The agricultural biotechnology segment of the bioscience industry has progressed rapidly since its first crops were planted less than 15 years ago. Bioscience-enabled crops were first planted in 1996 and exceeded 2.3 billion acres in 2009, representing "approximately 70 million repeat decisions by farmers to grow these crops."[17]

- Agricultural biotechnology produces plants with built-in protection against disease and insects, resulting in reduced pesticide usage.
- Bioscience-produced crops decrease erosion because harmful weeds are controlled while the crops thrive, promoting tillage systems that save the soil, conserve soil moisture and nutrients, preserve earthworm populations, and reduce sediment runoff into watersheds.
- Enhanced crops make it possible to obtain higher crop yields by effectively controlling disease, insects and weeds, enabling farmers to produce more food at lower costs. Higher yields of crops generated by agricultural biotechnology companies have been reported by a number of sources, including the World Bank, Nuffield Council on Bioethics, and a joint consultation of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO).

13 Ibid., page 14.

14 Ibid., page 2.

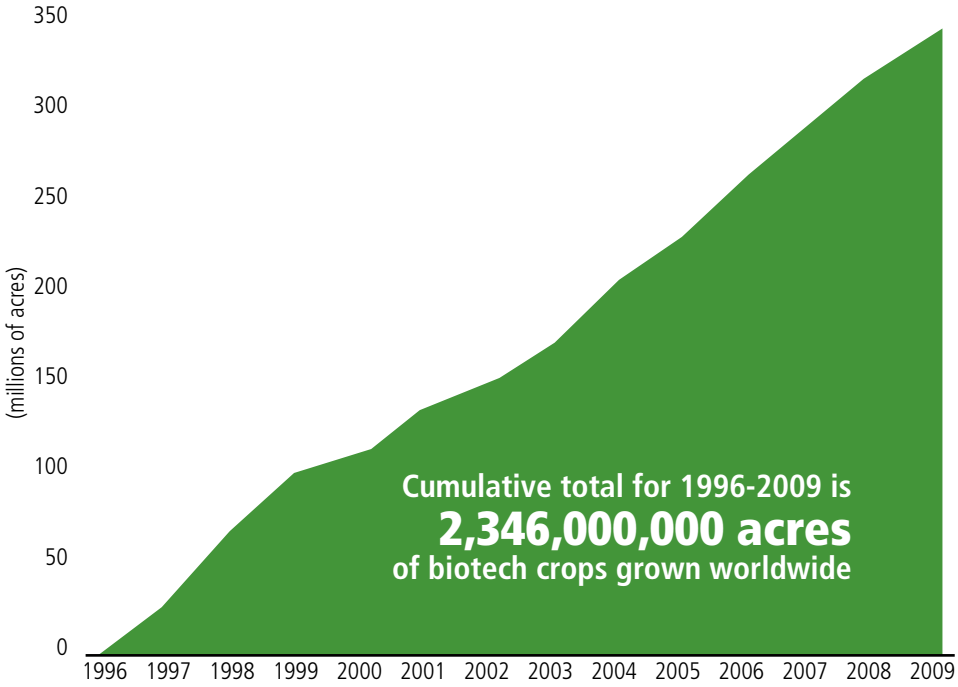
15 Oberman, Raoul. *Sustainable Biofuels Growth: Hurdles and Outcomes*, McKinsey & Company, June 2010, page 9. *http://biofuelsandclimate.files.wordpress.com/2010/06/2010-bio-mckinsey-presentation-vf.pdf* (accessed on December 21, 2010).

16 "Heal, Fuel, Feed: Biotech Can Do All Three - Sustainably", *BIOtechNOW (e-Newsletter)*, June 2010. *http://biotech-now.org/2010/05/12/heal-fuel-feed-biotech-can-do-all-three-sustainably* (accessed December 21, 2010).

17 Healing, Fueling, Feeding: How Biotechnology is Enriching Your Life, BIO (Biotechnology Industry Organization), June 2010, page 56. *http://www.valueofbiotech.com/sites/default/files/pdfs/ValueofBiotechFINAL.pdf* (accessed December 21, 2010).

- Agricultural biotechnology allows for the more efficient use of farmland. According to the House Subcommittee on Basic Research, "Crops that can withstand drought conditions, high salinity, or toxic materials, for example could enable populations living in currently non-arable regions to farm their land, reducing the pressure on other regions of the world, such as rainforests, that are currently being converted to farmland."[18]
- The use of biotechnologies, such as biosensors, can ensure the safety of our food and water supplies and address the threat of major disease outbreaks.
- The use of agricultural biotechnology increases the profitability of farming and offers opportunities for new and expanding industries.

Figure 1-1: Total Acres of Biotech Crops Grown in 2009[19]



18 "Benefits of Agricultural Biotechnology." BIO (Biotechnology Industry Organization) *http://www.bio.org/foodag/background/epabenefits.asp* (accessed December 10, 2010).

19 *Healing, Fueling, Feeding: How Biotechnology is Enriching Your Life*, BIO (Biotechnology Industry Organization), June 2010, page 56. *http://www.valueofbiotech.com/sites/default/files/pdfs/ValueofBiotechFINAL.pdf* (accessed December 21, 2010).

Life Science Industry: Rapid Growth Has Led to Major Economic Impact

The life science industry has grown rapidly, in part due to the high growth of the biotechnology industry since its beginnings roughly 30 years ago. As Table 1-1 indicates, overall U.S. bioscience revenue generated by publicly traded companies exceeded $577 billion in 2009, producing overall net income of $75 billion.[20]

Table 1-1: Bioscience Financial Performance by Subsector and Net Income, FY 2009[21]

Bioscience Subsector	Public Firms in Dataset	FY 2009 Revenue		FY 2009 Net Income	
		$ Millions	% of Industry	$ Millions	% of Industry
Agricultural Feedstock & Chemicals	34	$120,242	21%	$7,734	10%
Drugs & Pharmaceuticals	383	$329,661	57%	$58,009	78%
Medical Devices & Equipment	182	$106,016	18%	$7,121	10%
Research, Testing & Medical Laboratories	50	$21,430	4%	$1,680	2%
Industry Total	**649**	**$577,349**	**100%**	**$74,544**	**100%**

As it relates specifically to biotechnology, revenue of publicly traded biotechnology firms grew 12% to $90 billion in 2008.[22] The biotechnology industry is clearly in its growth phase and is approaching profitability; according to Ernst & Young, the global industry's net loss shrank from $3.0 billion in 2007 to $1.4 billion in 2008, and the U.S. biotech industry reached aggregate profitability for the first time.[23]

One reason for the attractiveness of the life science industry relative to other industries is that it is less impacted by economic downturns. "The life sciences industries were largely immune to the global recession of 2008-10. Unlike industries such as automotive, none of the large pharmaceutical manufacturers faced bankruptcy or needed large government bail-outs. Most companies even maintained profit margins that would be the envy of competitors in other industry segments," according to a white paper released by Deloitte Touche Tohmatsu.[24]

20 *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page 4. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

21 Ibid.

22 Giovannetti, Glen T. and Jaggi, Gautam. Beyond Borders: Global Biotechnology Report 2010, Ernst and Young, page 27. *http://www.ey.com/Publication/vwLUAssets/Beyond_borders_2010/$FILE/Beyond_borders_2010.pdf* (accessed December 21, 2010).

23 Ibid., page 27, 34

24 *The Future of Life Sciences Industries: Aftermath of the Global Recession*, Deloitte, page 4. *http://www.deloitte.com/assets/Dcom-Global/Local%20Assets/Documents/LSHC/2010%20Future%20of%20the%20life%20sciences%20industries%20report_web.pdf* (accessed on December 21, 2010).

Economic Impact from Life Science Industry

The economic and therapeutic impact associated with the bioscience sector is clearly significant and growing. Job creation in the bioscience industry has also been robust, has a large multiplier effect on the creation of additional jobs, and is expected to continue to outperform other industries. Battelle reports that total employment in the U.S. bioscience sector grew to 1.4 million in 2008.[25]

Table 1-2: U.S. Bioscience Employment

Bioscience Subsector	2008 Employment	Change in Employment, 2001–2008	Change in Employment, 2007–2008
Agricultural Feedstock & Chemicals	114,793	1.9%	4.6%
Drugs & Pharmaceuticals	311,882	2.3%	-2.3%
Medical Devices & Equipment	435,509	2.0%	2.4%
Research, Testing & Medical Laboratories	558,140	46.1%	2.1%
Total U.S. Bioscience	**1,420,324**	**15.8%**	**1.4%**

Table 1-2 shows that between 2001 and 2008 (the latest year for which data is available), bioscience employment growth was 15.8%, adding nearly 200,000 jobs.[26] Compared to the 3.5% growth rate for the national private sector, the bioscience industry job growth was 4.5 times higher.[27] Battelle also calculates that the total employment impact of the bioscience sector is eight million jobs, based on the additional jobs created as a result of the sector's direct jobs.[28] On a national basis, for every new bioscience job, another 5.8 jobs are created.[29]

The sector also continues to be a source of high-wage employment. Bioscience wages increased by 10.1% (inflation adjusted) from 2001 to 2008, compared to 3.2% for the private sector.[30]

Average annual bioscience income per employee was $77,595 compared to the average annual wage for the total U.S. private sector of $45,229.

Source: *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page ii. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

Biologics: A Key Driver of Life Science Industry Growth

While the market for conventional drugs continues to grow, the market for biologics is growing much more rapidly. According to EvaluatePharma, total prescription and over-the-counter drug sales were up 10% annually worldwide from 2000 to 2008; biologics were a key driver of this growth and were up 18% annually in the period, compared to conventional drug sales, which increased 8%

25 *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page ii. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

26 Ibid.

27 Ibid.

28 Ibid., pages 19-20.

29 Ibid.

30 Ibid.

Biologics

Biologics are larger molecule drugs derived from living organisms or their products and have historically been developed primarily by biotechnology companies.

annually in the period.[31] Biologics are expected to continue to gain market share as many of the top conventional drugs have near-term patent expirations looming.

Clearly, the importance of biologics in disease treatment is growing. In 2000, only one of the top ten selling drugs was a biologic (Epogen/Procrit). By 2008, this number had grown to five of the top ten. Forecasts released by EvaluatePharma in its "*World Preview 2016*"[32] report project that Abbott Laboratories' Humira (a biological product) will become the top-selling product in 2012 with sales of $8.3 billion and will retain its top spot through 2016 when sales could exceed $10 billion. As Table 1-3 indicates, the importance of biotech products is expected to continue to increase, with biologics comprising eight of the expected top ten therapeutic products by 2016.

Table 1-3: Projected Ranking of Top Selling Products in 2016

Rank	Product	Company(s)	Therapeutic Subcategory	Technology	2009	2016	CAGR (09-16)
1	Humira	Abbott Laboratories/Eisai	Other anti-rheumatics	Monoclonal antibody	5.6	10.1	9%
2	Avastin	Roche	Anti-neoplastic MAbs	Monoclonal antibody	5.7	8.9	6%
3	Enbrel	Amgen/Pfizer/Takeda	Other anti-rheumatics	Recombinant product	6.5	7.3	2%
4	Rituxan	Roche/Biogen Idec	Anti-neoplastic MAbs	Monoclonal antibody	5.6	6.8	3%
5	Crestor	AstraZeneca/Shionogi/Chiesi	Anti-hyperlipidaemics	Small molecule chemistry	4.8	6.3	4%
6	Herceptin	Roche	Anti-neoplastic MAbs	Monoclonal antibody	4.9	6.2	3%
7	Remicade	Johnson & Johnson/Merck & Co/ Mitsubishi Tanabe	Other anti-rheumatics	Monoclonal antibody	5.9	5.7	0%
8	Lantus	Sanofi-Aventis	Anti-diabetics	Recombinant product	4.3	5.3	3%
9	Advair/ Seretide	GlaxoSmithKline/Almirall/Others	Other bronchodilators	Small molecule chemistry	8.0	5.2	-6%
10	Prolia	Amgen/Daiichi Sankyo/GlaxoSmithKline	Bone calcium regulators	Monoclonal antibody	0	5.2	—

Source: EvaluatePharma 5/3/2010

The growing importance of biologics is also supported by Lehman Brothers research on growth trends by therapeutic categories. The growth projected between 2007 and 2012 in the top four therapeutic categories is driven by biologics:[33]

- Inflammation (12% growth per year) – driven by the shift from cheaper NSAIDS to higher-priced biologics such as Humira, Remicade, Enbrel, and Orencia.

31 "Biotechs Set to Dominate Drug Growth", *EP Vantage*, June 17, 2009. *http://www.evaluatepharma.com/Universal/View.aspx?type=Story&id=188700&isEPVantage=yes* (accessed on December 21, 2010).

32 "World Preview 2016", EvaluatePharma, May 3, 2010. *http://www.evaluatepharma.com/EvaluatePharma_World_Preview_2016.aspx* (accessed on December 21, 2010).

33 "Which Therapeutic Categories Are Growing the Fastest? Global and US Sales Growth of Branded Drugs by Therapeutic Category, 2005-2012E", *PAREXEL's Bio/Pharmaceutical R&D Statistical Sourcebook 2009/2010*. 2009, page 35.

- Vaccines (12%) – driven by growth in markets such as HPV (human papilloma virus), pediatric, meningitis, influenza, and other vaccine families through the penetration of biologics.
- Dermatology (10%) – driven by the psoriasis market; the chief products spearheading the growth in this market are biologics.
- Cancer (8%) – driven by biologics such as Avastin, Rituxan, Velcade, Erbitux, and Herceptin.

The Importance of Start-Up Companies to Industry Growth

Entrepreneurs and bioscience start-up companies played an important role in the growth outlined above and will continue to be a critical component in the industry's future. Small businesses with fewer than 500 employees accounted for 65 percent of the net new jobs created during the 1993-2009 period.[34] In their first year, new firms collectively add an average of three million jobs, while older companies lose one million jobs annually.[35]

Most successful biotech drugs emerge from start-ups.[36] According to AdvaMed, 28% of the medical technology industry's research and development spending comes from smaller companies.[37] While these start-up companies may leave the ultimate commercialization of their products to larger companies, the life science industry is highly dependent on discoveries initially developed by start-ups.

Biomanufacturing

Biogen Idec is one of several biotechnology companies with dedicated biological bulk-manufacturing facilities. These facilities include a 250,000-square-foot large-scale manufacturing (LSM) plant in Research Triangle Park. The LSM has 90,000 liters of bioreactor capacity and is one of the largest biologic manufacturing facilities of its kind in the world.[A] This facility has already received industry recognition for its exceptional design, innovative modular construction methods, and strong safety record – including the prestigious "Facility of the Year Award for Operational Excellence"[B] announced in January 2010. Biogen Idec employs approximately 850 people in the Research Triangle area.[C]

Source: [A] "Manufacturing", Biogen Idec. *http://www.biogenidec.com/research_manufacturing.aspx?ID=5779* (accessed on December 21, 2010). [B] Facility of the Year Awards are sponsored jointly by the International Society for Pharmaceutical Engineering, the group's associated trade show, INTERPHEX, and by *Pharmaceutical Processing* magazine. *http://www.facilityoftheyear.org/foyawinners2010* (accessed on December 31, 2010). [C] "Biogen RTP Wins Global Award", North Carolina Biotechnology Center, News and Events, January 12, 2010. *http://www.ncbiotech.org/article/biogen-rtp-wins-global-award* (accessed on December 21, 2010).

34 "Frequently Asked Questions" Office of Advocacy, U.S. Small Business Administration. *http://www.sba.gov/advo/stats/sbfaq.pdf* (accessed on December 21, 2010).

35 Kane, Tim. *The Importance of Startups in Job Creation and Job Destruction*. Kauffman Foundation, July 2010, page 2. *http://www.kauffman.org/uploadedFiles/firm_formation_importance_of_startups.pdf* (accessed on December 21, 2010).

36 Johnson, Ken. "PhRMA Statement Regarding Benefits of U.S. Innovation", PhRMA, August 25, 2009. *http://www.phrma.org/news_room/press_releases/phrma_statement_regarding_benefits_of_u.s._innovation* (accessed on December 21, 2010).

37 "About Our Industry", AdvaMed. *http://www.advamed.org/MemberPortal/About/Industry* (accessed on December 21, 2010).

Tremendous Opportunity for Growth in Life Science Industry

Despite the industry's healing, fueling, feeding and economic impacts to date, a great deal of opportunity for growth remains ahead for the life science industry. As such, localities competing successfully to build and attract companies in the industry are expected to reap significant rewards in terms of job growth and overall economic impact. Several trends that provide optimism behind the growth prospects for the industry are described below.

Highly Prevalent Diseases Remain Poorly Addressed by Current Treatments

Despite the strong growth in the overall life science industry and biotech industry specifically, many highly prevalent diseases remain poorly addressed by current treatments, implying that the industry has a great deal of room to grow. In 2008, analysts at Lehman Brothers studied data from the Centers for Disease Control and Prevention, National Health Statistics surveys, and National Institutes of Health to identify unmet medical needs by therapeutic category. This study identified many common diseases (each with a U.S. prevalence greater than three million patients) that remain poorly addressed by current therapeutics including: obesity, Alzheimer's disease, arthritis, chronic obstructive pulmonary disease, depression, cancers, pain, urinary incontinence, and congestive heart failure/ arrhythmia.[38]

Aging of Population and Other Trends Resulting in Rapid Growth in Highly Prevalent Diseases

While the mortality rates and prevalence of some diseases is declining due to the availability of new treatments and preventive measures, epidemiologic and environmental factors are driving the increasing prevalence of a number of common diseases. Three representative examples are Alzheimer's disease, diabetes and asthma. Alzheimer's disease is the most common form of dementia, and current therapeutics are unable to stop the disease from progressing.[39] In 2007, there were roughly five million Americans with Alzheimer's disease, but the U.S. prevalence is expected to increase to nearly 16 million by 2050[40] in large part due to the aging of the population. Exacerbating the societal and economic impact of the disease is the fact that patients with Alzheimer's may live 10-15 years after diagnosis, therefore having a long-term impact on the patients and their families.[41]

38 "Pharma/Biotech Pipelines and Unmet Medical Need: A 2008 Analysis", *PAREXEL's Bio/ Pharmaceutical R&D Statistical Sourcebook 2009/2010*, page 77.

39 "What is Alzheimer's?", Alzheimer's Association. *http://www.alz.org/alzheimers_disease_what_is_alzheimers.asp* (accessed on December 21, 2010).

40 2010 Alzheimer's Disease Facts and Figures. Alzheimer's Association, page 14. *http://www.alz.org/documents_custom/report_alzfactsfigures2010.pdf* (accessed on December 21, 2010).

41 Anderson, Pauline. "Global Prevalence of Alzheimer's Disease Set to Double Every 20 Years", Medscape Medical News, September 24, 2009. *http://www.medscape.com/viewarticle/709450* (accessed on December 21, 2010).

Growth in the diabetes population is being driven by the aging of the population as well as the sedentary lifestyle and poor eating habits of many Americans. In 2007, the Centers for Disease Control reported that more than 23.6 million Americans had diabetes – up from 18.2 million in 2002. [42,43] The number of Americans with diabetes more than tripled between 1980 and 2008.[44] In 2007, the direct and indirect costs associated with diabetes were $174 billion.[45]

The prevalence of asthma grew to 23.3 million in the U.S. in 2008, and asthma accounted for 14.4 million in lost school days and 14.2 million in lost work days in that year.[46] While the rate of increase in asthma prevalence has slowed somewhat, the prevalence had still grown 3% annually over the previous five years.[47] Some believe that this increase may be due in part to environmental factors.[48]

New Technologies Allowing Researchers to Focus on More Targets

According to researchers at Accenture Technology Labs, pharmaceuticals are currently directed at no more than 500 targets in the human body.[49] Genomic research is expected to yield drugs designed to interact with a far greater number of biological targets, resulting in enhanced efficacy and reduced toxicity in well-defined patient populations. This research is also expected to allow scientists to focus on up to tens of thousands of targets.[50]

42 *National Diabetes Fact Sheet, 2007.* Centers for Disease Control, page 12. *http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf* (accessed on December 21, 2010).

43 *National Diabetes Fact Sheet, 2003.* Centers for Disease Control. *http://www.cdc.gov/diabetes/pubs/estimates.htm* (accessed on December 21, 2010).

44 "Diabetes Data and Trends. Number (in Millions) of Civilian, Non-Institutionalized Persons with Diagnosed Diabetes, United States, 1980–2008", Centers for Disease Control. *http://www.cdc.gov/diabetes/statistics/prev/national/figpersons.htm* (accessed on December 21, 2010).

45 *National Diabetes Fact Sheet, 2007.* Centers for Disease Control, page 12. *http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf* (accessed on December 21, 2010).

46 *Trends in Asthma Morbidity and Mortality.* American Lung Association, February 2010. *http://www.lungusa.org/finding-cures/our-research/trend-reports/asthma-trend-report.pdf* (accessed on December 21, 2010).

47 Ibid.

48 Priftis, K., et al. "Asthma symptoms and airway narrowing in children growing up in an urban versus rural environment", *Journal of Asthma* 46(3): 244-251, 2009.

49 Mesnage, Marion and Illsley, Martin. "Biotechnology: Out of the Labs and Into Every Industry", Accenture. January 2003. *http://www.accenture.com/Global/Research_and_Insights/Outlook/By_Alphabet/BiotechnologyIndustry.htm* (accessed on December 21, 2010).

50 Ibid.

Global Population Growth to Spur Agricultural Biotechnology Applications

The world population is currently just under seven billion people.[51] The United Nations projects that the population will reach 8.6 billion in 2035.[52] Since the global food supply may also need to double during this time period, the application of bioscience to the food supply is a global imperative.[53] As such, new approaches to enhancing the food supply, such as those described in the "Feeding" section above, will become even more pressing.

Demand for Biofuels Expected to Increase

As the population rises and traditional resources for fuel become more limited, demand for biofuels produced by the bioscience industry should continue to grow. According to the U.S. Department of Energy, "Cheap oil fuels America's economy—most of which is imported. Small changes in crude oil prices or supplies can have an enormous impact on our economy—increasing trade deficits, decreasing industrial investment, and lowering employment levels. Developing a strong industry for biomass fuels, power, and products in the United States will have tremendous economic benefits including trade deficit reduction, job creation, and the strengthening of agricultural markets."[54]

51 "U.S. and World Population Clocks", U.S. Census Bureau, *http://www.census.gov/main/www/popclock.html* (accessed December 21, 2010).

52 "World Population Prospects: The 2008 Revision Population Database", United Nations. *http://esa.un.org/unpp* (accessed December 21, 2010).

53 Healing, Fueling, Feeding: How Biotechnology is Enriching Your Life, BIO (Biotechnology Industry Organization), June 2010, page 58. *http://www.valueofbiotech.com/sites/default/files/pdfs/ValueofBiotechFINAL.pdf* (accessed December 21, 2010).

54 "Resources for Policymakers", U.S. DOE, Energy Efficiency and Renewable Energy. *http://www1.eere.energy.gov/biomass/for_policymakers.html* (accessed on December 21, 2010).

