University Cancer Research Fund

Annual Financial Report to the Joint Legislative Education Oversight Committee and the Office of State Budget and Management

Submitted November 1, 2012

in accordance with G.S. 116-29.1

A Message from the Chair

Five years ago, the General Assembly established the University Cancer Research Fund (UCRF) to help the University of North Carolina at Chapel Hill and its Cancer Center fight North Carolina's leading cause of death. Cancer affects one out of every three North Carolinians during their lifetime. The disease creates a significant health and economic impact across our state.

The UCRF has made a tremendous positive difference for North Carolina. Our state is a leader in innovative research to improve prevention, early detection, treatment and outcomes for cancer patients. The economic benefits have increased each year, and today every dollar invested by the state yields five dollars in return.

As Chair of the Cancer Research Fund Committee, I am pleased to present this annual report to show how North Carolina's support of the UCRF is paying off – not just in economic returns, but also through the research it supports that provides hope for people with this disease and saves lives. Below are some examples of the returns made possible by the UCRF:

- The hiring and retention of 129 outstanding cancer researchers at UNC;
- Publication of high-impact research findings in the world's top journals;
- Continued increases in extramural funding directly attributable to UCRF investment. This year alone, UNC received $88 million in new research funding from outside North Carolina directly attributable to UCRF;
- An increase in spin-off commercialization efforts and intellectual property, adding new innovations to the third-largest cluster of life science industries in the nation;
- A growing economic impact on North Carolina, reaching $293.8 million for FY 2011-2012 and totaling $968 million over five years. During its first four years UCRF created more than 5,000 new jobs; and
- Advancement of large-scale projects designed to better understand the cancer problems in North Carolina from the genetic to the community level, and participation in global collaborations aimed at eradicating this disease.

Thank you again for your ongoing support for the University Cancer Research Fund – on behalf of the cancer patients we are serving, the professionals involved in their care, and the researchers who are working to pave the way for better cancer care in North Carolina and beyond.

Sincerely,

H. Holden Thorp

Holden Thorp, PhD
Chair, Cancer Research Fund Committee

EXECUTIVE SUMMARY

In 2007 – the year cancer became the leading cause of death in North Carolina – the General Assembly created the University Cancer Research Fund (UCRF) to provide ongoing state support for cancer research. Annually, more than 40,000 North Carolinians are diagnosed with cancer, and the disease claims almost 17,500 lives.

The legislature determined that the state should provide a minimum of $50 million annually for cancer research under UNC Hospitals, the UNC Lineberger Cancer Center, or both. Supported by tobacco settlement funds, taxes on non-cigarette tobacco products such as snuff, and state appropriations, the Fund initially received $25 million in 2007 and $40 million in 2008 before reaching its full funding amount of $50 million in 2009. The Fund has dropped slightly below that level after 2010 due to a shortfall in non-cigarette tobacco product sales receipts.

Investments from the Fund are guided by a Strategic Plan adopted in 2009 that focuses resources on areas where they can have maximum impact – a limited number of strategic research priorities, selective opportunities and initiatives, and critical infrastructure. Under the Strategic Plan, the Fund's main research priorities are:

- to understand how genetic changes play a role in cancer,
- to develop new therapies to treat patients, and
- to optimize North Carolinians' cancer outcomes.

Opportunistic initiatives include the Innovation Awards, a fiercely competitive program that promotes groundbreaking research projects with a high likelihood of success and impact. The field of cancer research changes rapidly, and to be a national leader we need to be able to selectively invest in new areas. Critical infrastructure encompasses technology, training and other core resources, as well as promoting clinical excellence and outreach across the state.

The Cancer Research Fund Committee, the legislatively established oversight committee for the Fund, has published regular reports on the Fund's activities since 2008. In 2011, the General Assembly required an annual financial report including UCRF's effects on the state's economy, details on expenditures of UCRF monies and outside funds leveraged by UCRF support, and other performance measures.

Our second financial report submitted under this requirement demonstrates that the University Cancer Research Fund has had a significant economic impact on the state of North Carolina. From 2008 to 2012, the UCRF had the following economic impacts:

- Had an overall economic impact that reached $293.8 million in FY 2011-2012 and totaled $968 million over the years since UCRF inception, including $420.9 million in direct impact and $547.2 million in indirect and induced effects.
- Increased return on investment each year, exceeding a 5 to 1 return in FY 2011-2012.
- Created the equivalent of 5,056 new jobs through FY 2011, based on an independent economic evaluation.

One key area of economic impact is growth in funding from sources outside the state. UCRF has shown its effectiveness in increasing funds brought to North Carolina for cancer research.