Challenges Facing Growth of Life Science Industry

While the impact that bioscience-based products and services has on our welfare is enormous and wide-ranging (health, food, fuel, revenue, employment), it is accompanied by significant challenges in advancing a product from discovery to commercialization. Chapter 3 of this strategic plan will focus on specific gaps and challenges facing North Carolina's life science industry. On an industry-wide level, much of the commercialization challenge is associated with the high cost and high risk of failure associated with the development of bioscience-related products, particularly biopharmaceuticals.

High Costs and High Risk of Failure Associated with Life Science Product Development

According to a study by the Tufts Center for the Study of Drug Development, there is only a 16% success rate for drugs entering clinical trials (drug trials in people rather than animals).[55] In a Boston Globe article, Peter Wirth, Executive Vice President of Genzyme Corporation stated, "It takes a billion dollars to develop a drug. The critical dilemma now is: how are we going to pay for innovation?"[56] Tufts estimated the average cost to develop a new biotech drug at $1.2 billion in 2006.[57] Even more pessimistic is research released in 2003 by Bain & Company, a consulting firm, which stated that this cost is more on the order of $1.7 billion, including such factors as marketing and advertising expenses.[58] Because of the long period before research and development (R&D) pays off in net income, companies with revenues below $100 million do not, on average, record positive net income; the 79 public bioscience companies with over $1 billion in revenue generate nearly all of the net income for the bioscience industry.[59]

Unclear Future for Basic Research Funding

One area that could present future challenges for the bioscience industry relates to academic bioscience R&D funding. Bioscience R&D expenditures were nearly $32 billion in 2008, representing 60% of all U.S. academic R&D.[60] Academic bioscience research grew by 22% from 2004 to 2008.[61]

55 *Outlook 2010*. Tufts Center for the Study of Drug Development, Tufts University, page 4.

56 Weisman, Robert. "Biotech firms feel funding squeeze",, *The Boston Globe*, October 2, 2009.

57 *Outlook 2010*. Tufts Center for the Study of Drug Development, Tufts University, page 3.

58 "Has the Pharmaceutical Blockbuster Model Gone Bust?" Bain & Company, December 8, 2003. *http://www.bain.com/bainweb/About/press_release_detail.asp?id=14243&menu_url=for_the_media.asp* (accessed on December 21, 2010).

59 *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page 3. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

60 Ibid., page 41.

61 Ibid., page 41.

"While helping to meet some critical needs resulting from previous budget shortfalls, the funding provided by the ARRA was unprecedented and short-term. Scientific research is an on-going process that requires strong, predictable funding year-in and year-out. A funding tap that runs hot and cold wreaks havoc on the research process and diminishes our ability to benefit from the innovations that flow from it. It is essential to America's global competitiveness and long-term economic health that the U.S. invest in basic research significantly and consistently year-over-year."

Source: *Sparking Economic Growth*, The Science Coalition. April 2010, page 14. *http://www.sciencecoalition.org/successstories/resources/pdf/Sparking%20Economic%20Growth%20Full%20Report%20FINAL%204-5-10.pdf* (accessed on December 21, 2010).

Federal research funding is a major source of bioscience-related research support, providing some 60% of basic research funding.[62] Some institutions are concerned about future levels of such funding. The National Institutes of Health (NIH) funds intramural research (research conducted on-site at the NIH campuses), extramural research (generally university-based) and early-stage company R&D (via its Small Business Innovation Research [SBIR] and related grants programs). In 2009, NIH baseline funding of $21.5 billion declined 7.5% from the previous year.[63] An additional $4.4 billion of research was funded by the American Recovery and Reinvestment Act of 2009 (ARRA).[64] When commenting on the welcome influx of ARRA money, Alan Eisenberg, Executive Vice President for Emerging Companies and Business Development at BIO, said, "The NIH money granted for basic biomedical research could have a beneficial, long-run effect on biotech firms, which will help bring promising discoveries from the lab to commercial viability."[65] However, overall NIH funding has been flat since 2003, which is a cause of concern within the bioscience industry.[66]

Decline in Venture Capital Funding and Initial Public Offerings

As is described in much more detail in Chapter 3, venture capital funding for bioscience companies and growth companies in general has declined significantly. Additionally, venture capital groups appear to be more focused on later-stage companies than in the past, leaving a wide funding gap for early-stage companies. Finally, initial public offering activity has declined (as further delineated in Chapter 3), leaving companies with fewer funding options as they move into expensive late-stage clinical trials.

62 *Sparking Economic Growth*, The Science Coalition. April 2010, page 3. *http://www.sciencecoalition.org/successstories/resources/pdf/Sparking%20Economic%20Growth%20Full%20Report%20FINAL%204-5-10.pdf* (accessed on December 21, 2010).

63 Battelle/BIO State Bioscience Initiatives 2010, Battelle Technology Partnership Practice, May 2010, pages 42-43. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

64 Ibid., page 42.

65 *Biotech: Lifting Big Pharma's Prospects with Biologics*, PricewaterhouseCoopers. May 2009. *http://www.pwc.com/en_GX/gx/pharma-life-sciences/pdf/biotech-final.pdf* (accessed on December 21, 2010).

66 Battelle/BIO State Bioscience Initiatives 2010, Battelle Technology Partnership Practice. May 2010, page 42. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

Life Science Opportunity Put in Context of Challenges Ahead

This chapter presented the major effects that the life science industry is having on human health, our food supply, and fueling the economy. The growth in the industry has resulted in an impressive jobs and tax base, and this rapid growth is expected to continue as a result of a range of factors described earlier. However, combining the high cost of taking a product from the discovery phase to commercialization with questions around sources of funding for such research and development, funding gaps arise that must be bridged and product development challenges occur that need to be surmounted. Only those companies (and the localities in which they are based) that are able to bridge these gaps and surmount these challenges will be successful in benefiting from the continued growth in the life science industry.

The next chapter describes how North Carolina has grown into a leading hub for the life science industry through successes across a range of subsectors within the industry. North Carolina has developed several distinctive strengths, which have resulted in its strong industry position, and these strengths are also described. However, as detailed in Chapter 3, the state faces a number of challenges to building upon its leadership position, and failure to confront these challenges will negatively impact the state's ability to benefit from the tremendous growth likely ahead for the bioscience industry. As such, the balance of this report, Chapters 4-7, presents several strategies to successfully overcome these challenges.

CHAPTER 2:

Life Science Opportunity in North Carolina

North Carolina's early and long-term commitment to biotechnology has played a key role in establishing a large and growing life science industry in the state. This chapter details the strong positive impact that the life science industry has had on North Carolina as well as several of the factors behind the state's success in the industry to date. While North Carolina appears poised to garner more than its fair share of the tremendous life science market opportunity described in Chapter 1, this chapter also describes a few "disconnects" which must be addressed to ensure that the state's success in the life science industry to date is continued in the coming decades.

North Carolina's Life Science Industry's Large and Growing Statewide Economic Impact

North Carolina was early in seeing the economic opportunity associated with establishing a strong biotechnology industry, as part of the state's transition from a traditional economy based on textiles, tobacco and furniture. The creation of the North Carolina Biotechnology Center (the Biotechnology Center) in 1984 and consistent state funding of the Center since reflect the state's commitment to further growing the sector. This investment has begun to yield tangible benefits for North Carolina in that the state is now home to the third largest number of biotechnology companies among all states,[1] and has built a strong bioscience jobs and tax base.

> *"The reason we are ahead of the curve is because for 15 years we've invested in the biotech industry and it's paying dividends."*
>
> —Norris Tolson, President/CEO, North Carolina Biotechnology Center[2]

Strong Growth in High-Paying Jobs

North Carolina's biotechnology sector provides a major economic boost to the state. Total biotechnology-related employment (direct & indirect) grew to more than 226,000 jobs with payroll and benefits totaling $12.7 billion in 2008.[3]

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1 *Beyond Borders: The Global Biotechnology Report*, Ernst & Young, 2006.

2 Friedman, Bob. "Biotech could pave NC's path out of the recession", *Business Leader Magazine (NC-Triangle)*, September-October 2010, page 38-39.

3 *2010 Evidence and Opportunity: Biotechnology Impacts in North Carolina*, Battelle Technology Partnership Practice, 2010, page i, vi.

Biotechnology is responsible for $64.6 billion in total economic output and generates $1.9 billion in state and local taxes as shown in Table 2-1.[4]

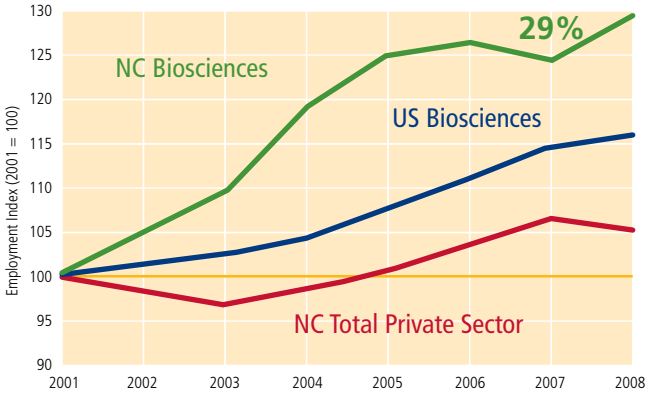
Table 2-1: Total (Direct and Indirect) Economic Impact of Biotechnology in North Carolina

	2010 Reported Impact	2008 Reported Impact	Change 2008–2010
Employment	226,823	180,007	46,816 jobs increase
Employment Compensation	$12.7 billion	$9.4 billion	$3.3 billion increase
Business Volume (Economic Output)	$64.6 billion	$45.8 billion	$18.7 billion increase
State and Local Taxes	$1.92 billion	$1.44 billion	$0.48 billion increase

Note: Data in the 2010 economic impact report are from 2008, and data in the 2008 report are from 2006.

Bioscience employment in the state grew 29% from 2001 to 2008,[5] which was nearly twice the national bioscience sector growth rate and more than five times that of North Carolina's total private sector. Furthermore, Figure 2-1 reflects that employment growth in the state's bioscience industry tended to be positive during periods when employment in the state's private sector was in decline (2001-3, 2007-8), demonstrating that this industry may indeed be able to weather periods of economic decline far better than others.

Figure 2-1: Rapid Employment Growth in North Carolina's Bioscience Industry



When compared to the other top ten states in overall bioscience employment, North Carolina's job growth during 2001-2008 outpaced all states except Massachusetts.[6] Further, the Biotechnology Center predicts that the state could see an additional 65,000 – 70,000 biotechnology jobs throughout North Carolina by 2020.[7]

Not only has the state's life science industry grown rapidly (even in challenging economic times), but salaries are comparatively quite high in the industry. Wages for North Carolina's bioscience workers rose to an average salary of $74,829 in 2008, which was $35,000 more than the state's average private-sector salary.[8]

It is important to note that this growth brings additional collateral economic benefit to support sectors not directly represented in these data:

4 Ibid.

5 Ibid., page 8.

6 Ibid., page 27.

7 Friedman, Bob. "Biotech could pave NC's path out of the recession", *Business Leader Magazine (NC-Triangle)*, September-October 2010, page 38-39.

8 *2010 Evidence and Opportunity: Biotechnology Impacts in North Carolina*, Battelle Technology Partnership Practice, 2010, page 13.

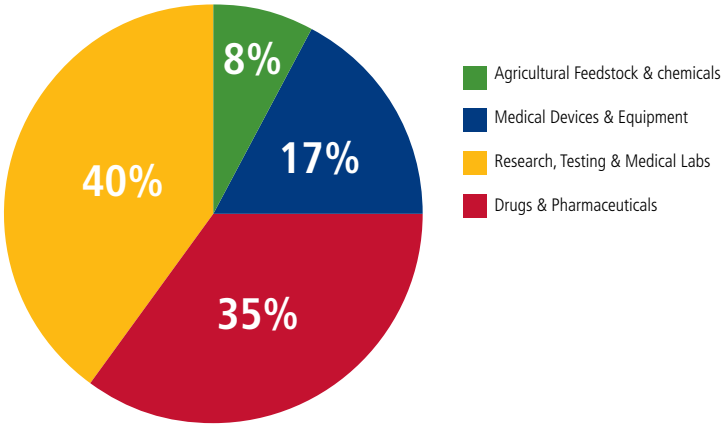
"The life sciences are an engine of job creation with a high "multiplier" rate – they create a lot of jobs indirectly. In addition to elite, Ph.D.-level positions, the life sciences create a range of jobs, including support and manufacturing roles ideal for workers transitioning from declining industries such as furniture or textiles. If North Carolina is to climb out of the recession permanently, it will do so on the shoulders of good-paying, sustainable jobs like these."

—Art Pappas, Founder and Managing Partner, Pappas Ventures[9]

Unusually Diverse Life Science Community

While many states have one or two strong niches within the bioscience sector, North Carolina has a notably diverse employment composition.[10]

Figure 2-2: Breadth of North Carolina's Bioscience Industry – Employment Composition



National statistics corroborate the unusual breadth of life science research and commercialization found in the state. Based on 2001-2008 employment metrics, North Carolina is one of only five states specialized in three of these four bioscience subsectors (Agricultural Feedstock & Chemicals; Research, Testing & Medical Labs; and Drugs & Pharmaceuticals), and is one of the top seven states in employment growth in the Medical Devices & Equipment subsector.[11] In addition to being a major U.S. hub for biopharmaceutical research and development, North Carolina is home to the headquarters of three of the top ten contract research organizations (CROs) in the world, with a combined global market share of

The Hamner

The Hamner Institutes for Health Sciences is a nonprofit organization located in Research Triangle Park whose mission is to "improve public health through better predictive assessments of chemical and drug safety while helping to develop new breakthrough medicines and diagnostics." The Hamner routinely collaborates with federal agencies such as the Centers for Disease Control, the Environmental Protection Agency and the Food and Drug Administration. In 2008, the Hamner-UNC Center for Drug Safety Sciences was formed to foster new alliances between academia, industry and government regulatory agencies to advance public health research, education and scientifically informed policies.

9 Pappas, Arthur M. "Legislators aid N.C. life sciences", *News & Observer*, Raleigh, NC. Point of View. July 16, 2010. *http://www.ncbioscience.org/news_and_events/documents/ArtPappas-NOOpEd7-16-2010.pdf* (accessed on December 21, 2010).

10 *2010 Evidence and Opportunity: Biotechnology Impacts in North Carolina*, Battelle Technology Partnership Practice, 2010, page 10.

11 *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page iv. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

PHOTO © MEDICAGO

Tobacco: Creating Jobs, Saving Lives

In the past, tobacco has had a negative impact on human health. But in Research Triangle Park, one company plans to use tobacco instead to *save* lives. **Medicago**, a Montreal-based pharmaceutical company, is using the plant as a tool for producing flu vaccines. Medicago recently chose Research Triangle Park for its 90,000 square foot manufacturing facility, which will create up to 85 jobs.

North Carolina's tobacco history also resulted in the founding of **Targacept**, which is now one of North Carolina's leading public bioscience companies. Targacept was started in 1997 based on research originating at R.J. Reynolds Tobacco Company (RJR) and is headquarted in Winston-Salem. Its drug candidates are aimed at treating a wide range of disorders, including Alzheimer's disease, depression, Parkinson's disease, ADHD, and schizophrenia.

27%.[12] In addition to North Carolina's strengths in human health fields, four of the top five U.S. agricultural companies have significant biotechnology research operations in the state.

The North Carolina Biotechnology Center recently launched several initiatives to further broaden North Carolina's life science industry base. The Centers of Innovation (COI) grant program catalyzes development and strengthening of new industry sectors within the North Carolina economy by making innovation and commercialization a strategic priority. COIs represent partnerships between the Biotechnology Center, university researchers, technology transfer officers, industrial partners, nonprofit stakeholders and policymakers. COIs have been created to support the state's medical device, oncology-focused drug discovery, nanobiotechnology and marine biotechnology subsectors. Each of these subsectors has attained some degree of critical research mass across the state but previously lacked a state-wide infrastructure and public-private cohesion to satisfactorily drive these sectors towards commercialization and economic impact.

More recently, the *30 in 10 Agbiotech Initiative* was launched, with a goal of expanding the commercial contributions from local agricultural biotechnology efforts to the state's agri-economy, thereby growing the agriculture component of the gross state product ($70.1 billion at the time of that report) by $30 billion in ten years.[13] The economic benefits of this initiative will be strongly realized in rural areas most impacted by challenges in the state's traditional industries such as textiles, tobacco and furniture.

12 *The Top 10 Contract Research Organizations*, Business Insights, March 2009.

13 *30 in 10: Growing North Carolina's AgBiotech Landscape*, North Carolina Biotechnology Center, 2009, page 4. *http://www.ncbiotech.org/sites/default/files/agbiotech_30in10_2.pdf* (accessed on December 22, 2010).

Life Science Efforts Spread Across the State

While much of North Carolina's life science momentum is concentrated in the Research Triangle region, it should be noted that there are significant research, development and commercialization efforts spread across the state. In addition to Targacept, the Piedmont Triad region boasts other significant life science assets, including TransTech Pharma, Tengion, Banner PharmaCaps, Wake Forest University and its new Institute for Regenerative Medicine. Gaia Herbs and other natural products-focused businesses have concentrated in the western part of the state. The greater Charlotte area is home to UNC-Charlotte and the new North Carolina Research Campus in Kannapolis. Eastern North Carolina is represented by East Carolina University (Greenville) and Avoca, a manufacturer of fragrance from clary sage in Merry Hill, N.C. The southeast is represented by PPD (one of the world's largest contract research organizations), UNC-Wilmington, the UNCW Center for Marine Science and its biotechnology commercialization incubator (MARBIONC), AAI Pharma (Wilmington) and Pfizer Poultry Health (Laurinburg). Life science-related manufacturing efforts are particularly well-distributed across the state, including Novozymes (Franklinton), Novartis (Holly Springs), Pfizer/Wyeth (Sanford), Metrics (Greenville) and DSM (Greenville).

To further cultivate and leverage the life science advantages specific to each of these regions, the Biotechnology Center has opened regional offices in Winston-Salem, Charlotte, Greenville, Wilmington and Asheville. Additionally, the Biotechnology Center currently has active loans to biotechnology companies in all parts of the state.

North Carolina Research Campus

The North Carolina Research Campus (NCRC) was established in Kannapolis to foster research collaborations in the areas of biotechnology, health and nutrition. NCRC is a public-private partnership between benefactor David H. Murdock and the state of North Carolina. The Campus supports researchers from eight North Carolina universities, industry partners and not-for-profit institutions with core facilities offering state-of-the art discovery tools and an abundance of laboratory and office space.

PHOTO © NC RESEARCH CAMPUS

Key Drivers of North Carolina's Life Science Industry Growth

The North Carolina life science industry has clearly established a great deal of momentum which must be continued over the coming decades in order to fully reap the economic benefits. This momentum has been built through the leveraging of a vast, diverse and uncommon array of assets found in the state. The availability of these assets will continue to be critical as the state seeks to further build its strong position in the life science industry.

Among the most critical of these building blocks are:

- an abundance of world-class research institutions (including university, government and nonprofit laboratories) and their associated technology transfer and commercialization efforts
- a base of large corporations with significant operations in the state (which contributes human capital at all levels)
- the global headquarters for many top contract research (CRO) businesses
- a support infrastructure facilitated in part by entities such as the North Carolina Biotechnology Center, the Council for Entrepreneurial Development (CED), and the Small Business and Technology Development Center (SBTDC)
- a biotechnology- and entrepreneur-friendly state government and business climate

Several of the key drivers behind the growth of North Carolina's life science industry are described in the following sections.

Big Business Starts with Tiny Particles

Advanced Liquid Logic, a Research Triangle Park firm spun out of Duke University with the help of several Biotechnology Center loans, is developing high-speed diagnostic tests that use nano-sized droplets of fluids. This "lab-on-a-chip" technology performs complex laboratory operations on miniscule "microfluidic" platforms. Advanced Liquid Logic is one of some 75 North Carolina companies developing nanobiotechnology applications.

Growth Spurred By Emerging Companies

The growth in the state's life science sector derives not only from the expansion of companies already established in North Carolina, but also from the creation of new companies and the relocation of other life science businesses to the state. The great majority of the state's life science companies are start-up companies with fewer than 50 employees. North Carolina's strong academic research institutions, along with numerous programs to nurture emerging companies, have driven high growth in the number of life science start-ups established here.

Many early-stage discoveries, which ultimately lead to commercialized products, come out of the state's leading academic research institutions. As described later in this chapter, Duke and UNC-Chapel Hill are both among the top 20 universities in research expenditures, but these two schools represent just the tip of the iceberg in terms of important life science research ongoing in the state. Work at these institutions is actively supported by the North Carolina Biotechnology Center and other statewide groups. For instance, the Biotechnology Center's Oliver Smithies Faculty Recruitment Grants program has provided $11 million to aid the state's

research institutions in recruiting 56 research faculty members who then founded ten companies and landed $542 million in other funding.[14]

Significant life science start-up company formation originates from the state's research universities. Table 2-2 shows the number of start-up companies created in 2008 to commercialize technologies invented at local universities.

Business and research loan funding provided through the Biotechnology Center is often the first external financing available to emerging life science companies in the state. More than half of all loans awarded by the Biotechnology Center have been made to companies spun out of the state's public or private universities, highlighting the continued prominence of university start-ups in the local demographic of early-stage companies. Many companies that benefit from Biotechnology Center loans either subsequently commercialize their products or are acquired. It is important to note that of the 57 companies in the Biotechnology Center's current loan portfolio, only one has more than 50 employees. This data point reflects the high number of early-stage, emerging life science companies based in North Carolina. (The Biotechnology Center loan program is described in further detail in Chapter 5.)

The Biotechnology Center also supports companies built to commercialize university inventions through its BATON program, which maps prequalified service providers and management candidates to promising nascent companies. In its three year history, the program has supported the creation of 17 university start-ups birthed at seven universities in the state.

Table 2-2: Start-Up Company Formation by North Carolina Universities in 2008

Institution	Startups Formed
Duke University	7
East Carolina University	1
North Carolina State University	5
UNC-Greensboro	2
UNC-Chapel Hill	5
UNC-Charlotte	3
Wake Forest	2
Total	**25**

Source: *AUTM U.S. Licensing Activity Survey, FY2008 Survey Summary*, Association of University Technology Managers, 2010, pages 47-51.

Employment Growth Driven By Larger Firms Locating Large Divisions Here

The list of major bioscience and related companies headquartered in North Carolina draws heavily from the biopharmaceuticals, diagnostics and CRO sectors. Of these, among the largest employers are: Laboratory Corporation of America (LabCorp), PPD, Talecris, RTI International, Quintiles, Spectrum-Carilion Labs, Banner PharmaCaps, bioMerieux, INC Research, AAI Pharma, Family Health International, Novella Clinical and Rho.

However, multinational corporations headquartered elsewhere but with significant operations in North Carolina are increasingly important contributors to the state's life science economy. The list of those that employ at least 300 North Carolinians includes companies from the biotechnology, pharmaceutical, medical device and agricultural biotechnology worlds such as: GlaxoSmithKline, Hospira, Baxter Healthcare, DSM, Syngenta Crop Protection, Pfizer, BD Technologies, Proctor & Gamble, Teleflex Medical, Biogen Idec, BASF Crop Protection, Bayer CropScience, Merck & Co., Thermo Fisher Scientific, Cook Medical, Covidien, Merck Biomanufacturing Network (Diosynth Biotechnology), Novo Nordisk, Novozymes, Sandoz, Eisai, Catalent Pharma Solutions and West Pharmaceuticals.[15]

14 North Carolina Biotechnology Center, "Grant Funding Proves Successful" brochure

15 Company Directory. North Carolina Biotechnology Center. *http://directory.ncbiotech.org* (accessed on December 21, 2010).

Job-Ready Employees, Day One

NCBioImpact is North Carolina's largest training consortium, delivering a full spectrum of industry-driven training for biomanufacturing and pharmaceutical production. This coordinated workforce training is provided through a variety of courses, certificates and degree programs developed as part of a first-in-class partnership between biomanufacturing businesses, universities, and the North Carolina Biotechnology Center.

BioNetwork offers a curriculum of short, industry-customized courses offered through the North Carolina Community College System that are designed to upgrade the skills of incumbent workers. North Carolina Central University's BRITE (Biomanufacturing Research Institute and Technology Enterprise) is preparing students for research careers in the biotechnology and biomanufacturing workplaces, particularly in the areas of drug discovery and manufacturing process development. BTEC (Biomanufacturing Training and Education Center), located on North Carolina State University's Centennial Campus, deploys a system of advanced, hands-on training and education in a simulated cGMP (current Good Manufacturing Practice) environment using facilities and equipment that match those in place at the world's leading biomanufacturing companies.

Source: NCBIOIMPACT. *http://www.ncbioimpact.org* (accessed on December 22, 2010).

Workforce Development Programs Playing Key Role in Growth

North Carolina is particularly innovative with regards to its coordination of industry-driven workforce development efforts. Historically a training ground for Ph.D.-level researchers destined to ascend into the academic ranks, the state has methodically created and funded a first-in-class workforce training effort in coordination with its community colleges, universities, corporations and the North Carolina Biotechnology Center. These efforts have culminated in the creation of a biomanufacturing talent pool that has been instrumental in the successful recruitment of large manufacturing operations to the state in recent years.

> *"North Carolina's 'ace' was its ability to provide an instantaneous workforce."*
>
> —Joerg Reinhardt, CEO, Novartis Vaccines and Diagnostics, announcing the company's new flu vaccine biomanufacturing facility in Holly Springs[16]

These efforts were programmatically initiated with the introduction of the *BioWork* course, developed by the Biotechnology Center in partnership with the community college system and industry. In turn, biomanufacturing workforce development efforts have been extended under the *NCBioImpact* umbrella to include the university-scale programs, BRITE and BTEC (see sidebar). Finally, the Industrial Fellowship Program was recently created by the Biotechnology Center as a unique effort to transition promising academic researchers to scientific careers in industry. Statewide efforts in workforce development contributed to the Milken Institute's Biotech Index report ranking of the Research Triangle area as No. 1 in human capital and biotechnology workforce.[17]

North Carolina's Increasing Prominence as a Leader in Biomanufacturing

As indicated earlier, North Carolina has become a prominent location for manufacturing operations for pharmaceutical, biological and industrial products. When companies site their manufacturing operations in North Carolina, a large number of new positions for highly skilled workers typically become available. Some of the world's largest pharmaceutical companies have established new manufacturing facilities in in the state. Novartis Vaccines and Diagnostics chose Holly Springs over several other locations to locate a $267 million plant to produce a flu vaccine. Merck built a $300 million facility in Durham to produce vaccines for measles, mumps, rubella, chicken pox, and shingles. Both companies have since announced growth plans for these plants and the creation of additional jobs.

16 North Carolina Biotechnology Center. *http://www.ncbiotech.org/workforce-education/workforce-development* (accessed on January 4, 2011).

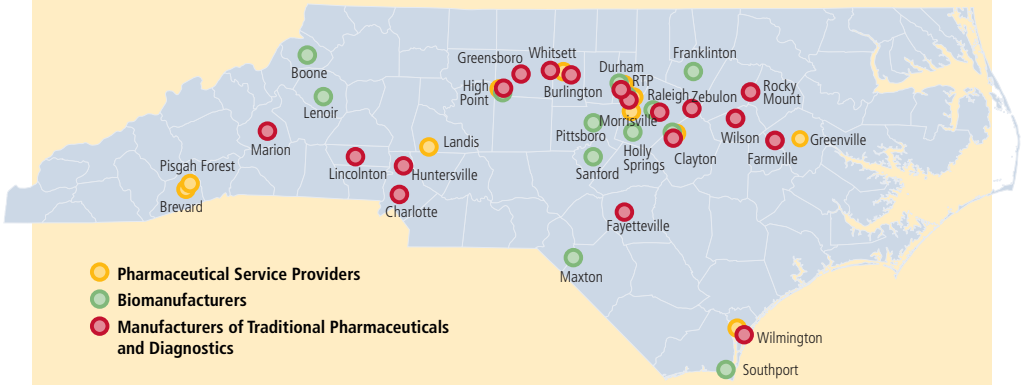
17 DeVol, Ross, Wong, Perry et al. *America's Biotech and Life Science Clusters: San Diego's Position and Economic Contributions*, Milken Institute, June 2004, page 3. *http://www.milkeninstitute.org/pdf/biotech_clusters.pdf* (accessed on December 22, 2010).

Novo Nordisk Pharmaceutical Industries and United Therapeutics, two companies with a long-term North Carolina presence, are also expanding their efforts in the state. As part of its $68 billion acquisition of Wyeth in 2009, Pfizer now operates a vaccine plant in Sanford. Pfizer Poultry health purchased North Carolina-based Embrex and now operates a poultry vaccine plant near Laurinburg. GlaxoSmithKline, Merck Biomanufacturing Network, Talecris, Biogen Idec and Novozymes all operate significant life science manufacturing facilities in North Carolina.

North Carolina's success in attracting biomanufacturing operations in part has resulted from strategic efforts to provide these companies with a skilled technical workforce, as mentioned earlier. Additionally, the availability of affordable land and substantial water resources is often cited as a competitive advantage for North Carolina.

Biomanufacturing

Whether it is physical infrastructure, human resources or support companies, North Carolina provides what a biomanufacturing facility needs. More than 50 companies manufacturing biologics, pharmaceuticals and diagnostics already call North Carolina home. These companies, including Biogen Idec, GlaxoSmithKline, Novozymes, Pfizer, and Talecris, operate some of the largest and most unique facilities of their kind.



North Carolina's Vaccine Development Cluster

One of the most significant recent trends in the biopharmaceutical industry has been the rapid growth of the vaccine development sector. Numerous public-private partnerships are being forged to establish new vaccine production technologies to facilitate the rapid development of strain-specific vaccines in response to the occurrence of pandemics. Global vaccine sales reached $19 billion in 2008 and are expected to grow 15% annually over the next five years. North Carolina's biomanufacturing workforce and infrastructure strengths are proving to be major contributors to a growing vaccine production cluster in the state. Pfizer, Novartis, Merck, GlaxoSmithKline and Medicago each now have major vaccine R&D and/or production facilities in the state. This formidable cluster is further enriched with up-and-coming homegrown R&D companies such as Alaeras, AlphaVax, Argos Therapeutics, ArboVax, Global Vaccines, Greer Labs, ImmunoBiosciences, Liquidia, Peptagen, Pique Therapeutics and SoyMeds, which are developing new vaccines and vaccine-enabling technologies.

Source: *Biotech 2010 Life Sciences: Adapting for Success*, Burrill & Company, 2010, page 37.

"Disconnects" That Could Impact Future Growth and Economic Impact

North Carolina has developed into a leading life science hub, resulting in a highly positive impact on the state's economy. However, it is vitally important to understand that the economic momentum to date, while encouraging, is in no way a guarantee for future economic growth. The presence of the commercialization components currently available in the state may not be sufficient to take these economic gains to the next level.

Upon deeper inspection, there are "disconnects" that suggest breakdowns in the flow of life science commercialization efforts within the state; indeed, exploration of these disparities may help to define factors that disrupt the state's ability to fully realize the economic potential of this industry.

Few Revenue-Generating Public Companies Headquartered Here

Although North Carolina ranks third in the nation in number of biotechnology companies, few established biotechnology companies are headquartered here. According to Ernst & Young, in 2009 there were 313 public biotechnology companies headquartered in the U.S. and only 10 (3%) of those companies were based in North Carolina.[18] Likewise, from *MedAdNews'* list of the top 100 public biotechnology companies worldwide based on revenues, only four are headquartered in North Carolina – Talecris, Inspire, Targacept, and Trimeris.[19] By comparison, 25 of the top 100 are based in California, 15 in Massachusetts, eight in New York, seven in Maryland, and five in New Jersey.[20] Table 2-3 shows how North Carolina's life science industry compares to the U.S. industry overall on several relevant metrics.

18 Giovannetti, Glen T. and Jaggi, Gautam. *Beyond Borders: Global Biotechnology Report 2010*, Ernst and Young. *http://www.ey.com/Publication/vwLUAssets/Beyond_borders_2010/$FILE/Beyond_borders_2010.pdf* (accessed December 21, 2010).

19 "Top 100 Biotechnology Companies: A mixed bag for biotech", *MedAdNews*, 29(6), June 2010.

20 Ibid.

Table 2-3: North Carolina Life Science Industry Relative to U.S. Life Science Industry (Dollars in Millions)

	N.C.	U.S.	N.C. (% of U.S.)	Sector
Jobs (2008)[A]	53,615	1,420,324	4%	Bioscience
Biotechnology Patents (2009)[B]	126	6,125	2%	Biotechnology
National Institutes of Health Funding (2009)[C]	$1,141	$25,838	4%	Bioscience
VC Funding Rounds (1H10)[D]	4	111	4%	Bioscience
VC Funding Rounds (2009)[E]	12	273	4%	Bioscience
Public Companies (2009)[F]	10	313	3%	Biotechnology
Revenue of Headquartered Public Companies (2009)[G]	$1,916	$56,637	3%	Biotechnology
R&D of Headquartered Public Companies (2009)[H]	$332	$17,179	2%	Biotechnology
Revenue of Headquartered Public Companies ex Talecris (2009)[I]	$383	$55,104	0.7%	Biotechnology

Source: [A] 2010 Evidence and Opportunity: Biotechnology Impacts in North Carolina, Battelle Technology Partnership Practice, 2010, page iii. [B] Based on a search of the U.S. Patent and Trademark Office patent database. [C] "Dollars Awarded by State for 2009", Research Portfolio Online Reporting Tools (RePORT), National Institutes of Health. *http://report.nih.gov/award/trends/State_Congressional/StateOverview.cfm* (accessed December 22, 2010). [D] Trend Analysis: 1Q10 Bioscience VC, M&A and IPO Overview; Trend Analysis: 2Q10 Bioscience VC, M&A and IPO Overview, OnBioVC. [E] Trend Analysis: 2009 Bioscience VC, M&A and IPO Overview, OnBioVC. *http://onbiovc.com/wp-content/uploads/2010/02/onbiovc-trend-analysis-2009-year-in-review.pdf* (accessed on December 22, 2010). [F] Giovannetti, Glen T. and Jaggi, Gautam. Beyond Borders: Global Biotechnology Report 2010, Ernst and Young. *http://www.ey.com/Publication/vwLUAssets/Beyond_borders_2010/$FILE/Beyond_borders_2010.pdf* (accessed December 21, 2010). [G] Ibid. [H] Ibid. [I] Ibid.; Talecris 2009 10-K; North Carolina Biotechnology Center data.

North Carolina's biotechnology industry employment growth has been impressive, especially given that employment has already surpassed the goal of creating 48,000 biotechnology-related jobs by 2013 set in a January 2004 strategic plan that was spearheaded by former Governors James B. Hunt, Jr. and James G. Martin.[21] Yet when considered in context, this number represents only 4% of all U.S. biotechnology employment because the great majority of the biotechnology companies based here are small start-ups.

To continue and potentially accelerate the growth of North Carolina's life science industry, it will be important to convert more of the state's promising start-ups into established, revenue-generating companies.

21 *New Jobs Across North Carolina: A Strategic Plan for Growing the Economy Statewide through Biotechnology*, North Carolina Biotechnology Center, January 2004, pages 4-5.

The Largest IPO of 2009

North Carolina-based Talecris Biotherapeutics raised $1.1 billion with its 2009 initial public offering. According to Michael Constantino, Ernst & Young's Managing Partner in Raleigh, "Following the transaction, the company's market capitalization was $2.3 billion; the PE (private equity) investors had received aggregate proceeds from dividends, sales of stock and other fees in excess of $1.3 billion; and the investors still controlled approximately 50% of Talecris' common stock – an incredibly successful outcome both for the business and its investors."

Source: Giovannetti, Glen T. and Jaggi, Gautam. *Beyond Borders: Global Biotechnology Report 2010*, Ernst and Young. *http://www.ey.com/Publication/vwLUAssets/Beyond_borders_2010/$FILE/Beyond_borders_2010.pdf* (accessed on January 4, 2011).

Acquisition of North Carolina Companies on the Cusp of Success

As described in more detail in Chapters 3 and 6, some of North Carolina's most promising life science companies have been acquired just as they were on the cusp of success and therefore would have soon begun providing major economic benefits to the state. Other North Carolina life science companies have been acquired after already achieving commercial success. For example, North Carolina's Talecris Biotherapeutics, already highly successful with $1.5 billion in 2009 revenue, has agreed to be acquired by the Spanish firm, Grifols.[22] While sale of a life science company is a common approach that founders and investors use to monetize their time and investments, it is important that North Carolina provide a support system and funding infrastructure to enable these companies to remain independent if they choose to do so. Although acquisition is often a positive result for the stockholders of these young entities, it often puts decisions relating to employment and long-term commitment to the state in the hands of entities based outside North Carolina.

Mixed Returns from Academic Bioscience Research

North Carolina is well known for the basic science research strengths of its leading academic research institutions; indeed, North Carolina ranks 5th in the U.S. with over $1.5 billion spent on academic bioscience research and development.[23] Additionally, both Duke and UNC-Chapel Hill are among the country's top 20 academic research institutions as ranked by research expenditures as shown in Table 2-4. However, in reviewing commercialization metrics such as patents, licenses and licensing income, the data are mixed as to whether these research expenditures are being maximized toward the commercialization of new products.

For instance, the state ranked only 14th among all states in terms of bioscience patents issued during the 2004-2009 period.[24] This ranking is also reflected in the fact that North Carolina's biotechnology patents only accounted for 2% of the country's biotechnology patents in 2009.[25] Table 2-4 indicates that the state's leading academic research institutions are having mixed levels of success in translating their research expenditures into patents filed and issued.

The data in Table 2-4 reflect mixed results on other commercialization metrics as well. For instance, North Carolina's top research institutions appear to be having success in executing licenses and options around their discoveries with commercial organizations. However, start-up formation and license income received by our universities tend to lag those of other leading universities (Wake

22 Bennett, Simeon and Sargent, Carey. "Grifols Agrees to Buy Talecris for $3 Billion", *Bloomberg Businessweek*, June 7, 2010. *http://www.businessweek.com/news/2010-06-07/grifols-agrees-to-buy-talecris-for-3-billion-update6-.html* (accessed on December 22, 2010).

23 *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page 42. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

24 Ibid.

25 North Carolina Biotechnology Center data.

Table 2-4: 2008 Technology Transfer Activity for North Carolina Universities (U.S. Rankings)

Institution	Research Expenditures	Invention Disclosures	New Patent Applications	U.S. Patents Issued	Licenses & Options Excecuted	Start-Ups Formed	License Income
Duke University	13	27	30	30	5	24	34
East Carolina University	175	166	159	140	155	109	112
North Carolina State University	45	38	29	22	13	32	N/A
UNC-Greensboro	159	154	166	156	132	81	152
UNC-Chapel Hill	20	52	72	55	18	36	78
UNC-Charlotte	165	118	85	112	161	67	160
Wake Forest University	101	111	N/A	85	96	88	8

Source: *AUTM U.S. Licensing Activity Survey, FY2008 Survey Summary*, Association of University Technology Managers, 2010.
Note: Data represent rankings among 184 reporting U.S. universities, hospitals and research institutes, and are not limited to life science research and commercialization.

Forest's licensing income for 2008 was largely influenced by a single blockbuster licensing program). These data suggest challenges that may be keeping North Carolina's discoveries from translating into start-up companies and, ultimately, product commercialization. In other words, the considerable research momentum of the state's research universities appears to not be uniformly maintained upon transition towards commercialization.

These data suggest a significant disconnect between North Carolina's strong academic research enterprise and the efficiency of translating that research into products that will be developed further in the state. As such, there appear to be untapped assets within North Carolina universities that could drive additional economic growth for the state.

Ensuring that North Carolina Maximizes its Life Science Opportunity

The life science industry is large and its economic impact is growing rapidly, as characterized in Chapter 1. Rapid growth preferentially brings economic benefits to regions with established life science industries and the building blocks necessary for expansion. For life science employment in particular, there exists an unusually high multiplier effect for additional jobs and services. Not surprisingly, the competition for the economic benefits associated with a thriving bioscience industry is fierce and increasingly global.

North Carolina has earned its status as one of a handful of global biotechnology industry hubs, and the state has enjoyed major economic benefits associated with its life science industry. Also, because key building blocks have been put in place, there are encouraging signs that the momentum established to date will continue, enabling the state to maintain its share of the industry opportunity described in Chapter 1. Moreover, with refinement of the building blocks already in place plus strategic investments in new programs, the state has the opportunity to not simply maintain status quo, but to accelerate the rate of its commercialization efforts (and the associated economic gains for the state).

Several concerning observations are identified in Chapter 2 that suggest that the flow along North Carolina's life science commercialization continuum is far from optimal and that, as a result, there are additional unrealized economic gains for the state being left on the table. Chapter 3 identifies several gaps that threaten the future growth of the state's bioscience industry. In subsequent chapters, we present a series of strategies to overcome these gaps and accelerate the commercialization of life sciences technologies in North Carolina.

CHAPTER 3:

Challenges Facing Commercialization of Life Science Technologies in North Carolina

The development of this report was prompted by a legislative bill requesting that the North Carolina Biotechnology Center prepare "a strategic plan to accelerate the commercialization of life science technologies and discoveries being developed in universities and private companies in North Carolina and the related development and production of new commercial products."[1] As such, the first step in the development of this strategic plan was to understand the challenges (gaps) that represent significant obstacles to such commercialization. Once these obstacles were clearly elucidated, the focus shifted to developing strategies that would surmount the challenges (bridge the gaps) to ultimately accelerate the commercialization of life science technologies in North Carolina. Chapter 3 describes these challenges and why they exist. Chapters 4, 5, 6 and 7 detail several strategies for bridging these gaps.

To ascertain the major challenges facing companies and universities seeking to commercialize their technologies, the authors received input from more than 50 key stakeholders involved in North Carolina's life science community. Leaders from numerous small and large companies, university technology transfer offices, investment groups, banks, service providers and non-profit organizations all provided input. Their views on both the challenges to commercialization and potential solutions are central to this report.

According to most of the stakeholders surveyed, North Carolina's primary challenge in commercializing life science technologies is funding. While a dearth of early-stage funding was frequently noted as an obstacle, the limited availability of late-stage funding to build facilities and production lines was also deemed to be a key challenge for the state's industry. In addition to early-stage and late-stage funding challenges, the state's limited number of experienced life science executives with product development, commercialization and financing experience was viewed as a significant impediment to bringing products to market successfully. These three key challenges are described in the balance of this chapter.

The key challenges facing the commercialization of life science technologies in North Carolina are the early-stage funding gap, the late-stage (debt) funding gap, and the management gap.

1 General Assembly of North Carolina, Session 2009, Session Law 2010-31, Senate Bill 897.

The Early-Stage Funding Gap

> *"What we need is more direct risk capital, rather than more support resources. This means more venture capitalists and angel investors actually funding more local technology."*
>
> —Greg Mossinghoff, CEO, Novolipids, Inc.

> *"The critical challenge we face is that the vast majority of innovations arising in university labs are at a very early stage of development. We typically have limited data and while there often is a significant potential market, the technology is far too unproven to attract venture investment or a commercial partner."*
>
> —Cathy Innes, Director, Office of Technology Development, The University of North Carolina at Chapel Hill

The majority of respondents providing input on the major challenges facing commercialization echoed the need for more early-stage life science funding in North Carolina. North Carolina is the home to leading academic research institutions and 537 biotechnology companies[2] (Ernst & Young ranked North Carolina #3 among states based on number of biotechnology companies[3]). However, as mentioned in Chapter 2, the state has struggled to produce companies that generate significant revenue and/or become publicly traded companies.

In 2009, there were only 10 publicly traded biotechnology companies (as defined by Ernst & Young) headquartered in North Carolina with total revenue of $1.9 billion (of which $1.5 billion was generated by one company, Talecris, which has agreed to be acquired by Grifols S.A. of Spain). Nationwide, in 2009, there were 313 public biotechnology companies generating $56.6 billion in total revenue.[4] As such, only 3% of the nation's public biotechnology companies are based in North Carolina, accounting for 3% of the total U.S. revenue generated by public biotech companies. While North Carolina has the third highest number of biotechnology companies, the state is outside of the top five in terms of number of publicly traded biotechnology companies.[5] Most of the stakeholders interviewed believe that a critical shortage of early-stage funding in North Carolina is a key obstacle deterring companies from successfully navigating product development—successful product development often results in the establishment of a revenue-generating public company. Company executives and technology transfer officers viewed this early-stage funding shortage to be especially challenging.

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2 North Carolina Biotechnology Center Company Directory Benchmark, 3rd Quarter 2010.

3 *Beyond Borders: Global Biotechnology Report 2006*, Ernst and Young, page 24. *http://www.ey.com/Publication/vwLUAssets/Global_Biotechnology_Report_2006/$FILE/0511-0689191%20BB%203-16%20v3%20TO%20PRINT.pdf* (accessed on December 22, 2010).

4 Giovannetti, Glen T. and Jaggi, Gautam. B*eyond Borders: Global Biotechnology Report 2010*, Ernst and Young, page 58. *http://www.ey.com/Publication/vwLUAssets/Beyond_borders_2010/$FILE/Beyond_borders_2010.pdf* (accessed December 21, 2010).

5 Morningstar Document Research, Public companies by Morningstar Industry Classification.

The early-stage funding gap (sometimes referred to as the "valley of death") has been defined as the gap in between the funding that the National Institutes of Health may provide for basic research, and the downstream financing that investors supply once promising technologies are sufficiently developed.[6] As shown in Figure 3-1, this gap occurs for North Carolina companies when they have progressed beyond the stage where early-stage funding vehicles (such as federal grants or North Carolina Biotechnology Center loans) are typically useful, but these companies have not yet progressed to the point where they are able to attract venture capital funding or strategic partners.

The early-stage funding gap has been defined as the gap in between the funding that the National Institutes of Health may provide for basic research, and the downstream financing that investors supply once promising technologies are sufficiently developed.