- In FY 2011-2012, $88 million in extramural funding is directly linked to faculty who were recruited or retained by UCRF funds, or to the results of innovation grants, technology and infrastructure investments by UCRF.
- UCRF has helped to spark a significant increase in UNC's federal funding compared to other universities, at a time when overall federal funding levels have fallen or remained flat.

This funding growth is due to the world-class faculty members who have been recruited or retained, or whose work has been enhanced, using UCRF funds.

While some economic and health outcomes of the University Cancer Research Fund investment are quantifiable, the long-term effects this research could have on the overall health of North Carolinians will be seen in the years to come. In the meantime, the Strategic Plan has guided UCRF investments that have helped make UNC a national leader in several areas of cancer research and care. Some of the research highlights include:

Understanding the Role of Genetics in Cancer Causation and Treatment

In the past year, our UCRF investment in Next Generation sequencing, high content data storage, bioinformatics, and statistical genetics has placed UNC Lineberger faculty at the forefront of the world's cancer genomics efforts. Funded by more than $30 million in grant funds from outside North Carolina, including the National Cancer Institute's Cancer Genome Atlas program, UNC became the world leader in RNA sequencing from patient tumors. Highlights of this work were published in three papers in one of the world's leading journals, *Nature*. These high-impact publications described the results in colon cancer, lung cancer, and breast cancer. UNC faculty member Charles Perou, PhD, led the national effort in breast cancer, and was the central author of the breast cancer publication with UNC's Katherine Hoadley, PhD. The national impact of this work was demonstrated in a front-page story in the New York Times and Dr. Perou's appearance on CBS News.

Developing Novel Therapeutics

Our chemical biology and drug discovery investment in small molecule drugs for cancer is one of only a handful funded by the NCI in the country. Several drug development projects funded by NIH have focused on cancer targets derived from the work of Cancer Center scientists. These efforts are creating small molecule drugs that are beginning to show efficacy in pre-clinical models. This year saw the patenting and first publication of a new series of molecules targeting pediatric acute lymphatic leukemia (ALL). Additional grants were obtained and molecules patented that target the processes responsible for disordered gene regulation in cancer. The continued development of our mouse model of human cancer program has resulted in over 20 publications and over $10 million in new grants.

Optimizing NC Cancer Outcomes

UCRF investment in faculty recruitment and the development of our North Carolina Integrated Cancer Information Surveillance System (ICISS) has helped recruit Ethan Basch, MD, a recognized leader in cancer outcomes from Memorial-Sloan Kettering. He has begun to organize the existing faculty in the schools of medicine and public health. A groundbreaking article from this group, published in the *Journal of the American Medical Association*, evaluated radiation therapy for prostate cancer, assessing the treatment outcome and toxicity of various types of radiation therapy. A major finding was that the expensive new technology, "proton beam therapy," resulted in outcomes and toxicity similar to current state-of-the-art prostate radiotherapy. Since proton beam therapy installations are multimillion-dollar

investments, this type of comparative effectiveness research and evaluation is crucial and will diminish the escalation in cancer health care costs.

Clinical Excellence and Infrastructure

The ongoing research support provided by the UCRF complements the North Carolina General Assembly's major capital investment in UNC Health Care's N.C. Cancer Hospital, serving patients from all 100 counties. Opened in 2009, the new hospital has enabled us to take care of the citizens of North Carolina by expanding both space and our multidisciplinary approach to care. It allows us to be a referral center for citizens from across the state. And with the increase in population and aging, North Carolina's cancer burden is expected to double over the next two decades. The seven-story hospital provides more space and newer technology to serve more patients and enhance care. The hospital also serves as the clinical home of the UNC Lineberger Comprehensive Cancer Center – one of the most highly rated of the 41 such National Cancer Institute-designated centers in the country.

With a state that is 500 miles across, it is difficult for patients to travel long distances for their care. That is why UCRF and UNC developed and continue to support a clinical research network and telemedicine program, expanding the ability of patients to be seen close to home yet participate in the latest cancer care advances. The telemedicine effort is developing a physician call-in tumor board process by which local oncologists can seek the expertise of UNC oncologists with full ability to digitally observe pathology slides and imaging tests.

The expansion of the clinical program and the clinical trials network is enabling an even greater sophistication in our clinical research program. Our geneticists have derived new molecular tests that help oncologists determine the prognosis and potentially the best care pathways for our patients. Novel imaging modalities in conjunction with the Biomedical Research Imaging Center are resulting in new ways of staging patients for more precise surgical approaches. New studies with patient samples are advancing our understanding of bone marrow transplant success and toxicity, with the aim of modifying treatment approaches. These and other clinical and translational research efforts are under way.