Figure 3-1: Current Environment for Life Science Companies – Early-Stage Funding Gap

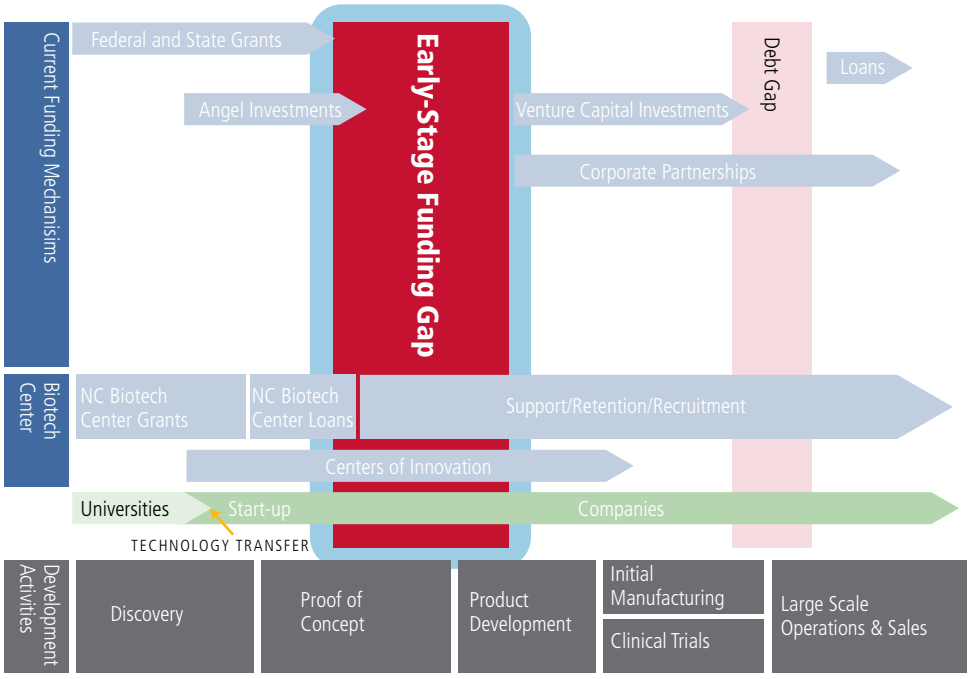


Figure 3-1 reflects the funding environment for North Carolina's life science companies, with several sources of funding (grants, North Carolina Biotechnology Center loans, angel funding) available for start-ups seeking initial proof of concept. However, once these companies move beyond that phase, they must navigate the early-stage funding gap during which limited or no funding options are available. Variations of Figure 3-1 will be used throughout the balance of this report to highlight the challenges facing North Carolina's life science companies and the recommended strategies to surmount these challenges.

For a traditional biotechnology company, this critical shortage of equity funding often occurs between initial preclinical proof of concept for a lead drug and early human trials of the drug. For a medical device company, this funding gap typically occurs closer in time to product commercialization. For a crop-based agricultural biotechnology company, this early-stage funding gap often occurs after proof of concept in a model plant when a new product still typically faces more than five

6 *Biotech 2009 Life Sciences: Navigating the Sea Change*, Burrill & Company, 2009, page 37.

years of development prior to commercialization. Clearly, the early-stage funding gap is prevalent across all subsectors of the life science industry. This early-stage funding gap has been exacerbated by: 1) venture capital firms progressively shifting their investments towards later-stage companies, 2) an overall reduction in life science venture capital funding nationwide, 3) a comparative shortage of venture capital groups based in North Carolina, and 4) limited bank funding for companies at this stage.

Venture Capital Firms Focusing Less on Early-Stage Opportunities

The typical venture fund term is ten years. As such, venture capital groups seek to "exit" their investments by year 10 of a fund's life, implying that the average exit is expected to occur 3-7 years following an initial investment. An exit typically occurs through one of two avenues: 1) sale of stock in the public market following an initial public offering (IPO), or 2) sale of stock as a result of the acquisition of a portfolio company. With the number of IPOs down relative to levels seen before the 2008 market decline (see Table 3-1) and with those IPOs typically occurring for later-stage companies than previously seen, exits have become more difficult to come by for life science venture groups.

Table 3-1: IPO Volume Rebounding in 2010 But Still Below That Seen Prior To 2008 Market Decline[7] (Dollars in Millions)

	Number of IPOs*	Total Offering Volume	Average Offering Size
2006	57	$5,117	$90
2007	86	$10,326	$120
2008	6	$470	$78
2009	12	$1,642	$137
First nine months of 2010	40	$3,460	$87

*Includes all companies that trade on U.S. exchanges and have had at least one U.S. venture investor

Because those exits which are occurring are typically occurring later in a company's life cycle, venture groups are making their investments later in the company's life cycle to allow for exits in the same time frame (3-7 years following investment) as with previous funds.

> *"Venture capital firms want to see more mature companies before they will invest…So, there's a gap."*[8]
>
> —Gary Glausser, Partner, Birchmere Ventures, Pittsburgh, PA

7 *Shaking the MoneyTree Q3 Update*, PricewaterhouseCoopers/National Venture Capital Association MoneyTree, Report, October, 2010, page 31.

8 Olson, Thomas. "Sparse funds stunt growth, biotech firms say", *Pittsburgh Tribune-Review*, August 25, 2010.

A key result of this shift in the life science venture funding environment is that the early-stage funding gap has widened. The level of study data required by venture groups has increased, and the higher level of funding required to generate such data means that North Carolina-based life science companies have often exhausted typical early-stage funding sources such as federal grants, North Carolina Biotechnology Center loans and angel funding prior to reaching a stage where they can attract venture capital funding. In other words, the early-stage funding gap has become progressively wider, leaving life science companies without the resources necessary to generate the data required to attract a venture capital investment and realize their commercial and economic promise.

The early-stage funding gap has become progressively wider, leaving life science companies without the resources necessary to generate the data required to attract a venture capital investment and realize their commercial and economic promise.

Venture Capital Funding in Life Science Sector Down Nationwide

The early-stage funding challenge has also been exacerbated by a decrease in overall life science venture capital funding, as shown in Table 3-2. In 2009, venture capital (VC) funding for biotechnology companies fell 19% to its lowest level since 2003. VC funding for medical technology companies fell 26% in 2009 to its lowest level since 2005. While VC funding in these two sectors rebounded somewhat in the first nine months of 2010, levels are still significantly below those in 2006-2008. These declines are consistent with a general decline in venture capital funding.

"Gone are the days when venture capitalists seemed to be falling all over one another to get a place on the ground floor of life science startups."

Source: Vinluan, Frank. "Fallback mode: Loans to grow", *Triangle Business Journal*, 26(5): 3, 31, October 8, 2010.

Table 3-2: Venture Capital Investments in Life Science Companies[9] (In Billions)

	2006	2007	2008	2009	First Nine Months of 2010
Biotechnology	$4.4	$5.2	$4.5	$3.6	$3.1
Medical Devices and Equipment	$2.8	$3.7	$3.5	$2.6	$1.9

Consistent with the decline in VC funding, the current number of active VC firms is down nearly one-third relative to ten years ago.[10] With total venture capital fundraising down 42% in 2009 compared to 2008 and fundraising tracking even lower in 2010,[11] the trend of lower VC investments in life science companies is likely to continue. According to Mark Heesen, president of the National Venture Capital Association, "With (venture) fund size getting smaller and fewer firms raising money, we are experiencing a period of time in which venture capital investment is consistently outpacing fundraising, creating an industry that will be considerably smaller in the next decade."[12] This outlook for the venture

9 *Shaking the MoneyTree Q3 Update*, PricewaterhouseCoopers/National Venture Capital Association MoneyTree , Report, October, 2010.

10 Crabtree, Penni. "Venture Capital firms facing tougher times", *The San Diego Union Tribune*, June 20, 2010. *http://www.signonsandiego.com/news/2010/jun/20/venture-capital-firms-facing-tougher-times* (accessed on December 22, 2010).

11 *Shaking the MoneyTree Q3 Update*, PricewaterhouseCoopers/National Venture Capital Association MoneyTree , Report, October, 2010, page 32.

12 *Pharmaceuticals and Life Sciences: Second Quarter Gains Fade*, PricewaterhouseCoopers, November 2010.

capital industry overall indicates that the early-stage funding gap is unlikely to be eliminated in the foreseeable future.

Limited Life Science Venture Fund Activity in North Carolina

It is generally challenging for life science companies to attract venture capital funding, given the reduced amount of funding available and the increased focus of VCs on later-stage investments. However, the challenge is especially difficult for North Carolina companies given the comparative shortage of North Carolina-based VCs and the few VCs based outside the state that are active in the state. This issue manifests itself in limited life science venture capital activity in North Carolina relative to states where leading life science-focused VCs are based. For instance, in 2009, there were 273 life science VC funding transactions in the U.S., of which 97 were for California-based companies, 51 were for Massachusetts-based companies and 12 were for North Carolina-based companies.[13] The data are similar for the first three quarters of 2010 during which there were 62 deals for California-based companies, 43 for Massachusetts-based companies and seven for North Carolina-based companies.[14] During the first three quarters of 2010, California and Massachusetts companies alone accounted for 61% of all life science VC funding transactions in the U.S.

Comments from two life science company executives in North Carolina summed up this issue:

> *"If NC wants to compete effectively with Boston and the West Coast in biotech and other startups it needs to look at the advantage those areas have in accessibility of funding for early stage companies."*
>
> —Malcolm Thomas, CEO, Arbovax, Inc.

> *"There are more VCs and other funding vehicles in CA/MA, so companies there have a greater number of opportunities to raise local funding."*
>
> —Mike Stocum, Managing Director, Personalized Medicine Partners

Only four active life science-focused venture capital groups with more than $100 million in capital under management are based in North Carolina, and none of these are among FierceBiotech's list of the top 17 life science focused venture capital groups.[15] (In fact, none of the top 100 venture capital groups are based in

13 *Trend Analysis: 2009 Bioscience VC, M&A and IPO Overview*, OnBioVC , 2010, page 10. *http://onbiovc.com/wp-content/uploads/2010/02/onbiovc-trend-analysis-2009-year-in-review.pdf* (accessed on December 22, 2010).

14 T*rend Analysis: 1Q10 Bioscience VC, M&A and IPO Overview; Trend Analysis: 2Q10 Bioscience VC, M&A and IPO Overview; Trend Analysis: 3Q10 Bioscience VC, M&A and IPO Overview* OnBioVC 2010.

15 Martino, Maureen and Myers, Calisha. "Top Venture Capital Firms", *FierceBiotech*, August 12, 2009. *http://www.fiercebiotech.com/special-reports/top-venture-capital-firms* (accessed on December 22, 2010).

North Carolina.[16]) In contrast, 12 of the top 17 have offices in California and six have offices in Massachusetts. While a few of these top life science focused VC groups, including Domain Associates, New Enterprise Associates and Quaker BioVentures, actively invest in North Carolina, most do not.

Part of the challenge is that venture capital firms tend to invest in geographic proximity to their offices since they have close relationships with management teams nearby, can keep closer watch on local companies, and do not have to travel long distances for visits and board meetings. One issue that makes it even more challenging for North Carolina companies to attract funding from out of state is that so many VCs are based in the San Francisco Bay Area, and there are currently no non-stop flights from there to the Raleigh-Durham area, where most of the state's life science companies are headquartered.

Of note, North Carolina is more competitive with other acknowledged biotechnology clusters with regards to NIH funding for basic science research. However, as shown in Table 3-3, a clear discrepancy exists between North Carolina's research and commercialization rankings.

Table 3-3: NIH Funding vs. Venture Capital Funding (In Millions)

	2009 NIH Funding[A,B]	2009 Life Science VC Funding[C]	NIH/Venture Ratio
North Carolina	$1,141	$197	5.8
California	$3,850	$2,011	1.9
Massachusetts	$2,833	$980	2.9

Source: [A] "Dollars Awarded by State for 2009", Research Portfolio Online Reporting Tools (RePORT), National Institutes of Health. *http://report.nih.gov/award/trends/State_Congressional/StateOverview.cfm* (accessed December 22, 2010). [B] "NIH Grants Funded by the American Recovery and Reinvestment Act of 2009", Research Portfolio Online Reporting Tools (RePORT), National Institutes of Health, FY2009 data. *http://report.nih.gov/recovery/arragrants.cfm* (accessed on December 22, 2010). [C] *Trend Analysis: 2009 Bioscience VC, M&A and IPO Overview, OnBioVC*, 2010, page 10. *http://onbiovc.com/wp-content/uploads/2010/02/onbiovc-trend-analysis-2009-year-in-review.pdf* (accessed on December 22, 2010).

These data suggest that the state's limited venture fund activity is not sufficient to efficiently translate academic research funding momentum into venture capital funding for North Carolina companies to the same extent as in other major life science centers. If the ratio of VC funding to NIH funding were comparable in North Carolina relative to California and Massachusetts, the local early-stage funding gap could be narrowed significantly.

16 Mukherjee, Sougata. "Triangle, N.C. Missing From List of Top 100 Venture Capital Firms", *Triangle Business Journal*, Triangle BizBlog, December 9, 2010. *http://www.bizjournals.com/triangle/blog/2010/12/triangle-nc-missing-from-top-vc-list.html* (accessed on December 22, 2010).

Banks Not Actively Lending to Early-Stage Life Science Companies

If equity funding is difficult to attract for early-stage North Carolina-based companies with early evidence of proof of concept, why not seek debt financing? North Carolina is an international banking center, home to Bank of America, Wachovia/Wells Fargo, BB&T, RBC (USA) and many other commercial banks. Unfortunately, traditional commercial banks are not active lenders to high risk life science companies without collateral assets. Even venture banks active in North Carolina are typically focused on companies that have already received venture funding. Venture banks rely heavily on institutional investors such as venture capital groups, and a key part of the venture bank's decision to make a loan is focused on the bank's relationships with existing investors in the prospective banking client. As such, as venture capitalists have edged toward later-stage investments, venture banks have focused their loan portfolios on later-stage companies. For traditional biotechnology companies, the result is that debt funding from venture banks is typically not an option until products are well into clinical trials.

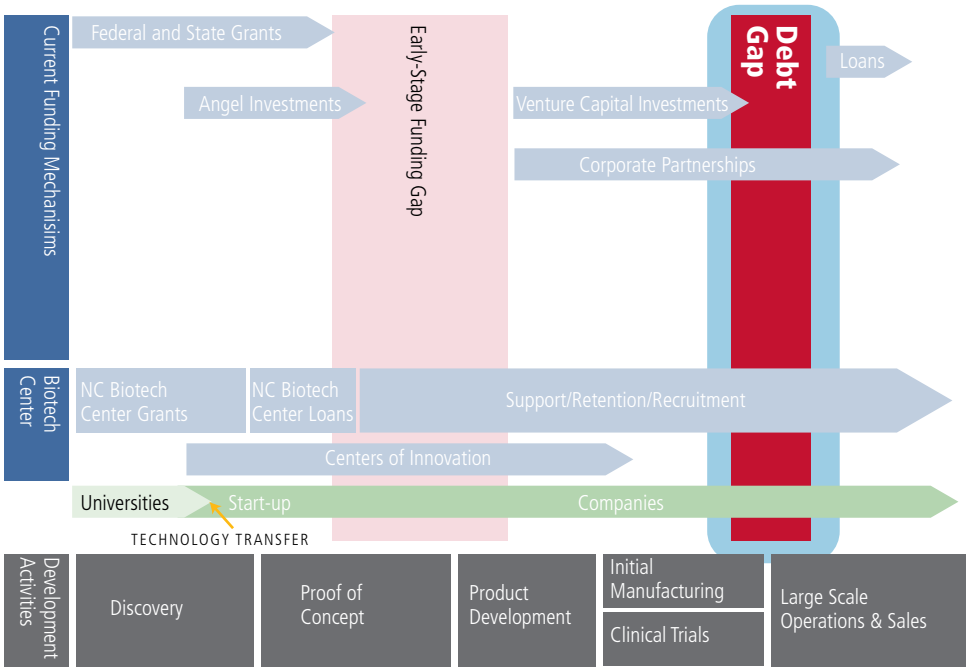
The Late-Stage Funding Gap

> *"In my experience, it is extremely difficult to find local banks or investment firms in North Carolina who are willing to fund a late-stage product development company like Avioq. This despite the fact that the company has no debt, an FDA approved product in the market, and several long term contracts with customers."*
>
> —Cham Chetty, CEO, Avioq, Inc.

Later-stage companies face a funding gap which is as challenging as the early-stage funding gap. This late-stage funding gap is also known as the debt funding gap and is highlighted in Figure 3-2. Companies caught in this gap typically have no sales and limited assets other than intellectual property, and have a product that is being readied for the market. At this point, such companies often require a significant cash infusion to finally capture their commercial opportunities. For a life science company, such debt funding is often employed to initiate or expand the company's manufacturing capabilities and sometimes to build sales and marketing efforts or complete late-stage product development.

The late-stage funding gap (also known as the debt funding gap) is faced by life science companies that require a significant cash infusion to finally capture their commercial opportunities.

Figure 3-2: Current Environment for Life Science Companies – Debt Gap



Companies in North Carolina have found it difficult to access such debt funding. While there are fewer companies facing this late-stage funding gap as compared to the early-stage funding gap, these companies typically require larger amounts of funding. A survey conducted by the North Carolina Biosciences Organization (NCBIO) and the North Carolina Biotechnology Center in 2008 identified nearly a dozen later-stage North Carolina life science companies which would

be interested in accessing such debt funding. These companies were estimated to represent between $75 and $125 million in total loan demand.[17]

The shortage of debt financing available for companies such as these stems from the limited number of banks willing to make loans to companies that are still in the development stage or are just beginning to market a product and are not yet cash flow positive. A few firms such as Silicon Valley Bank, Square 1 Bank, and MidCap Financial provide such services to North Carolina-based life science companies, yet many local companies continue to struggle to access such funding, as reflected below:

> *"We need funding to build facilities with specialized equipment to manufacture our product. The funding environment in North Carolina is not supportive due to the limited number of banks and venture capital groups based here."*
>
> —Tim Bertram, Senior Vice President, Tengion, Inc.

Importantly, receipt of debt funding can often represent an inflection point in hiring new employees for manufacturing or commercializing a new product. In many cases, early-stage life science companies are able to operate virtually, meaning that they have few employees and use outside contractors (based in North Carolina and elsewhere) for much of their product development and initial manufacturing needs. Later-stage companies, on the other hand, typically expand their employee base to initiate larger-scale manufacturing and market products. As such, a new approach to bridging the debt funding gap (as discussed more fully in Chapter 6) would be expected to greatly increase the number of life science jobs in North Carolina.

Life Science Companies Face Unique Challenges

Unlike many manufacturers, life science companies are often required to demonstrate – as a condition to regulatory approval by the Food and Drug Administration – that new products will be both safe and effective when produced at commercial scale. In the case of biotechnology drugs, such a demonstration typically requires the use of manufacturing facilities that may cost between $10 million and $50+ million to construct. Emerging companies, which typically are developing their first commercial products, are challenged to obtain financing for such substantial investments because they do not have an existing portfolio of approved products and associated revenues to fund the debt service for such loans.

Although conventional bridge loans might ordinarily be available for start-up manufacturing facilities, most banks and other conventional financing institutions lack the expertise to underwrite applications involving such technically challenging businesses as the commercialization of new drug products. Consequently, the existing market for financial services fails to meet the needs of many life science companies preparing to commercialize their products.

17 *Life Science Development Corporation Fact Sheet*, NCBIO, 2009. *http://www.ncbioscience.org/news_and_events/documents/LSCDFactSheet.doc* (accessed on December 22, 2010).

In the absence of such financing, life science companies entering the later stages of product development typically have only two options – to be acquired by (or out-license a product to) a much larger life science company, or to make arrangements with existing firms to contract manufacture sufficient quantities of new therapeutic compounds to meet the needs of clinical trials required for product approval.

Keeping Life Science Companies and Their Manufacturing Capabilities in North Carolina

While North Carolina is home to a few contract biomanufacturing operations, most such facilities are located outside the state. Consequently, when emerging life science companies elect to use a contract manufacturer, the jobs and investment associated with those manufacturing facilities usually are shifted out-of-state. Perhaps more importantly, contract manufacturing is typically not an option for companies whose products have certain unusual properties or are based on innovative new manufacturing techniques. Such truly innovative products often represent "disruptive technologies" that become the high-growth products of tomorrow's markets. The opportunity to keep the development of such products in North Carolina is disproportionately important to our state's future as a leading player in the life science sector.

North Carolina also loses investment and job creation opportunities when emerging companies are forced to "sell-out" to larger, more established life science firms. Large, multinational pharmaceutical and biotechnology companies have the capacity to site new manufacturing operations anywhere in the world. Experience shows that these firms are able to command significant economic development incentives when selecting sites for new or expanded manufacturing facilities.

As such, filling the debt funding gap is especially important since construction and build-out of manufacturing facilities in North Carolina greatly increases the likelihood that maturing companies on the verge of making a real economic impact in the state are able to remain here.

Filling the debt funding gap greatly increases the likelihood that maturing companies on the verge of making a real economic impact in the state are able to remain here.

Moreover, the establishment of manufacturing capabilities is typically accompanied by a significant spike in the employment base. Historically, the growth in North Carolina's life science community has been slowed by the acquisition of some of its brightest prospects. Life science companies such as Triangle Pharmaceuticals, Serenex, and Addrenex were on the verge of commercializing their first product or moving into late-stage drug development when they were acquired—ultimately their North Carolina employee bases dwindled.

Increasing the availability of late-stage funding would enable more maturing North Carolina-based companies to move into late-stage development or develop manufacturing and commercialization infrastructures here. The presence of manufacturing facilities tends to be a strong geographic anchor (in part because regulatory approval of the manufacturing facility may take two years or more), thereby making it likely that operations will remain in North Carolina even after an acquisition. Transferring manufacturing to another site is risky, expensive and time-consuming, especially for a late-stage drug or one that has already reached the market.

Attracting Life Science Companies to North Carolina

Availability of additional debt funding resources could also be an effective tool for attracting later-stage or commercial life science companies from other locations to move to North Carolina. In addition, a number of companies are recruitment targets for North Carolina for whom a new debt funding vehicle could be a critical deciding factor. Such companies are typically larger, with nearer-term opportunity for significant employment increases.

The Management Gap

The success of North Carolina's life science commercialization efforts is tightly linked to the ability of each of its companies to raise the capital and broker the partnerships necessary to graduate through each successive stage of company development. The CEO and other members of the executive management team are typically responsible for fundraising, strategic planning, risk management and undeterred motivational drive. Additionally, these executives are ultimately responsible for synchronizing the many interweaving factors associated with the development and commercialization of a biotechnology product.

By numerous accounts, there is an insufficient supply of local serial entrepreneurs and top-tier executives relative to the number of commercial opportunities being generated within North Carolina. The limited size of this talent pool constitutes a rate-limiting step that prevents more promising life science companies from reaching a commercial plateau that reaps economic benefit to the state in the form of jobs and revenue.

North Carolina faces a management gap resulting from an insufficient supply of local serial entrepreneurs and top-tier executives relative to the number of commercial opportunities being generated within the state.

Background: Entrepreneurial Life Science Management

High growth, high risk life science discovery companies are, by nature, entrepreneurial endeavors. These companies face:

- an arduous, multi-step evolution in the development of the technology (and the business)
- a requirement of vast amounts of cash (from a variety of investment sources) before realizing the first dollar of revenue
- a myriad of complex intellectual property and regulatory considerations
- a shifting market and customer target
- a need to attract, engage and maintain a diverse set of technology and business partners

It is understandable that it takes a special type of executive to create and grow a successful life science company. Actually, a successful company typically engages several executives over its life cycle, as its needs evolve with growth. Each stage of company development is associated with a distinct set of challenges that requires a leader with stage-specific skills who understands all of the moving parts and has the ability to navigate with agility through a myriad of complex issues. Orchestration of these complexities requires a command of the underlying science, intellectual property, regulatory affairs, product development, board and investor management, manufacturing, workforce, and sales and marketing.

For the inception-stage company funded solely with money from its founders, the ideal CEO candidate may be the builder and shaper of a vision who understands and synchronizes all company activities, finds the compelling story and focuses the company efforts accordingly. Further, this individual has a knack for effectively channeling the energy of the inventor and corporate team, has a passion for building opportunities from scratch, is resourceful at finding start-up funding and managing risk, and is willing to work for an equity stake in the

company. There are few individuals with these characteristics coupled with a track record of success.

Many (if not most) entrepreneurial companies must eventually obtain venture capital funding and/or develop strategic partnerships in order to grow in the absence of a revenue stream. It is therefore necessary for these companies to put an executive in place that has a successful track record in securing equity-based funding or key co-development relationships. Moreover, the needs and priorities of the company evolve as it matures, typically necessitating an expansion of the management team to include new skill sets and connections. Once invested in a company, a venture capital firm will typically assume a voting board seat to oversee its investment and the activities of the CEO. It is not unusual for a key investor to make wholesale changes to the management team.

The Management Gap in North Carolina

As described earlier, there is a clear disconnect between the global prominence of North Carolina as a research powerhouse (as measured by research grant dollars obtained by academic faculty and the number of early-stage life science companies formed around technologies invented in the state), and the relative absence of mature companies successfully commercializing those research discoveries. As life science companies progress toward later-stage development and product commercialization, a concomitant maturation of managerial skills and funding/partnering connections is required to grow these companies.

When surveyed recently by the North Carolina Biotechnology Center, investors, company CEOs, entrepreneurial support agency executives and others routinely pointed to a shortage of top-tier executives as a key factor impeding the state's collective life science commercialization efforts:

> *"The other missing link that comes to mind is a good bullpen of successful serial entrepreneurs and their understudies."*
>
> —James Green, Chief Business Officer, BHV Pharma, Inc.

> *"North Carolina needs more commercialization expertise (it's a management issue), including marketing, CEOs, CFOs"*
>
> —Jeff Basham, Vice President, Business Development, Metrics

Surveyed investors pointed to the state's management gap as a key challenge to product commercialization much more frequently than other types of stakeholders. Venture funds hinge their investments on the presence of previously successful entrepreneurial executives—such executives are only abundant in a few biotechnology hubs such as California and Massachusetts. The co-location of dominant venture capital funds and seasoned management is, therefore, not coincidental. North Carolina has lost promising companies because top-tier management is not locally available or willing to relocate to the state.

The relative lack of depth of the local management talent pool compared with other life science clusters is a widely held belief that has not been carefully studied and whose evidence is largely anecdotal in nature. One such illustration is provided by Don Alexander, VP for Life Sciences Development and Commercialization for Carlyle & Conlan, a North Carolina-based executive search firm. Mr. Alexander pointed to a search that he performed for a Boston-based company, which had a Phase III asset and others in the pipeline. The company was looking for a business development executive who not only brought licensing experience, but who had witnessed all aspects of commercialization, including building a specialty sales force. He found ten candidates in the Boston area who fit this description; in North Carolina, there were, at best, three candidates, none of whom had participated at all stages of commercial development and launch.

Recruiting Life Science Executives to North Carolina

It is a challenge for North Carolina companies to recruit highly experienced life science company executives. This challenge exists despite the state's biotechnology hub stacking up quite well from a quality of life standpoint,[18] and a recent study by ExecuNet indicated that quality of life is now a Top 5 consideration for CEOs considering a new engagement.[19]

As with investors, the absence of direct flights to the West Coast may hinder the recruitment of life science executives to North Carolina. Transfers mean long days, multi-day visits and/or high risk of layovers. A CEO intending to raise money from sources on the West Coast realizes that these investors have investment options closer to home and may only find a periodic trip to North Carolina for board meetings or scouting new investment opportunities to be worthwhile if there are multiple investments being managed regionally.

Assurance of re-employability is also a key concern for some executives considering a position in North Carolina, since the state is commonly perceived as having few established life science companies headquartered here with products on the market or in late-stage development. Executives tend to preferentially relocate to places which have a number of other companies within their sector of expertise, so that they have options at the end of their current stint that do not require relocation.

18 Thomas, G. Scott. "Quality of life? Raleigh ranks No. 1 among large U.S. metros" *Triangle Business Journal*, May 24, 2010. *http://www.bizjournals.com/triangle/stories/2010/05/24/daily11.html* (accessed on December 22, 2010).

19 *2010 Executive Retention Report: Executives Discreetly Exploring Career Options and Why the Boss Doesn't Know*, Finnegan/Mackenzie and ExecuNet, Inc., 2010, page 5. *http://www.execunet.com/promo/pdf/ExecuNet_R_Executive_Retention_Report_Finnegan_2010.pdf* (accessed on December 22, 2010).

Benefits from Expanding the Executive Talent Pool

Expanding the pool of credible serial entrepreneurs and top-tier executive management available to lead North Carolina life science companies should serve to draw more out-of-state investment and partnership opportunities for North Carolina based-companies. These additional investments and partnerships would be expected to result in the commercialization of more life science products in the state, thereby increasing employment in the industry in a sustainable fashion. It is further assumed that these outcomes will drive the relocation of other companies to North Carolina, resulting in long-term economic benefit for the state.

While there is a talent pool of credible management available locally, the numbers are thin relative to the innovations being birthed and patented by the local universities and elsewhere. As a state, North Carolina must find ways to grow the base of quality life science entrepreneurs available to lead these companies, as well as other executive level management for when companies move beyond the entrepreneurial phase. Expansion of strong local entrepreneurial training and support mechanisms will be important, but will likely need to be coupled to an aggressive and coordinated campaign to recruit established management talent from outside the state.

Surmounting the Three Challenges Described in This Chapter

The early-stage funding gap, debt funding gap and management gap all pose significant challenges to North Carolina life science companies seeking to commercialize their products. For North Carolina to continue to build upon its strong position in the life science industry and to avoid being surpassed by other states, new initiatives must be developed and ongoing initiatives must be enhanced to overcome these challenges. The continuation of the strong and growing economic impact from the life science industry on North Carolina as described in Chapter 2 depends on successful implementation and coordination of such strategies. Coordination is important since strategies to bridge the funding gaps will not lead to an acceleration of the commercialization of life science technologies without a strong pool of executives available to run the funded companies. Alternatively, strategies to bridge the management gap will only be successful if capital is available to the new executives. These strategies and their expected benefits are detailed in subsequent chapters.

Chapters 4 and 5 describe programs to enable emerging bioscience companies in the state to progress to and through the early-stage funding gap. Chapter 6 focuses on a new fund to help companies cross the debt funding gap. Finally, Chapter 7 details several initiatives for attracting experienced life science executives from outside the state and developing more homegrown successful executives to bridge the management gap.

CHAPTER 4:

Early-Stage Life Science Fund

RECOMMENDATION: *Development of an Early-Stage Life Science Investment Fund to support promising North Carolina-based companies that have achieved significant proof of concept but are not yet candidates for venture capital funding*

THE FIRST RECOMMENDATION in this strategic plan is the development of a new investment fund designed to help close the early-stage funding gap described in Chapter 3. According to the stakeholders we surveyed, this gap is the most daunting challenge facing commercialization of life science technologies in North Carolina. This gap has been exacerbated by: 1) a shift in venture capital investments toward later-stage companies, 2) decreased venture capital funding nationwide, and 3) limited activity of venture capitalists and venture banks in North Carolina. For North Carolina to remain competitive with other life science centers, new bridges must be developed that enable companies to proceed from early proof of concept to the point where they have sufficient evidence to attract venture capital investors or partners. Without such bridges, many promising companies in North Carolina will be unable to progress toward product commercialization, profitability, and a concomitant large expansion in employee base.

Identification and hiring of an experienced life science venture investor or investor team to develop a business plan, establish and manage a new Early-Stage Life Science Fund (ESLSF) is recommended. This fund would be designed to provide the funding necessary to enable promising early-stage life science companies to make it across the early-stage funding gap, thereby positioning them to achieve strategic partnerships or venture capital funding on the other side.

Identification and hiring of an experienced life science venture investor or investor team to develop a business plan, establish and manage a new Early-Stage Life Science Fund (ESLSF) is recommended.

Development of the ESLSF

> *"The biggest thing NC needs is more capital directed at life sciences. Possibly think about setting up an actual early stage fund where limited partners earn tax incentives for contributing capital* ***...Management teams and entrepreneurs will follow the money."***
>
> —James Green, Chief Business Officer, BHV Pharma
> *[highlighting added by James Green]*

A potential framework for the ESLSF is shown in Table 4-1. Again, it is important to note that the fund's ultimate investment criteria, structure and terms would be determined by an experienced life science venture investor or investor team that would be hired to develop and manage the fund. It is expected that the ESLSF would focus on promising emerging North Carolina life science companies that are at an earlier stage of development than normally targeted by most venture capital funds.

The fund's ultimate investment criteria, structure and terms would be determined by an experienced life science venture investor or investor team that would be hired to develop and manage the fund.

Table 4-1: Anticipated Framework of the Early-Stage Life Science Fund

Expected Fund Size	To be determined; however, a $50 million investment fund is envisioned
Focus of Fund	Biotechnology/pharmaceutical, medical device, agricultural biotechnology companies
Stage of Companies	Companies with clear evidence pointing to likelihood of successful commercialization; fund size would allow for follow-on funding in later rounds
Fund Management	A highly experienced life science investor or investor team would be identified and hired and a board of advisors with corporate, investment, research and clinical experience in the life science field would be appointed
Investment Guidelines	The ESLSF will only fund companies with a significant presence in North Carolina; portfolio companies will be required to remain in North Carolina for at least three years following an ESLSF investment
Fund Structure/Term	Evergreen

Investment Focus

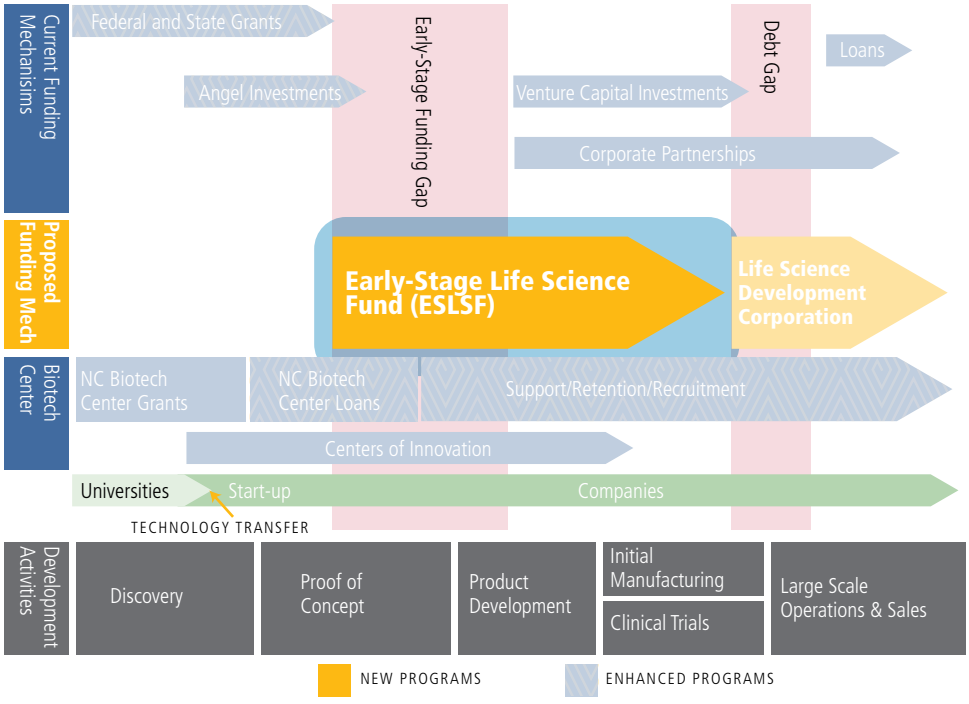
It is anticipated that the ESLSF's investments could be structured as equity investments or convertible debt and would be limited to life science companies, including human health-focused biotechnology and pharmaceutical companies, medical device companies and agricultural biotechnology companies. Since a primary goal of the ESLSF would be to support companies navigating the early-stage funding gap, the fund's investment focus would be on companies that have gathered initial data demonstrating proof of concept of their product/technology but that do not yet have enough evidence or are too far from a potential exit to attract outside venture capital funding. The ESLSF's "sweet spot" for initial investments in portfolio companies would be seed-stage investments in companies developing:

The fund's investment focus would be on companies that have gathered initial data demonstrating proof of concept of their product/technology but that do not yet have enough evidence or are too far from a potential exit to attract outside venture capital funding.

- Therapeutics (both small and large molecule drugs) and vaccines with positive early preclinical data
- Diagnostics with a validated approach and time to market of roughly three years
- Medical devices in late preclinical or early clinical trials
- Agricultural biotechnology products that have been optimized and have been the subject of positive field studies

As envisoned here, the ESLSF is intended to leverage, rather than to replace or supplement, current funding vehicles for university-based technologies or recent start-up companies. At these earlier phases, federal grants, North Carolina Biotechnology Center grants and loans, and angel investments are available. The expansion of these funding programs (described in Chapter 5) should go a long way toward funding the progression of technologies through these very early phases. Rather, the ESLSF would be expected to fill the funding void between where Biotechnology Center loans and angel funding are applicable (during development of early proof of principle) and the point in time when companies are able to start attracting venture capital funding. Figure 4-1 shows how the ESLSF is expected to fit in with the funding vehicles available to North Carolina life science companies before and after the early-stage funding gap.

Figure 4-1: Environment Incorporating Strategic Plan Programs – ESLSF



As highlighted in Figure 4-1, the goal in developing the ESLSF would be to provide a first venture-backed investment in a strong company that is struggling through the early-stage funding gap. Most likely, the ESLSF would be structured to make

follow-on investments as portfolio companies move through and exit this funding gap, since follow-on investments would preserve the ESLSF's ownership in the company and be crucial to supporting the company's progress toward product commercialization. For each investment round, it is anticipated that the ESLSF would seek to be part of a syndicate of investors.

A key requirement for the ESLSF would be to focus its investments in companies that are headquartered in North Carolina. However, companies headquartered elsewhere, but with a significant base in the state, may also be considered. A "significant base" might constitute a research and development laboratory or a manufacturing site; however, a company with only an executive or sales representative residing in the state would not qualify. Portfolio companies would be required to remain in North Carolina for at least three years following an investment.

While the fund's management team will ultimately select the investment criteria for the fund, such investment criteria can be expected to include:

- Experience and capabilities of management team
- Size of market opportunity
- Level of sustainable competitive advantage
- Ability to address an unmet need that is of interest to future partners, investors and customers
- Strength of intellectual property
- Clear plan and path to commercialization
- Evidence of proof of concept which results in an increased likelihood of success relative to other companies at the same stage of development
- Prior funding from external sources such as grants, loans and angel funding (beyond friends and family)

Like most venture funds, the ESLSF and its co-investors may recruit new executives to run the portfolio companies. Experienced executives will be integral to ensuring that the portfolio companies are successful and are able to attract additional funding in the future. Having well-qualified executives with strong track records will be key to drawing additional venture capital investors to these companies, and therefore, essential to the ESLSF's long-term success. (As noted in Chapter 3, the investors contacted as part of this report frequently noted the management gap as the state's top challenge in developing and commercializing products.) Strategies to grow North Carolina's base of successful life science executives are detailed in Chapter 7 of this report.

Having well-qualified executives with strong track records will be key to drawing additional venture capital investors to these companies, and therefore, essential to the ESLSF's long-term success.

Fund Structure

One of the criteria to be presented to the fund management team will be to explore the possibility of establishing the ESLSF as an evergreen fund; that is, "a fund that reinvests its profits in order to ensure the availability of capital for future investments."[1] In other words, the returns generated by the ESLSF's loan payoffs and exits from portfolio companies would be returned to the fund rather than being distributed. Through this structure, the ESLSF would be expected to be self-sustaining following initial funding as long as: 1) the initial funding is large enough to support investments for long enough to begin having some investments realized, and 2) portfolio company selection is successful. A key advantage of developing an evergreen fund is that rather than being limited to the ten-year life of a typical venture capital fund, the ESLSF would be able to make investments in North Carolina-based early-stage companies for the foreseeable future.

Two examples of evergreen funds are the Maryland Venture Fund and GlaxoSmithKline's SR One fund. The Maryland Venture Fund was started in 1994 and received $10-$15 million from the State of Maryland in 1994-1998[2] (see additional detail on this fund later in Chapter 4). From 1994 to 2008, the fund invested over $65 million in Maryland-based companies and returned $60 million in investment distributions back to the fund. These investments resulted in 2,000-3,000 jobs and more than $1.2 billion in additional investments in the fund's portfolio companies.[3] While the Maryland Venture Fund now appears to be struggling to survive given sluggish recent returns,[4] the fund's 15+ year life and economic development impact from a limited initial funding base is notable.

SR One is the venture capital arm of GlaxoSmithKline, a leading pharmaceutical company with its U.S. headquarters in North Carolina. The fund was founded in 1985 and has invested more than $600 million in 25 companies to date. Returns have been reinvested back into the fund. Many of these companies have been the subject of initial public offerings and/or acquisitions. The SR One fund is heavily focused on biotechnology and invests globally in companies at all stages of development. The fund's managers credit the fund's evergreen structure as a key factor in the long-term success of the fund.

Fund Objectives

The ESLSF will be expected to have two consistent objectives: 1) generate sufficient positive returns to sustain the fund, and 2) expand North Carolina's life science employee base and state/local taxes generated by the industry directly and indirectly. Such a fund could help North Carolina-based life science companies

The ESLSF is expected to have two primary objectives: 1) generate sufficient positive returns to sustain the fund, and 2) expand North Carolina's life science employee base and state/local taxes generated by the industry directly and indirectly.

1 "Private Equity Glossary", Tuck School of Business at Dartmouth Center for Private Equity and Entrepreneurship. *http://mba.tuck.dartmouth.edu/pecenter/resources/glossary_d_h.html#evergreenfund* (accessed on December 22, 2010).

2 Dickson, Frank. "Maryland Venture Fund", Maryland Department of Business & Economic Development, 2009, Slide 3. *http://www.cdfa.net/cdfa/cdfaweb.nsf/fbaad5956b2928b086256efa005c5f78/2765d7eb151adfb4862575f900548516/$FILE/Dickson%20-%20MD%20Venture%20Fund.pdf* (accessed December 22, 2010).

3 Ibid.

4 Schultz, Sue. "Money is running low at Maryland's venture fund", *Washington Business Journal*, April 20, 2009.

transition through the early-stage funding gap, positioning portfolio companies for subsequent funding from other sources and incenting them to remain and grow in the state. The ESLSF could also be an excellent tool to attract emerging life science companies to North Carolina. Since the investments are expected to be syndicated, the ESLSF will likely attract additional funding sources for North Carolina-based companies. Finally, the evergreen structure would enable the fund to have a long-term impact on technology commercialization, company growth and job creation in the state.

A key measure of success for the ESLSF would be its ability to attract other investors to its portfolio companies to fund their development through the early-stage funding gap and beyond. It is expected that the ESLSF fund development team would notify venture fund investors globally of the ESLSF's goals, investment targets and interest in co-investing in North Carolina-based companies. Since the managers of the ESLSF will be experienced life science venture investors, they will already have relationships with leading life science venture investors in California, Massachusetts and elsewhere. These relationships will be supplemented by those maintained by the ESLSF's advisory board and important stakeholders throughout the state such as life science executives, venture fund managers and individuals within the North Carolina Biotechnology Center, the Council for Entrepreneurial Development (CED) and other organizations.

Sources of Funding

Funds will be requested from the State of North Carolina to initiate the Early-Stage Life Science Fund. The partners involved in this strategic plan, including the North Carolina Biotechnology Center, NCBIO, the Small Business and Technology Development Center (SBTDC) and the North Carolina Department of Commerce, will each commit significant resources to identifying and hiring an experienced investment team and providing "back office" operations of the ESLSF as necessary. Additional funding may be pursued from other sources, such as university endowments, corporations and philanthropic organizations.

Investment Funds Developed in Other States

According to the Battelle/BIO State Bioscience Initiatives 2010 report, venture investments for start-up life science companies have not only abruptly declined in the past several years, but those investments that were made were heavily geographically concentrated; about 70 percent of the total venture capital invested from 2004 – 2009 went to firms located in one of five states: California, Massachusetts, New Jersey, Pennsylvania, and Texas.[5] In light of the early-stage funding gap (which is especially challenging in states where VCs are less active), many states seeking to aggressively grow their bioscience industry have established venture-like programs to fund select companies in the hopes of creating economic benefit for their states. Two of these state programs in the Southeast region are described below.

Maryland Venture Fund

The Maryland Venture Fund (MVF) (briefly described above) appears to be a leader among state-run funds. The Maryland Venture Fund is part of Governor Martin O'Malley's $1.3 billion Biotech 2020 plan to cultivate investment and growth in the local biotechnology industry. MVF is an evergreen fund which historically received annual allocations from the Maryland State Legislature. The fund is comprised of a seed program ($50,000-$150,000 investments) and an early-stage equity fund ($150,000-$500,000 investments) and makes direct investments in technology and life science companies as well as indirect investments in venture capital funds. Approximately 60% of the MVF is invested in technology companies, and 40% is invested in life science companies in the areas of therapeutics, medical devices, and diagnostics. The MVF is managed by employees of Maryland's Department of Business and Economic Development who have relevant domain experience. Unlike traditional venture capital fund managers, MVF managers do not take board seats on behalf of the fund.

From 1994 to 2008, the fund invested over $65 million in Maryland-based companies and returned $60 million in distributions to be reinvested. The MVF also provided operating funds of more than $20 million for economic development initiatives. As stated earlier, the MVF's investments resulted in more than 2,000 jobs and $1.2 billion in additional investments in the fund's portfolio companies.

Kentucky Seed Capital Fund

The Kentucky Seed Capital Fund (KSCF) was started in 2005 with more than $5 million in funding and invests in early-stage companies that specialize in biotechnology, health care services, medical devices, and health care information technology. Unlike the MVF which received initial funding from the State of Maryland, the KSCF has received funding from a range of state, non-profit and for-profit organizations. The KSCF invests in companies based in Kentucky or Southern Indiana that are not yet able to attract venture fund interest. The KSCF typically takes a lead position in funding rounds and is led by two managing partners, who had previously held positions at Humana, Baxter and Eli Lilly.