The legislature also funded the Imaging Research Building to expand research efforts in drug development, nanotechnology, cutting-edge imaging research, and fundamental approaches to cancer biology. Scheduled to open in the winter of 2014, the facility will house state-of-the-art research labs and radiographic equipment that will speed the discovery of new drugs and treatments. Some technologies will be available in only a few other places in the world. The facility's interdisciplinary approach and physical linkage to the Lineberger Building will integrate researchers from the schools of pharmacy and medicine and the College of Arts and Sciences. This linkage juxtaposes cancer science and clinical research, accelerating the discovery of new therapies; devising molecular imaging techniques for early detection; improving targeting and delivery of drugs by using nanotechnology; and enabling other breakthroughs.

These capital investments and UCRF are leading to more clinical trials, more outside grants, and more world-class researchers working in North Carolina. It has enabled job creation, spinoff companies and private-sector collaborations. And most importantly, it has enhanced our understanding of cancer and our efforts to eradicate it.

ECONOMIC IMPACT

Under the UCRF Strategic Plan, creating jobs and enhancing North Carolina's economy is a key principle guiding the investment of resources. Each year, the Fund's economic return to our state has grown, exceeding a 5-to-1 return on investment in 2012. The UCRF has directly supported thousands of faculty and staff jobs, has led to important capital investments, and has strengthened the university's research capacity. Increased intramural funding, intellectual property, private-sector partnerships and spinoff commercialization opportunities are among the additional economic benefits for North Carolina.

Estimated Impact

To assess whether UCRF is achieving its goal of stimulating the economy, UNC hired the UNC Center for Competitive Economies (C3E) at the Frank Hawkins Kenan Institute of Private Enterprise to replicate the economic evaluation conducted in 2011 by SRA International. Using the same methodology used by SRA International, the C3E estimated the UCRF's immediate and ongoing impact on state income growth and employment. The Fund's overall economic impact was estimated as the sum of its direct and indirect and induced economic impacts. Direct impact resulted from two major sources: expenditures from UCRF itself and expenditure of directly UCRF-attributable research funds awarded to UNC by federal, foundation, and other sources. The indirect and induced impact was calculated by applying standard multipliers to direct expenditures.

From 2008 to 2012, UCRF total allocation (adjusted for tax receipt shortfalls) was $209.0 million, including $47.8 million in FY 2011-2012. Assuming a mid-range multiplier for the indirect impact, C3E estimated that:

- **The overall economic impact of UCRF expenditures on North Carolina's income from 2008-2012 is $968.0 million.** The total includes $420.9 million in direct impact and $547.1 million in indirect and induced impact
- **The $47.8 million allocation in FY 2011-2012 resulted in an economic impact of $293.8 million -- approximately $5 in additional impact for every dollar expended.**

UNC Fiscal Year	2008	2009	2010	2011	2012	Total
Direct Impact at UNC (millions)						
Personnel Expenditures *	3.3	16.5	25.4	26.0	27.3	**98.6**
Capital Investment and Other Non-Personnel Expenditures *	3.2	17.8	22.3	22.2	12.5	**77.9**
Extramural Research Support **	5.0	24.8	57.4	69.2	88.0	**244.4**
Total Direct Impact (millions)	11.5	59.1	105.1	117.4	127.7	**420.9**
Indirect & Induced Impact on NC Income * **	15.0	76.8	136.6	152.6	166.1	**547.2**
Total Impact on NC Income	**26.5**	**135.9**	**241.7**	**270.0**	**293.8**	**968.0**

* Mid-range case: assumes partial out-of-state "leakage" of fringe benefits (50%) and capital purchases (50%)
** UCRF-attributable Extramural Research Support indexed by grants received by faculty newly hired or retained, plus grants to those receiving Innovation Awards or generated through UCRF-funded infrastructure
*** Assumes Direct Impact multiplier of 1.3, consistent with recent applications

UCRF has generated a significant number of jobs:

- **Over its first four years UCRF expenditures created an estimated 5,056 new jobs.** The estimate, developed by SRA International, was based on the effects of UCRF expenditures on North Carolina employment from 2008-2011. It assumed an employment multiplier of 17.25 jobs/$1M in direct impact spending, an approach that is consistent with U.S. Department of Commerce methodology and base-case multiplier assumptions in National Institutes of Health economic impact analyses. In FY 2012, UCRF direct impact increased by over $10 million and created additional jobs.