5 *Battelle/BIO State Bioscience Initiatives 2010*, Battelle Technology Partnership Practice, May 2010, page xii. *http://www.bio.org/local/battelle2010/Battelle_Report_2010.pdf* (accessed on December 22, 2010).

ESLSF to Aid in Bridging Early-Stage Funding Gap in North Carolina

The ESLSF would be expected to advance North Carolina's most promising life science companies through the early-stage funding gap for the foreseeable future. While the fund size has yet to be determined, even a $50 million fund will only be able to fund a small minority of North Carolina's emerging life science companies. However, preliminary calculations indicate that a $50 million fund would be sufficient to ensure that the ESLSF can, through highly selective investments, become self-sustaining and support economic development in North Carolina for many years to come. The ESLSF's experienced management team and advisory board will be required to focus on those companies most likely to grow in North Carolina, bringing additional jobs and taxes to the state.

> *"Emerging companies need money in between angel funding and VC funding—there is a big hole between proof of concept and Phase I/II studies."*
>
> —Steve Peterson, CEO, Trana Discovery, Inc.

The Early-Stage Life Science Fund is a new investment vehicle recommended in this strategic plan to help bridge the early-stage funding gap. This gap has been described as a key challenge facing commercialization of life science technologies by company executives, technology transfer offices, non-profit organizations and banks throughout North Carolina. As envisioned here, the ESLSF would provide the needed financial resources to promising companies prepared to progress from the proof of concept phase to the point where they would be able to attract venture capital or strategic partner funding. As such, the ESLSF would complement those funding mechanisms that are already in place to assist life science companies in achieving early proof of concept. Recommendations regarding enhancements to these existing funding mechanisms are detailed in the next chapter.

The ESLSF would play a major role in accelerating the commercialization of life science technologies and discoveries in North Carolina by helping to bridge the early-stage funding gap. ESLSF investments would enable many promising North Carolina companies to progress to late-stage clinical development and product commercialization, stimulating the employment and other economic impacts that follow.

CHAPTER 5:

Expansion of Existing Programs to Support Start-Up and Early-Stage Companies

RECOMMENDATION: *Expand the North Carolina Biotechnology Center loan, SBIR Matching and QBV tax credit programs to provide additional financial support to start-up and early-stage life science companies in the state*

Financial resources available to life science companies struggling through the aforementioned early-stage funding gap are limited; the Early-Stage Life Science Fund recommended in Chapter 4 would be expected to help companies bridge this gap. Chapter 5 focuses on existing funding programs available in North Carolina to life science start-ups developing preliminary proof of concept around their technologies and products. These earlier-stage companies may be 1-4 years from reaching the early-stage funding gap, and they typically require less cash since they are performing smaller, less expensive studies. For biotechnology companies, proof of concept can be gained through in vitro and small animal studies (in contrast to companies crossing the early-stage funding gap, which may be at the stage of performing much more expensive large animal studies and Phase 1 and Phase 2 clinical trials).

Examples of start-up and very early-stage funding vehicles include North Carolina Biotechnology Center loans, federal SBIR grants and funding from angel investors. These vehicles typically provide from $30,000 to $2,000,000 per funding event. In this chapter, approaches to leverage or expand these three key funding vehicles to improve support for early-stage life science companies in North Carolina are discussed. Expansion of these programs is expected to enable more companies to develop the proof of concept data and business savvy required for transition to a stage of company development that warrants investment consideration from seed-stage funds like the ESLSF. The initiatives described in this chapter would not only allow more companies to benefit from these programs but also could move those companies further along the product development continuum.

Expansion of North Carolina Biotechnology Center Loan Program

The Biotechnology Center opened in 1984 when Governor James B. Hunt, Jr. and other state leaders sought to capitalize on the economic promise of what was then a new industry. The Biotechnology Center's mission is to provide long-term economic and societal benefits to North Carolina through support of biotechnology research, business, education and strategic policy statewide. As part of its economic development mission, the Center began providing grants to companies in 1984 and made its first company loan in 1989. To date, the Center has awarded more than $22.7 million in loans and grants to emerging biotechnology companies. These companies have received subsequent funding of more than $2.35 billion. Thus, for every dollar awarded to biotechnology companies by the Biotechnology Center, those companies have gone on to receive an average of $103 from other sources. Biotechnology Center funding is clearly helping these companies to grow, and additional funding for its loan programs would enable more North Carolina-based biotechnology companies to move their products forward, hire more employees and attract additional funding from other sources within the state and beyond.

A $3 million increase in recurring funds to the Biotechnology Center loan program would support the expansion of the current loan programs, while also allowing the program to provide assistance to companies entering the early-stage funding gap.

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Review of Loan Programs

The Biotechnology Center offers loans of $30,000 to $250,000 to promising emerging life science companies located in North Carolina. These loans are deployed to support companies as they start up, perform early research projects and ultimately carry out activities that would be expected to lead to initial institutional funding. The Biotechnology Center provides these companies with low-interest rate loans made at one percent above the prevailing prime rate. The loans typically have a three-year term, with repayment through a balloon payment (principal plus accrued interest) on the maturity date. These loans are only available to companies based in North Carolina; in fact, if a loan portfolio company leaves the state, its unpaid loan is called due immediately.

The Biotechnology Center staff performs rigorous due diligence on all loan applications that includes the use of technology and domain specific expert reviewers and a formal review by a subcommittee of the Center's board of directors for loans exceeding $75,000. As such, the process is highly selective—fewer than half of all companies expressing interest ultimately receive a Biotechnology Center loan.

In fiscal years 2008-2010, the Biotechnology Center awarded $5.4 million in loans to 38 North Carolina-based life science companies. All but three of these companies remain in business in North Carolina today.

Impact of Loan Programs

For many start-up and early-stage life science companies, Biotechnology Center loans are the only outside funding option beyond federal grants. Venture capital groups typically will not invest until a product or technology is further developed, and there are only a few angel funds in the state that actively invest in life science companies. Consequently, these Biotechnology Center loans are extremely important to North Carolina's early-stage life science companies; often, they are the difference between a new company successfully starting up and one never getting off the ground.

"The loan program operated by the Biotech Center, which is headed by Norris Tolson, has proved to be a lifeline for many companies."

Source: Vinluan, Frank. "Fallback Mode: Loans to Grow", *Triangle Business Journal*, 26(5): 3, 31. October 8, 2010.

The loan programs support the Biotechnology Center's mission of providing long-term economic and societal benefits to North Carolina by enabling scientific discoveries to grow into companies with a substantial number of employees and a good deal of evidence supporting the potential of those discoveries.

> *"Early stage companies, which are the source of most new good jobs, are often very fragile in the formative stages. The North Carolina Biotechnology Center has made a critical difference in helping Affinergy grow through the formative stage into a potentially very successful company."*
>
> —Peyton Anderson, CEO, Affinergy

While many loan recipients are located in the Research Triangle area, the programs are actively promoted throughout the state, and the Center's current loan portfolio includes companies from all regions of the state. Loan recipients have also included a number of agricultural biotechnology companies; two of these companies, Agile Sciences and Piedmont Pharmaceuticals, recently announced major partnerships with top agricultural biotechnology companies.

In order for the Biotechnology Center's loan programs to have the desired economic development impact, these loans have to provide recipients with a springboard that positions them to access funding from other sources. The many companies that were seeded with Biotechnology Center loans and were subsequently successful in raising additional funding clearly indicates that the loan programs are helpful in financing the earliest stages of company development. A number of these companies, such as Embrex, Ridge Diagnostics and Trimeris, have gone on to commercialize their products. Others, such as Sphinx Pharmaceuticals, Ercole Biotech and Addrenex, produced early successes and were ultimately acquired.

For the loan funds to continue to have their economic development impact, loans must be repaid so that the returned funds can be used for future loans. Due in part to the rigorous due diligence performed prior to making a loan, the great majority of Biotechnology Center loans are paid off despite the nascent stage of the loan portfolio companies.

Biofuel Breakthroughs Start at the Roots

GrassRoots Biotechnology is converting some green Duke University research into a biofuel business. GrassRoots' core technology monitors how genes control plant growth from within tiny developing roots. Nudging that activity by flipping certain genetic "switches" can transform these plants into more efficient feedstock for ethanol distillation – biofuel. Like many North Carolina life science companies, it received start-up help, including a $25,000 loan, from the Biotechnology Center. GrassRoots has subsequently gone on to raise nearly $1.5 million from government agencies and other sources.

Types of Loans

The North Carolina Biotechnology Center has four loan programs available to life science companies headquartered (or with operations primarily based) in North Carolina. These loans provide pre-seed funding to achieve critical milestones associated with the commercial development of their technologies. The loan program is staged to be responsive to the technical and business needs of applicant companies across the early phases of their life cycle.

The types of Biotechnology Center loans available to North Carolina-based companies are described in Table 5-1 and in more detail below:

Table 5-1: Types of Biotechnology Center Loans

Loan Type	Awards Provided	Amount Awarded
Company Inception (CIL) Maximum Award: $30,000 Includes *BDL and *TML from 2008	FY08 – 8	FY08 – $229,040
	FY09 – 10	FY09 – $425,000
	FY10 – 5	FY10 – $148,407
Small Business Innovation Research (RBL) Maximum Award: $75,000	FY08 – 0	FY08 – $0
	FY09 – 0	FY09 – $0
	FY10 – 0	FY10 – $0
Small Business Research (SRL) Maximum Award: $250,000	FY08 – 6	FY08 – $890,027
	FY09 – 6	FY09 – $1,448,000
	FY10 – 5	FY10 – $749,050
Strategic Growth (SGL) Maximum Award: $250,000	FY08 – 3	FY08 – $608,000
	FY09 – 2	FY09 – $423,000
	FY10 – 2	FY10 – $500,000

* BDL=Business Development Loan; TML=Technology Enhancement & Acceleration Model Loan
Note: For RBL, SRL and SGL awards, the Biotechnology Center takes an equity position in the company in the form of warrants equivalent to 25% of the principal amount of the loan.

"Stephen Butts, former vice president of Addrenex Pharmaceuticals, says Biotech Center loans played a role in helping the company get to the point where it was acquired by Sciele Pharma for $29 million last year. Rather than pursue venture capital funding, Addrenex obtained a Biotech Center loan to develop its drug candidate to the point where it attracted angel investors and then a licensing deal with Sciele. 'For Addrenex, the loans were absolutely critical,' he says."

Source: Vinluan, Frank. "Fallback Mode: Loans to Grow", *Triangle Business Journal*, 26(5): 3, 31. October 8, 2010.

Company Inception Loan (CIL): Awards of up to $30,000 are available through the CIL Program to fund inception-stage, non-research company activities. Examples of approvable activities include: business start-up legal expenses; development of a business plan; market research and competitive intelligence; hiring a key consultant for grants writing, regulatory strategy development or product development guidance; patent landscape analysis; and travel to a key conference, partner or investor. Other than the initial stake of money from the founders, friends and family, CIL funding is often the first money into a recipient company.

SBIR Bridge Loan (RBL): Small Business Innovation Research (SBIR) grants are offered by various federal agencies to fund research undertaken by U.S.-owned small businesses. The Center's RBL Program leverages a company's grants writing effort and initial SBIR success by providing gap funding of up to $75,000 to maintain technology development momentum between phases of the federal

grants. Coupled with the state-funded SBIR/STTR Matching Program, the RBL Program provides North Carolina companies with ample incentive to secure federal SBIR grants funding. While the Biotechnology Center has not awarded an RBL recently, the large volume of SBIR grants in North Carolina suggests that this program will become more active in 2011 and beyond.

Small Business Research Loan (SRL): The SRL is the Biotechnology Center's flagship loan, providing up to $250,000 to fund a research project designed to achieve a commercially meaningful technology development milestone. A funded project may help a company establish technical feasibility or proof of concept, overcome a regulatory hurdle, or otherwise reduce technology risk from a product development or investment perspective. Ercole (a UNC-Chapel Hill spinout) used an SRL award to fund a project to establish *in vivo* proof of principle for using its alternative RNA splice modulating oligonucleotides as a treatment for rheumatoid arthritis and Crohn's disease. The company was sold in 2008 to AVI BioPharma in a deal estimated to be worth $9 million.

Strategic Growth Loan (SGL): The SGL program provides a company with up to $250,000 to match a simultaneous investment by an accredited angel network or venture capital fund. The applicant company is expected to have already achieved a significant technical milestone (*e.g.*, early proof of concept) sufficient to attract investor interest. It is expected that an awarded SGL will fund corporate development activities that will directly lead to additional funding or partnering success for the applicant. As part of its due diligence process, the Biotechnology Center undertakes an independent review of the co-investor as well as the applicant. This award has been particularly successful at helping to elicit angel investment in North Carolina life science opportunities from both North Carolina and out-of-state funds (which are typically reluctant to make long-term or geographically distant investments). For example, Precision Human BioLaboratory (now Ridge Diagnostics) used SGL awards made in 2007 and 2009 to secure a combined $602,500 investment from KI Investment Holdings, LLC (San Diego, CA) and launch its depression diagnostic in 2010.

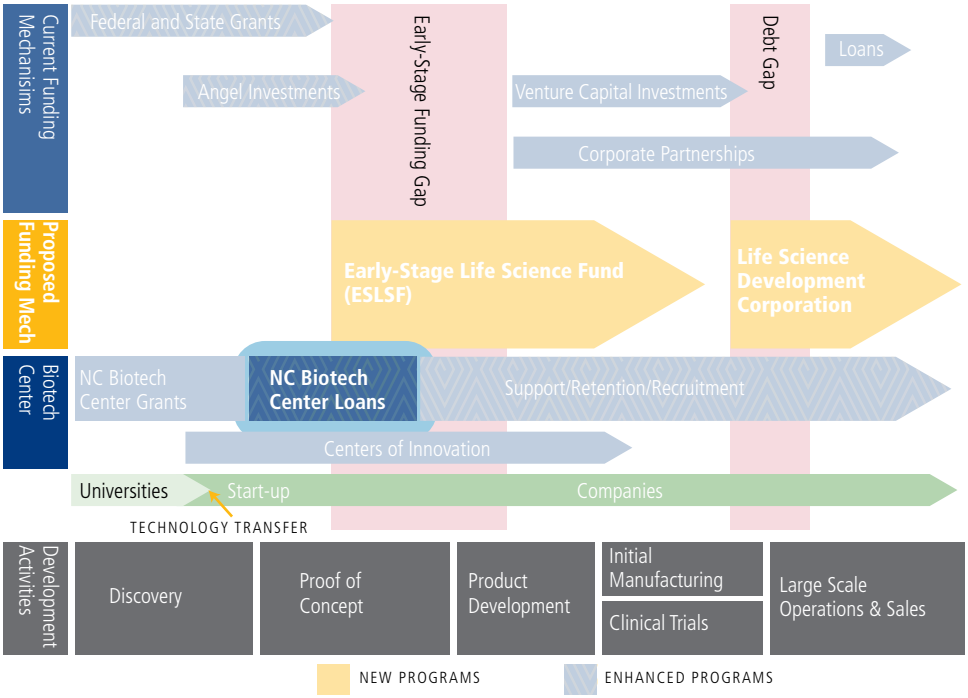
Potential Benefits from Expansion of Biotechnology Center Loan Program

For fiscal years 2008-2011, the North Carolina Biotechnology Center's annual loan award budget has been limited. In fiscal 2011, the loan budget allows for the awarding of roughly four Small Business Research Loans, two Strategic Growth Loans, one SBIR Bridge Loan and seven Company Inception Loans. A recurring increase in the Biotechnology Center loan program by $3 million could benefit North Carolina-based life science companies in two ways:

- By expanding the number of SRLs and SGLs to support more companies developing early proof of concept data relating to their technologies
- By enabling the Biotechnology Center to expand the SGL program to include a focus on companies which already have proof of concept data and are standing on the brink of the early-stage funding gap

Both of these approaches support the larger goal of this strategic plan, which is to move more of North Carolina's many promising life science discoveries and start-up companies toward commercialization. Figure 5-1 highlights the stage of bioscience companies that would benefit from the recommended expansion of the Biotechnology Center loan programs. Note that the addition of the expanded SGL program would allow the impact of the overall Biotechnology Center loan program to extend well into the early-stage funding gap to assist companies preparing for the more expensive demands of product development.

Figure 5-1: Environment Incorporating Strategic Plan Programs – Biotechnology Center Loan Program Expansion



Expansion of SRL and Current SGL Funding By $1 Million Annually: Expanding the number of $250,000 SRLs and SGLs would support companies that have completed the start-up process but remain at an extremely early stage of product development. While rigorous due diligence and selectivity would remain a hallmark of the Biotechnology Center's process, there are many companies with strong prospects that are unable to receive an SRL or SGL each year because of funding limitations.

Introduction of an Expanded SGL Program Through $2 Million Annual Allocation: An expansion in the loan budget could also be employed toward the development of a new type of loan that would provide promising life science companies with financial support as they enter the early-stage funding gap. Companies which would be appropriate for the expanded SGL would have already achieved evidence of proof of concept, potentially funded through a previous SRL or current SGL. These expanded SGLs might be awarded concurrent with angel funding or soon thereafter, but before a company would be able to attract venture capital funding. As a result of the higher cost of development for these

later-stage companies, the expanded SGLs would be larger than the SRLs and current SGLs, likely in the range of $500,000 in maximum funding. Work funded by the expanded SGLs would be expected to result in a company that would be suitable for investment from either the Early-Stage Life Science Fund (as described in Chapter 4) or seed-stage venture capital funds.

Projected Impact of Loan Programs Expansion: The recurring $3 million North Carolina Biotechnology Center loan budget increase recommended here would provide for four additional SGL/SRLs and four expanded SGLs per year. The Biotechnology Center expects that companies receiving these additional loans would go on to receive follow-on funding consistent with past loans, implying that the additional $3 million in annual loan awards would lead to follow-on funding exceeding $300 million for the North Carolina companies receiving these loans. Such funding would be expected to lead to new hires and continued development toward commercialization. Enhanced support of the SRL/SGL programs and the initiation of an expanded SGL program would be important in helping North Carolina-based life science companies surmount the most daunting obstacle for early-stage companies, the early-stage funding gap. In sum, these enhanced and expanded loan programs can be expected to provide for increased employment in the sector, further economic development and the attraction of outside funding from angel and venture investors, banks, and grant organizations.

Increase Appropriation for SBIR/STTR Matching Program

The North Carolina SBIR/STTR Matching Funds Program ("the Matching Program") provides matching grants to North Carolina-based small businesses that have been awarded federal Phase I Small Business Innovation Research (SBIR) or Small Business Technology Transfer (STTR) awards. Based upon the historical success of North Carolina companies competing for Phase I Awards, matching all of the expected applicants at the maximum amount allowable would require $5 million each fiscal year. Funding for the Matching Program has decreased substantially from its $5.0 million level in fiscal 2007 to $1.5 million for fiscal 2011.

It is recommended here that the SBIR/STTR Matching Funds Program receive an annual recurring appropriation of $5 million to maximize its ability to help North Carolina high-tech businesses develop and commercialize technologies, create more well-paying jobs, and generate the kinds of innovation critical for making the state a leader in the global economy.

It is recommended here that the SBIR/STTR Matching Funds Program receive an annual recurring appropriation of $5 million to maximize its ability to help North Carolina high-tech businesses develop and commercialize technologies, create more well-paying jobs, and generate the kinds of innovation critical for making the state a leader in the global economy.

SBIR/STTR Matching Program: History and Purpose

The SBIR and STTR programs grant competitive awards to small businesses for Phase I proof of principle research and development (R&D) and Phase II early-stage product development. Combined, these two highly competitive, peer-reviewed programs are the single largest source of early-stage capital for U.S. small businesses (more than $2 billion annually). Recognizing that one of North Carolina's greatest economic development opportunities is in bridging the gap between its internationally regarded innovation capacity and the creation of small businesses that can commercialize it, a bipartisan coalition of North Carolina lawmakers established the SBIR/STTR Matching Funds Program (§ 143B-437.80-81) during the 2005 legislative session.

The specific objectives of the Matching Program are to:

1. Increase the amount of federal research and development dollars received by North Carolina small businesses
2. Help North Carolina small businesses bridge the funding gap period between the final Phase I payment and the first Phase II payment in the federal SBIR/STTR program
3. Increase the intensity of the research and development conducted under Phase I, making North Carolina small businesses more competitive in the competition for Phase II funds
4. Encourage the establishment and growth of high-quality, advanced technology firms in the North Carolina

SBIR/STTR Matching Program: Structure and Funding

To accomplish its objectives, the Matching Program matches funds that a North Carolina business receives under a federal SBIR/STTR Phase I award, up to a maximum of $100,000. As summarized in Table 5-2, the Matching Program's appropriated funding has varied considerably throughout its six-year history, as have the number and size of matching awards it has made. More than 220 matching grants have been awarded to date, totaling nearly $16 million to more than 160 small businesses throughout North Carolina.[1]

Table 5-2. SBIR/STTR Matching Funds Program: Appropriations and Awards

FY	Appropriated $	Awarded #	Match Cap	Awarded $
2006	$1,000,000	25	$50K	$1,111,816
2007	$5,000,000	51	$100K	$4,553,917
2008	$4,830,000	49	$100K	$4,675,962
2009	$3,500,000	54	$75K	$3,968,588
2010	$700,000	22	$50K	$1,018,939
2011	$1,500,000	19 (ongoing)	$30K	$569,016 (ongoing)
Total	**$16,530,000**	**220**	**N/A**	**$15,898,231**

At its highest appropriated funding level ($5 million) in fiscal 2007, the Matching Program made 51 matching awards and was able to provide the full match amount allowable under its guidelines ($100,000). At its lowest appropriated funding level ($700,000) in fiscal 2010, however, it was able to make only 22 awards and for only half ($50,000) the match amount allowable under its guidelines. In general, as a result of funding decreases, both the number and the size of the matching grant awards has decreased over time, thus limiting this critical early-stage capital to eligible companies. Without adequate early-stage funding, such as the type of funding provided by the Matching Program, many of North Carolina's innovative technologies will remain in university laboratories and other research institutions, and their innovative benefits may never be realized.

Although the businesses receiving the Matching Program's grants vary in the types of activities they conduct, they reflect North Carolina's industry strengths overall. Consistent with the state's high rankings in biotechnology, nearly one-third of the businesses receiving the program's grants are involved in the biotechnology sector, and nearly half are in the life science sectors broadly.

All of the awardees fit well within the definition of a small business, as defined by the U.S. Small Business Administration as those companies having fewer than 500 employees. Roughly 75% of these firms have 10 employees or less, reflecting the high-growth, start-up nature of businesses receiving federal SBIR/STTR awards.

1 The source for all data in this section is the North Carolina Board of Science and Technology's *sciGrants* database. The data are collected from the small businesses via their matching grant application and subsequent Interim and Final Reports to the Board of Science and Technology.

Impact of SBIR/STTR Matching Program

To date, final reports for 120 projects, receiving more than $9.4 million in state matching funds from the Matching Program, have been submitted. This matching funding has helped the recipient small North Carolina businesses: 1) create more than 124 additional jobs—most at the professional/scientific, managerial, or technical level, 2) leverage more than $38 million in follow-on investments from other sources, 3) leverage more than $46 million in Phase II SBIR/STTR funding, and 4) advance innovative commercial technologies in numerous areas. These impacts are expected to expand as the grants become fully utilized to grow the small businesses. For example, the 120 completed projects are expected to produce 126 patentable products/processes with a total commercial value of more than $2 billion. Examples of such innovations in the life science sector have included a novel treatment for Parkinson's disease, a small, easy-to-operate body fluids analyzer, and a wearable environmental exposure monitor.

The small businesses receiving matching grants expect to license their innovative technologies to other businesses or organizations for further development and use. The lifetime monetized value of those licenses, which is estimated to be greater than $4 billion, will flow directly to the North Carolina small businesses that developed them.

The following testimonials, submitted by small businesses receiving a matching grant, emphasize the impact of the program:

> *"I cannot overemphasize the value of this grant to our company, our research, and our success. To receive this kind of funding so early in our research, and with so few strings attached, gave us an enormous advantage over other companies with whom we were competing for Phase II funds."*

> *"The matching funds program was the biggest single reason our company was able to weather the economic storm that occurred earlier in the year when SBIR funding ran very low. This enabled us to continue employment of all technical staff."*

Detailed Description of Recommendation

After administering the Matching Program for more than five years and awarding more than 220 matching grants to more than 160 companies throughout the state, the Board of Science and Technology is able to estimate how much funding is needed to meet the expected level of demand. On average, the number of Phase I matching SBIR/STTR matching grant applicants is 55, and the average value of the matching awards, assuming sufficient funding to make a full match, is $91,000. These data points suggest that the level of funding needed to fund the Matching Program fully is $5,005,000.

This full-funding level would enable small businesses to have a more successful Phase I project and be more competitive for a Phase II award. In addition, because the federal SBIR/STTR award-making agencies look more favorably upon proposals from small businesses that have matching funding, full funding for the Matching Program will likely increase the award rate of Phase I proposals.

In sum, full funding for the Matching Program will provide the greatest leverage by maximizing both the amount and the impact of the federal SBIR/STTR funding, as well as maximizing the probability of later-stage follow-on funding from Phase II SBIR/STTR awards and other investors in North Carolina small businesses.

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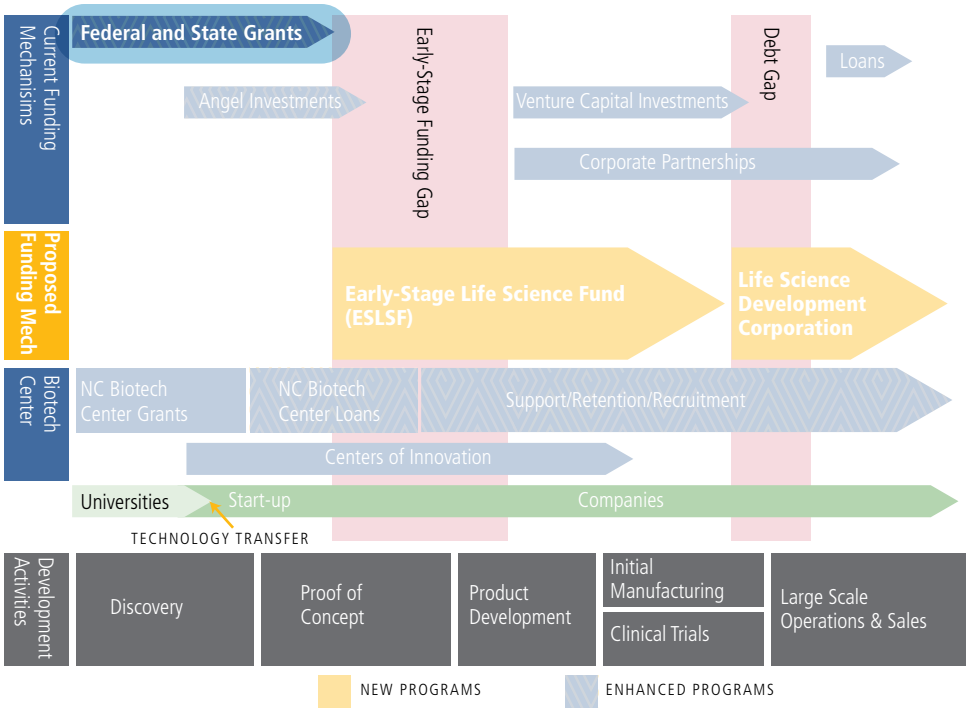
How an Expansion Would Benefit Commercialization of Life Science Technologies

Lack of access to early-stage capital is the most frequently cited impediment to small business development. That barrier is particularly high for small businesses in the life science sector, as their technologies are capital-intensive and complex. Thus, filling the financial gap between technology invention and commercialization would be expected to have a major positive impact on the commercialization of life science technologies in North Carolina. Figure 5-3 highlights where the expansion of the SBIR/STTR Matching Funds Program would impact emerging companies on the funding continuum.

Figure 5-3: Environment Incorporating Strategic Plan Programs – SBIR/STTR Matching Funds Program Expansion



In terms of North Carolina small businesses in the life science sector that receive SBIR/STTR awards, the estimated impact of full funding for North Carolina's SBIR/STTR Matching Funds Program[2] is expected to include:

- At least 20 additional life science jobs directly from the matching grants, and at least 31 additional life science jobs indirectly from federal Phase II awards, per year.
- At least $6.7 million in Phase II life science SBIR/STTR funding, per year.
- At least $1.8 billion in projected lifetime monetized value of life science licenses.
- At least $36 million in first-year retail sales and $336 million in third-year retail sales.

These impacts are significant considering the small size and early-stage nature of the businesses receiving these matching funds. Overall, increased funding for the SBIR/STTR Matching Funds Program would be expected to be of great benefit in moving technologies further down the development continuum to when larger amounts of funding are available through Biotechnology Center loans, angel funding, and, potentially, the ESLSF.

2 Based on the following assumptions, which derive from the Matching Program's descriptive and impact data presented above: (1) life science businesses—defined as those whose primary business activity is biotechnology, medical or pharmaceutical—account for 44% of all SBIR/STTR matching grant awardees, (2) annualized amounts are determined by dividing the overall impact measures for the Matching Program by three because only companies receiving awards in the Matching Program's first three years have completed Final Reports, and (3) the annual impact of full funding should be larger than what the overall impact measures above would predict because those overall measures are based partially on years in which the Matching Program was not fully funded.

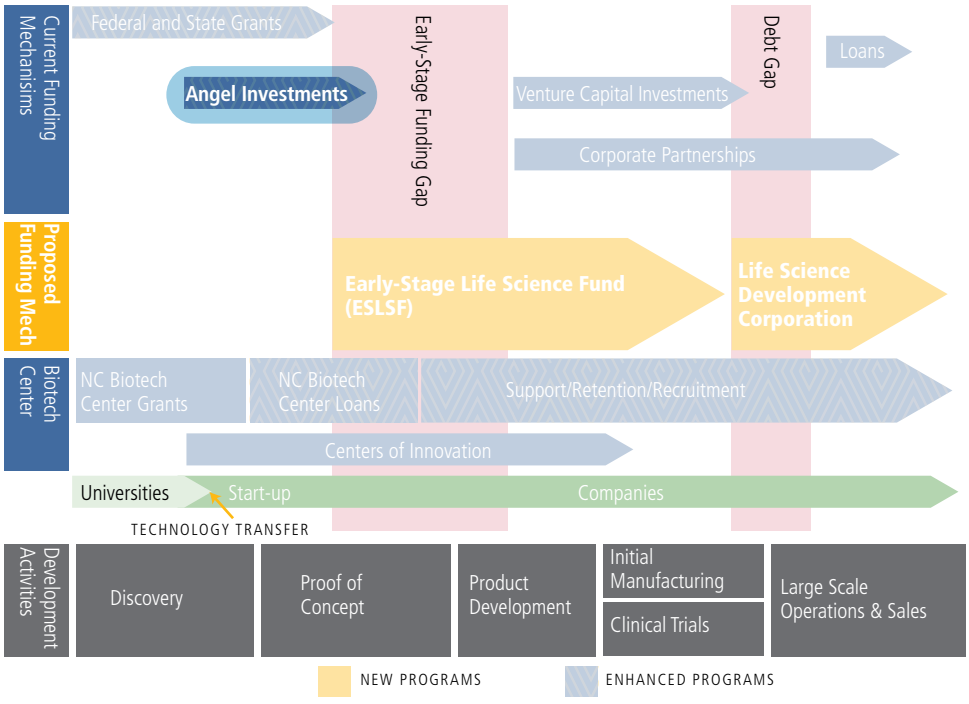
Expansion of North Carolina Qualified Business Venture (QBV) Tax Credit Program

The SBIR/STTR Matching Program is a valuable resource allowing North Carolina-based life science and technology companies to be more competitive with those located in other states. However, federal restrictions limit the types of companies eligible for SBIR awards as well as the types of expenses that can be funded through such grants. Another program that supports emerging companies in North Carolina that is not subject to such limitations is the Qualified Business Venture (QBV) tax credit program. The aim of the QBV program is to encourage more investment in early-stage companies by providing a 25% state tax credit to individual investors in qualified businesses. As a result, the QBV program improves the risk/reward profile of investments in angel/VC funds and emerging companies.

It is recommended that the tax credit allocated annually to the QBV program be increased from $7.5 million to $10 million and that a new class of institutional investors be allowed to participate in the program.

It is recommended that the tax credit allocated annually to the QBV program be increased from $7.5 million to $10 million and that a new class of institutional investors be allowed to participate in the program.

Figure 5-4: Environment Incorporating Strategic Plan Programs – QBV Tax Credit Program Expansion



Review of QBV Program

North Carolina's QBV tax credit offers incentives to individual investors interested in allocating capital to certain types of funds or businesses. These incentives make such investments more attractive, thereby increasing funding for emerging North Carolina businesses (focused on the life science or other industries). Specifically, North Carolina's QBV tax credit provides investors in qualified funds and businesses with up to a 25% credit against their state tax liability. For instance, if an individual investor makes a $100,000 investment in a qualified fund or small business, he or she could receive up to a $25,000 state tax credit, potentially having a major impact on the risk/reward profile of the investment.

The actual amount of the QBV tax credit for a specific individual investor depends on whether total QBV tax credits for the year reach the state's $7.5 million cap. If the total credit claims are less than the overall program cap, then each investor may receive a credit up to 25% of their investment or $50,000, whichever is less.[3] If the total request for tax credits exceeds the $7.5 million cap on credits, then all requests are allocated in proportion to the size of the credit claimed by each taxpayer. The cap has been exceeded six times in the past ten years with the cap ranging from $6.0 million to $7.5 million in that time period.

Business Qualification Process

Funds and companies must register with the Securities Division of the Department of the Secretary of State to become a qualified investment. Investments that qualify for the QBV tax credit are typically those made in angel or venture funds that actively invest in North Carolina's emerging companies or in the emerging companies themselves. More specifically, investments can be made in qualified businesses from three categories: Qualified Business Venture (QBV), Qualified Grantee Business (QGB), or Qualified Licensee Business (QLB). These categories are described in more detail in Table 5-3.

3 North Carolina General Statutes Sections 105-163.010 – 105-163.014.

Table 5-3: Allowable Business Categories for Qualified Investment Tax Credit

Business Type	Qualification Requirements
Qualified Business Venture (QBV)	The entity is primarily a manufacturing, processing, warehousing, wholesaling, research and development, or service-related business. The business must have been organized in the same year as the year in which it applies for registration or not have generated more than $5 million in gross revenues during its last fiscal year. The business cannot engage to any substantial degree in providing professional services, contracting or construction, selling or leasing at retail, investing, entertainment or recreation, or managing or operating real estate.
Qualified Grantee Business (QGB)	A business which during the three years prior to registration as a QGB has received a grant or other funding from a granting entity. A "granting entity" is an organization with the principal purpose of: 1) stimulating the development of the biotechnology industry, 2) stimulating economic development based on the advancement of science, engineering and technology, or 3) conducting research and development in electronic, photonic, information, or other technologies.
Qualified Licensee Business (QLB)	A business performing under a licensing agreement with an institution or university for the purpose of commercializing technology developed at that institution or university.

North Carolina's QBV Program Compared to Tax Credit Programs in Other States

Twenty-one states including North Carolina offer similar programs that differ along several attributes including percentage of investment credited, maximum allowable credit per investor, cap on total tax credits, and investor and company qualification requirements. North Carolina's QBV program offers comparatively smaller benefits than the average of those in the other 20 states that offer such a program:

- North Carolina currently will credit up to 25% of an investment into a qualified business. The average among programs in other states is 38%, with a low of 10% in New Jersey and a high of 100% in Hawaii.[4]
- North Carolina allows a maximum of a $50,000 annual credit per investor. Many states have caps on the allowable tax credit per investor, however the stipulations in each program vary considerably, making comparisons challenging. An estimated average among 18 state programs that have a defined cap is $265,000 per year with a range of $20,000 for Colorado up to $2,000,000 for Hawaii. Excluding both of

4 "State Strategies to Promote Angel Investment for Economic Growth", National Governors Association Center for Best Practices, Washington, D.C., 2010; "State Angel Investor Tax Credit Programs" Research Report 2010-R-0376, John Rappa, Office of Legislative Research, Connecticut General Assembly, September 29, 2010 (*http://www.cga.ct.gov/2010/rpt/2010-R-0376.htm*); unpublished comparative analysis of existing state tax credit programs communicated via e-mail by Dr. Paul Ulanch, Small Business and Technology Development Center, Dec. 20, 2010.

these outliers brings the average to a $171,875 maximum annual credit per investor with North Carolina and three other states falling on the low end of the range at $50,000.[5]

- North Carolina currently caps total QBV tax credits at $7.5 million (the initial cap that was instituted in 1996 was $6 million). The state's annual cap has been exceeded in six of the last ten years.[6] The average cap among 15 state programs that have a defined total credit cap is $14.2 million. Two of these states have a cap of only $750,000, and three states have no maximum annual credit.

History of QBV Program

Between 1988 and 2009, North Carolina has allowed $106 million in credits supporting investments of $637 million in qualified emerging companies. The number of individuals and pass-through entities applying for the credit peaked at 975 in 2000.[7] However, the impact of current economic conditions has reduced overall investment in the state's angel/VC funds and emerging companies, resulting in only 463 applications for credits claimed in 2009 (Table 5-4), the lowest since 1999. This steep decline in applications resulted in less than $5 million in credits being allowed in 2009, implying a significant reduction in funding for emerging companies in the state. Enhancements to the QBV program, as described later in this chapter, could play a role in generating a rebound in investing in North Carolina's emerging companies.

Table 5-4: QBV Program: Applications and Credits

Year of Investment	Applications Filed	Amount of Investment ($)	Year Credit Claimed	Total Credits Allowed ($)
2004	612	26,790,401	2005	5,889,109
2005	625	36,546,690	2006	7,000,000
2006	586	32,511,021	2007	6,549,418
2007	706	61,854,822	2008	7,000,000
2008	463	29,688,585	2009	4,983,538

Impact of QBV Program

Over the last four years, with $26 million in QBV credits supporting $161 million invested in qualified business ventures, 2,355 jobs were created at QBV-registered companies.[8] In essence, the program may have been responsible for

5 Ibid.

6 North Carolina Department of Revenue data, 1988-2009.

7 North Carolina Department of Revenue data, 1988-2009.

8 Qualified Business Registration 2007-2010 Annual Reports; prepared by Securities Division of the State of North Carolina Department of the Secretary of State.

roughly one new job for every $11,000 in tax credits. The QBV program, with the modifications recommended below, would be expected to create more jobs per $11,000 in tax credits because the new institutional investors involved in the program would likely attract additional large investments to QBV-registered companies, enabling these companies to grow faster and longer-term.

Expanding the QBV Program to Benefit Commercialization of Life Science Technologies

In a September 2010 report, the North Carolina Innovation Council recommended enhancing the QBV Program by raising the overall annual QBV cap to $10 million and expanding the eligibility for QBV tax credits to include institutional investors.[9] Specifically, the Council's recommendation called for $2 million of the QBV credits to be allocated to institutional investors, with unused credits from one group (institutional or individual) to be reallocated to the other group on an annual basis as necessary. ***These recommendations are endorsed in this plan.***

To attract institutional investors to take part in the program, ***a further recommendation would be that the maximum annual credit per investor be raised to $175,000*** to be comparable to the average maximum credit allowed in other states. A $50,000 maximum credit would be unlikely to influence an institution's investing decisions, but a $175,000 credit associated with a $1 – $2 million investment could have a significant impact on the institution's decision-making process.

These changes to the QBV Program would enable greater investments both in angel/VC funds as well as in individual emerging companies.

These changes to the program would enable greater investments both in angel/VC funds and also in individual emerging companies. The addition of institutional investors to the program would not only expand the number of entities involved in the program but also significantly increase the average investment size and therefore the average funding round size for a fund or company. Institutional investors are also likely to attract additional large investors (which may or may not be QBV eligible) to emerging companies (and the funds that invest in them) because these institutions are typically considered to be more experienced with access to more due diligence information than individual investors. Larger financing rounds mean that companies can progress further toward commercialization of their products without having to seek additional funding. The multiplier effect from these recommended enhancements to the QBV program are expected to be even higher than is seen with the current program due to the inclusion of institutional investors in the expanded QBV program.

9 NC Innovation Council, Committee 3 – Attracting Innovative Organizations, September 27, 2010.

Combining New and Existing Programs to Surmount the Early-Stage Funding Challenge

Overall, the enhancements to three existing programs described in this chapter are expected to drive additional early-stage funding for emerging companies in North Carolina. Such financing, when combined with the establishment of the Early-Stage Life Science Fund, should enable more North Carolina life science companies to progress to and through the early-stage funding gap to the point where they can garner the venture funding or strategic partnerships needed to drive them toward commercialization.

While Chapters 4 and 5 have focused on early-stage funding vehicles, Chapter 6 will introduce a new initiative to bridge another key funding gap identified by many key stakeholders in the state: the debt funding gap.

CHAPTER 6:

Life Science Development Corporation

RECOMMENDATION: *Create a Life Science Development Corporation to provide debt financing to later-stage companies seeking to build or expand manufacturing capabilities in North Carolina*

North Carolina life science companies face an uphill battle in securing debt financing for equipment and facilities necessary to manufacture their newly developed products. The creation of a new, non-profit Life Science Development Corporation (LSDC) is proposed to address this financing gap. Market surveys and interviews with potential borrowers suggest that a loan fund of approximately $70 million could be effectively deployed for this purpose. Creation of the proposed fund would require legislation to establish necessary authorities and tax benefits to support the program. If implemented, the proposal would allow North Carolina to significantly benefit from jobs and investments associated with early, small-scale production of new life science products, as well as from subsequent expansions required to support large-scale production. Of particular note, the proposed LSDC's contribution to growing domestic life science companies could be substantially less than the cost of economic development incentives typically required to lure manufacturing operations of established life science companies to the state.

As described in detail in Chapter 3, one of the most significant barriers to further growth of the state's life science cluster is the lack of financing opportunities for companies in need of initial-scale life science manufacturing facilities and other requisite first-product assets. In the absence of such financing, life science companies entering the later stages of product development typically have only two options, both of which often result in the company or its manufacturing capabilities residing outside North Carolina. The first option is to be acquired by a much larger life science company. The second option is to make arrangements with existing firms to contract manufacture sufficient pilot quantities of new products to meet the needs of regulatory testing required for market approval.

The recommendation to establish a new debt financing vehicle for companies in later-stage product development can be expected to 1) enable more North Carolina-based companies to successfully commercialize their products, 2) allow those companies to manufacture their products here, and 3) attract companies from elsewhere to establish and grow their manufacturing operations in North Carolina.

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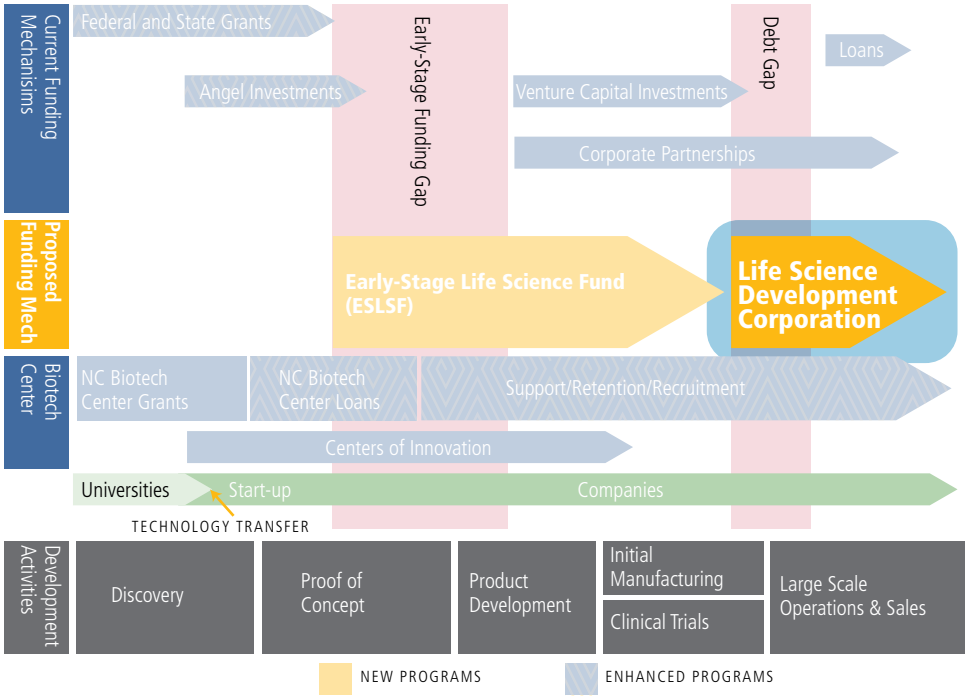
Proposed LSDC Loan Program

The creation of a new $70 million Life Science Development Corporation loan program is proposed to address the failure of North Carolina's existing financial markets to provide debt financing for new life science production facilities. This loan program would be supported by sophisticated technical underwriting resources necessary to successfully undertake life science facilities financing. The recommendation to initiate such a program is the strategic plan's primary solution to bridging the debt funding gap (otherwise referred to as the late-stage funding gap) as highlighted in Figure 6-1.

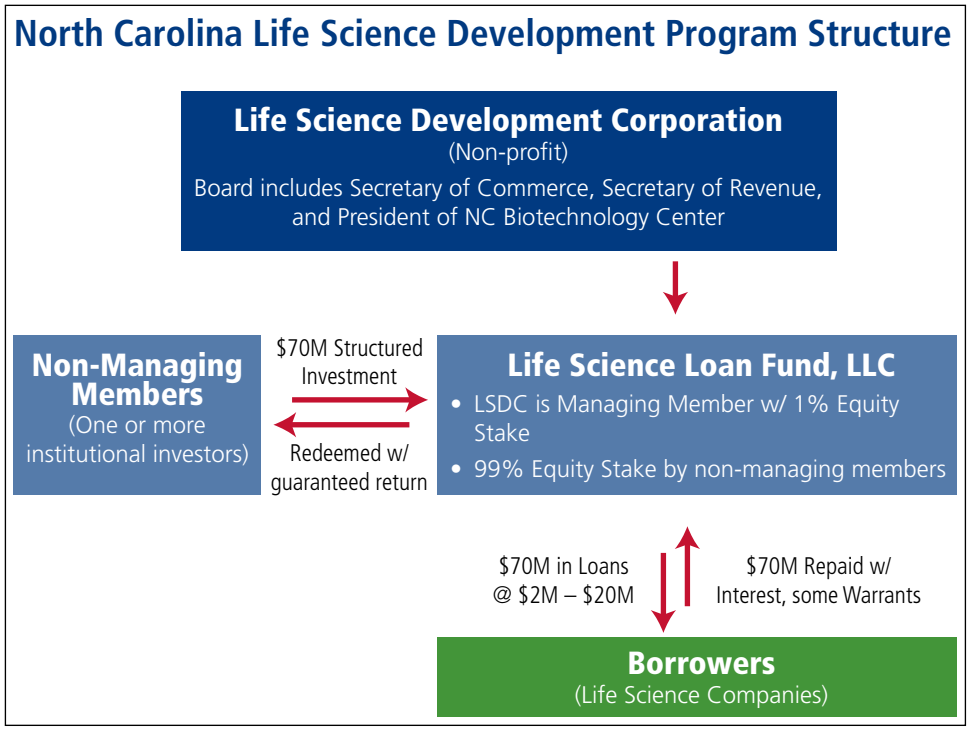
Figure 6-1: Environment Incorporating Strategic Plan Programs – Life Science Development Corporation



Given the significant uncertainties associated with product development, it is important for any financing program operating in the life science capital markets to assemble a portfolio of loans that appropriately diversifies the risks associated with such lending. A series of market surveys and focus groups conducted by the North Carolina Biotechnology Center and the North Carolina Biosciences Organization (NCBIO) in the autumn of 2008 suggested that near-term demand exists for more than $75 million of such facilities. It is believed that a loan portfolio of roughly this size would be of sufficient magnitude to achieve the necessary diversification and trigger meaningful economic benefit to the state.

The LSDC could be structured along the lines of Figure 6-2.

Figure 6-2: LSDC Program Structure



This structure involves an investment in the LSDC by one or more institutional investors—these investors would not be directly involved in the management of the LSDC. The return to these investors would be guaranteed by contingent tax credits that only become redeemable if the underlying loans made by the LSDC fail to achieve a predetermined rate of return.

A survey of recent innovation initiatives in other states shows that, during the last ten years, at least seven states created comparable structured investment vehicles to raise funding for programs designed to improve capital access for innovation-based companies. In these structured-investment programs, states including South Carolina, Utah, Ohio, and Michigan provide participating investors contingent tax credits that are redeemable in the event that the underlying investments fail to achieve predetermined rates of return. Monies from these structured investments are deployed as equity investments in venture funds that serve start-up companies in the supporting state. Although returns may vary across the portfolio of venture funds in which monies are invested, it is anticipated that the aggregate return across the entire portfolio will be more than sufficient to pay participating investors preferred dividends at the promised level. To date, states have authorized more than $900 million in contingent tax credits to support equity funds.

Although capital formation initiatives in other states have focused on equity investment programs, it is recommended that a loan program be the proposed structured investment vehicle for the LSDC. A properly structured venture debt program would offer the advantage of reducing investment risk through the use of security interests in financed facilities and equipment, while capturing potential upside investment returns through the use of convertible debentures or warrants for purchasing the stock of borrowing companies at favorable prices.

To achieve a diversified portfolio of practically-sized loans, the proposed LSDC would provide between $2 and $20 million debt financing packages to life science companies. The LSDC would hold security interests in equipment, buildings and real property financed with the loans. Loan durations would range from five to ten years. Borrowing companies could be required to escrow up to 10% of loan amounts as a reserve against default to mitigate risk; these companies would also pay application fees. As already noted, the loan fund could also take warrants for stock in the borrowing company.

Expected Benefits of the LSDC

The LSDC would provide North Carolina's promising life science companies with a clear funding path for financing the establishment of production facilities and other commercialization efforts that result in jobs for North Carolinians. The program will help prevent the emigration of companies, technologies and capital assets caused by the state's current lack of debt financing for life science manufacturing facilities. By providing a means for these firms to remain in North Carolina, the program will set the stage for later and more significant facility and workforce expansions. The LSDC would also be a significant tool for recruiting companies from other states to North Carolina.

When Maryland-based biotechnology company ACell considered moving its manufacturing operations from Indiana to Winston-Salem in 2010, it estimated the cost of building a new facility to house an anticipated 100 employees to be between $15 million and $30 million. When it was clear that North Carolina was unable to provide a loan-based incentive to the company to defray the initial cost of establishing a biomanufacturing facility, the company put its North Carolina moving plans on hold. According to Jim DeFrancesco, ACell's CEO, the company has not ruled out a move to North Carolina, but "it gets less and less likely as time goes on," adding that the company will need to grow soon, putting down roots in the process.

Source: "Maryland biotech halts Triad plans as legislation fails", *The Business Journal*, July 19, 2010, *http://www.bizjournals.com/triad/stories/2010/07/19/story1.html*.

Significant Job Creation Expected Once LSDC Is Established

It is not possible to estimate with certainty the amount of investment and numbers of new jobs that would accrue from establishment of the LSDC in North Carolina. However, in 2008, BIO and the North Carolina Biotechnology Center conducted a survey of existing North Carolina life science companies that might benefit from the proposed program. The survey identified more than $75 million worth of current or pending capital projects that would likely be benefited by the proposed fund. An estimated 100 to 250 immediate new jobs were associated with the pending investments.[1]

It is important to note that the potential jobs and investments identified by the survey represented only the immediate capital and employment needs of these companies. LSDC funding for these projects would be used to establish initial, small-scale production facilities. If the products associated with these projects were ultimately approved, then much larger investments and related workforce expansions would inevitably follow.

Jobs created by life science companies funded by the LSDC will typically enjoy above-average levels of pay, as well as clean, safe working environments. Furthermore, companies in the life science sector also are typically credited with higher than average economic impact multiples, meaning that the establishment and growth of such firms will have greater collateral impact on the economy than many other businesses.

1 The 2008 survey produced a "snapshot" of readily identifiable project opportunities for the proposed fund. The survey was not comprehensive, and did not attempt to measure the potential to attract out-of-state companies or investments to North Carolina.

Retention of Expanding Life Science Companies in North Carolina

LSDC loans are expected to result in North Carolina-based facility and workforce expansions at a higher rate than with other types of incentive or support programs. Because of the stringent regulatory compliance certifications and workforce training requirements for life science production facilities and operations, companies have strong incentives to expand in-place at the site of initial manufacture. By leveraging existing successful biomanufacturing workforce development programs, North Carolina is well-positioned to accommodate the subsequent expansion of companies at this stage.

The "stickiness" of established life science manufacturing operations is doubly important in the context of evaluating the benefits of the proposed LSDC. Because established operational manufacturing facilities are difficult to move, even emerging firms that are later acquired by larger life science companies are likely to retain a significant manufacturing footprint in North Carolina. This reality invites an alternative perspective in evaluating the potential benefits of the proposed LSDC. Specifically, North Carolina's own experience suggests that state-level incentive packages of more than $40 million can be required to attract large-scale biomanufacturing facilities to the state. Thus, if only two new "homegrown" biomanufacturing operations can be spawned through LSDC financing, the state could save as much as $80 million in incentives required to lure established life science companies representing an equivalent level of job creation and capital investment potential.

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Recruitment of Companies from Out-of-State

It should also be noted that the proposed LSDC will likely command the interest of early-stage life science companies outside of North Carolina. Even in states such as California and Massachusetts, where life science companies out-number those in North Carolina, nearly all development-stage firms with pre-approval manufacturing requirements face the same hurdles as companies in North Carolina, that is, how to finance expensive manufacturing facilities for a pre-revenue company.

In addition to a strong pool of existing domestic applicants, the LSDC program has the potential to further induce life science companies from other countries to relocate to North Carolina. In this scenario, the state would benefit not only from the maturing of existing in-state life science companies, it would also be in a position to harvest the "cream of the crop" among innovation-based emerging life science companies from across the globe.

Benefits Expected to Extend Beyond Biopharmaceutical Companies

Finally, while the LSDC primarily targets biopharmaceutical companies with pre-approval manufacturing needs, it is likely that the program will also benefit emerging companies developing a wide range of life science technologies. Development-stage companies in the regenerative medicine, personalized

medicine, nanobiotechnology, advanced medical devices, industrial biotechnology, and agricultural biotechnology sectors often have facilities financing needs, which make them difficult candidates for conventional financing options. LSDC will be positioned to materially assist such companies while at the same time further diversifying its loan portfolio.

Growing the State's Base of Executives to Lead Companies Through These Funding Challenges

While Chapters 4 and 5 of this report focused on potential solutions to the early-stage funding challenges experienced by North Carolina's life science companies, the Life Science Development Corporation described in this chapter is designed to bridge the funding gap faced by many later-stage companies. However, as emphasized in discussions with many business, academic and financial leaders in the state, funding is far from the only major challenge facing the state's life science companies. The primary non-financial challenge described by these leaders is the shortage of experienced life science executives in the state. This management gap is closely tied to the funding challenges faced by emerging life science companies—when investors and banks consider companies for an equity investment or loan, the quality of the management team is typically first on the list of selection criteria. Several programs to expand the state's bullpen of experienced life science executives are detailed in Chapter 7.

CHAPTER 7:

Strategies to Eliminate the Management Gap

RECOMMENDATION: *Develop a series of programs to support entrepreneurs based in North Carolina and to recruit successful executives from outside the state*

CHAPTERS 1 AND 2 PAINTED A PICTURE of the evolving global life science landscape, and North Carolina's position within this landscape. The state has developed an enviable life science enterprise with world class research and considerable commercial opportunity. Three key challenges were described in Chapter 3, each of which must be surmounted to fully tap the immense economic opportunity available to the state. This chapter is focused on new strategies to bridge the management gap facing many of the state's life science companies.

North Carolina is not without a base of distinguished life science executives. However, there are far more promising, innovation-driven companies at all stages of maturity than there are accomplished executives to lead them. In fact, one of the most commonly cited factors limiting North Carolina's ability to maximally leverage its rich life science research base into commercial products and services is the shortage of seasoned biotechnology executive management.

In this chapter, we outline a plan for increasing the number of experienced life science executives and entrepreneurs available to North Carolina life science companies. It is recommended that North Carolina's life science-focused institutions and companies implement the strategies outlined in this chapter to: (a) proactively recruit established executives from outside of North Carolina, and (b) support and expand the base of "homegrown" entrepreneurs.

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Increasing the number and depth of experienced, connected and successful life science executives through these means is expected to lead to greater commercial success for North Carolina companies, generate a greater willingness on the part of out-of-state funds to consider investments in local companies, and provide greater incentive for companies to relocate to North Carolina.

Recruiting Established Life Science Executives to North Carolina

Market North Carolina to Targeted Successful Out-of-State Executives

A proactive marketing campaign can be developed and directed to out-of-state executives who have successfully sold their most recent company and may be in the market for a new leadership opportunity. The initial contact to such an out-of-state executive would be made directly by a local high profile peer or investor. The purpose would be to provide an introduction to the state's life science sector, commercial resources, investors, and to North Carolina in general. Marketing materials would be created to reflect the breadth and depth of the research, commercialization and infrastructure landscape, similar to the packages routinely put together by the North Carolina Biotechnology Center for corporate recruitment prospects. Meetings could be coordinated through the Biotechnology Center and other organizations. The Center would also work with executive search firms and other partners to track life science company acquisition activity and develop leads to pursue.

> *"(We) need to bring in experienced CEOs/executives; every time a company gets acquired, we should send a letter to its top execs to have them visit and then give them the N.C. dog-and-pony show upon their visit."*
>
> —Jonathan Gindes (CFO) & Peyton Anderson (CEO), Affinergy

Additionally, a parallel effort could be directed at currently employed CEOs. A recent study indicated that 92% of currently employed CEOs are willing to talk to a headhunter.[1] An initial list of leading executives could be generated by polling local executives and investors.

This campaign would parallel some of the state's corporate recruitment efforts. Key marketing tools might include:

- A brochure highlighting the state's life science infrastructure and workforce, as well as the presence of a critical mass of North Carolina life science companies and corresponding leadership opportunities
- A description of several North Carolina life science leadership success stories
- A list of North Carolina-based executives willing to promote the state's life science-friendly business climate, including executives who have moved here from other states

1 *2010 Executive Retention Report: Executives Discreetly Exploring Career Options and Why the Boss Doesn't Know*, Finnegan/Mackenzie and ExecuNet, Inc., 2010, page 5. *http://www.execunet.com/promo/pdf/ExecuNet_R_Executive_Retention_Report_Finnegan_2010.pdf* (accessed on December 22, 2010).

- General information relating to cultural activities, recreational activities and quality of life in the state

Assurance of re-employability for subsequent opportunities is a very important issue for executives considering relocation. This concern should be addressed directly so that these executives are assured that there are multiple opportunities in the same geographic vicinity so that their next executive position will not necessitate a second relocation. Tactics that could provide potentially relocating executives with assurance on this issue include:

- Focusing initial marketing efforts to executives in sectors where there is critical mass of commercial activity (i.e., sectors with multiple North Carolina companies)
- Incorporating the Biotechnology Center's company database to facilitate searching by focus area to provide individuals who are being recruited for a position with a list of other North Carolina companies working in the same field

Adopt a Capital Gains Tax Exclusion for Founders and Investors in Early-Stage Companies

This proposal would provide a specific exemption from state capital gains taxes to founders and investors with initial stock investments in entrepreneurial businesses when they sell stock in their ventures.

North Carolina Governor Beverly Perdue has proposed a Small Business Start-Up Tax Relief ("Founder's Tax Credit") program that encourages investment in innovative small businesses by allowing favorable capital gains treatment of the founding interests in the business.[2] Specifically, this proposal would provide a specific exemption from state capital gains taxes to founders and investors with initial stock investments in entrepreneurial businesses when they sell stock in their ventures. Such a program could be an effective recruitment tool for drawing out-of-state executives to North Carolina leadership opportunities because it would provide another significant reason to start a company here rather than in another state.

Eligibility for this tax relief program would be extended to founders and investors supporting companies that qualify for the state's existing Qualified Business Venture Tax Credit (discussed in Chapter 5) and would thus effectively benefit investors in start-up companies with potential for rapid growth and job creation in North Carolina. The exclusion would be available only for stock issued after the effective date of the proposed legislation. Although the fiscal impact of the proposed exclusion will be driven largely by small, early-stage investments by individual investors, the overall economic leveraging impact of the proposal will be driven by follow-on investments, which are likely to be exponentially larger and typically not comprised of investments from individuals eligible for the capital gains exclusion. Moreover, the state is likely to derive material revenue gains from the proposed exclusion at the same time as the negative fiscal impacts of the exclusion are realized, since founders and follow-on investors are likely to sell stock at the same time upon sale of the company, which is the most common type of life science company liquidity event.

2 The North Carolina State Budget: Recommended Adjustments 2010-2011; *http://www.osbm.state.nc.us/files/pdf_files/2010_budget.pdf, page 34.*

With the exception of those states that do not have a state income tax (such as Florida, Texas and Washington) and therefore effectively do not tax capital gains, there is no comparable program in any other state. The closest may be the Virginia Innovation Investment Act, which would provide targeted, long-term capital gains tax exclusion for new investment in science and technology start-up companies in Virginia.[3] This legislation has been approved by the Virginia state legislature but, as of the writing of this report, had not yet been signed into law by the governor.

The capital gains tax exclusion concept carries the following benefits:

- Increases the availability of start-up capital by encouraging individuals to found and invest in North Carolina start-up companies
- Provides tax credits only for successful ventures (start-ups that do not succeed will not realize gains and will not receive tax benefits)
- Spurs economic growth and job creation before credits are taken
- Helps to attract experienced founders and investors from other states
- Encourages the creation of companies that will attract follow-on investments, and subsequent taxable gains, from venture funds and public equity markets

These benefits, should the capital gains tax exclusion be implemented, are likely to attract experienced life science executives and investors, thereby accelerating the commercialization of life science technologies in the state. In contrast,

> *"The current treatment of founders gains 'encourages' most successful entrepreneurs to move to other states with no tax on founders stock. N.C. not only loses the tax dollars it hopes to collect from these people, but it also loses those entrepreneurs who will start their next company in Florida or Texas and not North Carolina."*
>
> —Richard Holcomb, a serial entrepreneur[4]

Identify and Recruit Executives with North Carolina Ties

This approach would track executives with relationships to North Carolina. Examples of such North Carolina ties include being an alumnus of a North Carolina university, having children who attend one of these universities, and owning a second home in North Carolina. The Biotechnology Center already has a mechanism for identifying these individuals within its central contacts database. Such a mechanism can be utilized for both an initial outreach effort as well as part of a methodical follow up procedure.

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3 Website for Virginia State Senator Mark Herring: *www.markherring.org*; Senate Bill 428: *http://leg1.state.va.us/cgi-bin/legp504.exe?101+sum+SB428*.

4 Smith, Rick. "Perdue's 'Founder's Credit' could spark entrepreneurs, investors", *Local Tech Wire*, March 13, 2009 *http://localtechwire.com/business/local_tech_wire/venture/story/4732522/*.

As part of this concept, an office at the Biotechnology Center could be provided for use by such out-of-state executives and/or venture capital investors visiting North Carolina. This office could be made available on a first-come, first-served scheduling basis at no cost to the visitor. Occupants of the office could receive Internet access at no charge and have access to the Center's library and meeting rooms at in-state rates. As part of the program, local and out-of-state executive search firms would be made aware of this service and be encouraged to take advantage of this resource when bringing a recruiting prospect to North Carolina.

Coordinate Lobbying Efforts to Re-Institute Direct Flights to the West Coast

Executives for life science companies, venture capital groups and executive search firms have all corroborated that the lack of direct flights to/from the West Coast is a significant detriment to the ability of North Carolina companies to recruit experienced executives, attract investment and secure strategic partners. As such, it is recommended that statewide organizations such as NCBIO, the North Carolina Economic Developers Association (NCEDA), the North Carolina Technology Association (NCTA), the North Carolina Chamber and the North Carolina Department of Commerce develop a focused initiative to rally larger companies, venture capitalists and others to lobby airlines to establish at least one daily direct flight from Raleigh-Durham International Airport to/from San Francisco. When combined with other recommendations in this report, the establishment of such a direct flight should lead to a substantial increase in venture capital and strategic partnering activities, while also increasing the success rate for recruiting experienced biotechnology executives.

Support for North Carolina Entrepreneurs

Offer Stipends to Encourage Access to Entrepreneurial Education and Mentoring Programs

The state has an unusually strong cadre of entrepreneur support agencies and established entrepreneur training programs. Among these, North Carolina is home to two top 20 business schools[5] and a variety of non-profit business service organizations with an increasing focus on the life science industry. Existing programs that foster the growth of North Carolina's entrepreneurial base include:

- Duke University (Fuqua School of Business) – Center for Entrepreneurship and Innovation; Entrepreneur Affiliates Program, which connects business school students with seasoned executives
- North Carolina State University (Poole College of Management) – Life science-focused leadership training

5 "The Best U.S. Business Schools 2010", Bloomberg Businessweek, *http://www.businessweek.com/bschools/special_reports/20101111best_business_schools.htm*. (accessed on December 29, 2010) (Duke's Fuqua School of Business ranked #6 and the University of North Carolina's Kenan-Flagler Business School ranked #16.)

- The University of North Carolina at Chapel Hill (Kenan-Flagler Business School) – *Launching the Venture* and *Research to Revenue* courses
- Wake Forest University (Schools of Business) – Babcock Demon Incubator, which works to increase the number and quality of early-stage ventures in the Triad
- Council for Entrepreneurial Development (CED) – entrepreneurial education, networking, *FastTrac* (business planning program for start-up entrepreneurs), *Venture Mentoring Service* (new mentoring program for entrepreneurs)
- North Carolina Biotechnology Center – the BATON (Business Acceleration and Technology Out-licensing Network) Program that provides connections and guidance for first-time entrepreneurs
- Small Business and Technology Development Center (SBTDC) – *Investor Ready Entrepreneur* and *Power of Angel Investing* workshops, technology counselors, SBIR-related services

The value of these programs could be maximized to expand North Carolina's corps of life science-focused executives and also build a community of experienced business mentors. One mechanism for doing so is to create a stipend or subsidy for executives and product development professionals transitioning from careers in large corporate environments into entrepreneurial company leadership roles. Stipends could be managed by the Biotechnology Center and would be limited to first-time entrepreneurs to attend a formal, non-degree program tailored to life science entrepreneurism. These individuals bring a high level of relevant domain expertise and understanding of product development and/or commercialization, but may have little or no experience with entrepreneurism. Such a program would be expected to attract more experienced managers to entrepreneurial pursuits, while increasing the success rate for converting them into winning entrepreneurs.

Initiate North Carolina Biotechnology Center Executive-in-Residence Program

An Executive-in-Residence (EIR), based at the Biotechnology Center, could provide hands-on interim leadership for promising life science ventures in the state. As envisioned, the EIR would be a contract-based salaried position responsible for working directly with scientific inventors and others across multiple start-up companies to identify a compelling commercial story, develop a working business plan, focus the commercialization effort, manage the business, and recruit/groom a successor CEO. Other Biotechnology Center programs, such as BATON and the business loan programs, would closely support ventures managed by the EIR. The placement of a high-profile successful biotechnology executive like the EIR could be particularly helpful in recruiting permanent management for these start-up companies, particularly from out-of-state. A comparable public/private partnership model for sharing executives across multiple companies is employed

by the Pittsburgh Life Sciences Greenhouse[6] that provides funding and other services to promote the growth of western Pennsylvania's life science community.

Closing the Management Gap in Parallel with Implementing New Early- and Late-Stage Funding Initiatives

North Carolina clearly has many tools in place to grow the executive base required to effectively marshal the commercialization efforts of its life science companies. Presented in this chapter are several strategies to expand the homegrown management talent pool as well as to encourage top-tier executives to consider North Carolina as a source for opportunities and a viable launch pad for their next commercial adventure. This chapter suggests a number of partners that can effectively contribute to this effort; it will be critical that the roles of these stakeholders – drawn from the ranks of academic and non-profit entrepreneurism programs, government and the private sector – are carefully and strategically coordinated so as to maximally benefit this effort.

It is important that efforts to close the management gap be performed in parallel with the initiatives described in Chapters 4, 5 and 6 that will aid North Carolina companies in surmounting the funding challenges they face. Without access to funding, even highly skilled executives will be unable to move their companies toward product commercialization. On the other hand, without strong management, even companies with highly attractive products and technologies will not be able to attract the funding available. As such, it is recommended that the initiatives and programs described in this report be undertaken in a coordinated approach – one that synergistically increases the local availability of funding required to attract top-tier executives, and which simultaneously expands the base of strong executives able to attract additional funding for these early- and later-stage companies.

It is important that efforts to close the management gap be performed in parallel with the initiatives described in Chapters 4, 5 and 6 that will aid North Carolina companies in surmounting the funding challenges they face.

6 Stouffer, Rick. "Greenhouse program growing successful executives", *Pittsburgh Tribune-Review*, January 17, 2010.

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