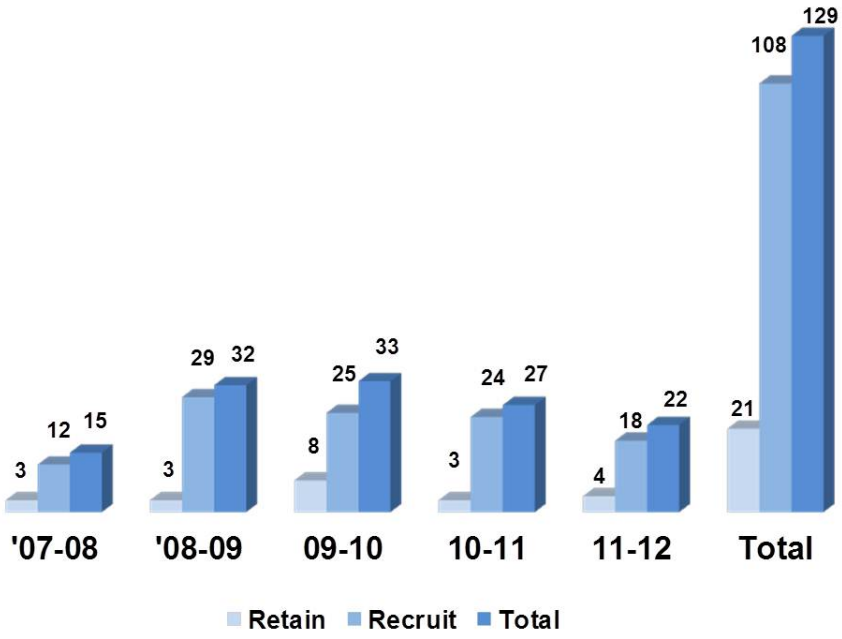
Faculty Job Creation and Retention

Faculty achievement drives the UCRF. They lead the teams that conduct the groundbreaking research to push the boundaries of our knowledge and advance cancer treatment, prevention and early detection. Faculty also hire staff, buy equipment, earn research funding from outside North Carolina, and train students and fellows. UCRF has had a tremendous positive impact on cancer research faculty at UNC:

- **Recruitment:** From 2007 through July 2012, UCRF has supported the recruitment of 108 faculty members in the College of Arts and Sciences, the Schools of Nursing, Public Health, Medicine, Pharmacy and Journalism and Mass Communication. These faculty members are developing a wide range of research programs in nanomedicine, quantitative biology, cancer genomics, health outcomes, health communications, multiple cancer types, and other areas critical to improving cancer prevention, diagnosis and treatment in our state.

- **Retention:** During the past five years, UCRF support has led to the retention of 21 faculty members.

Recruitment and Retention by Year



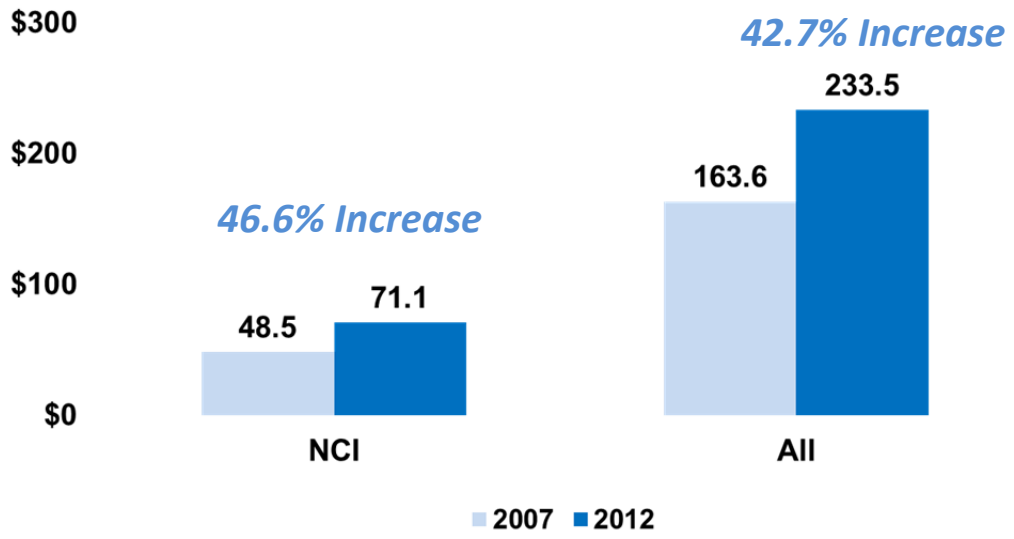
Extramural Funding Growth

Virtually all extramural funds come to UNC from outside North Carolina and add to the state's economy. The UCRF's Strategic Plan establishes extramural research funding – particularly competitive federal funding – as a key metric for UCRF success. Using this metric, UCRF funds are being invested effectively. They are leveraging extramural research funds for North Carolina at a time when national funding levels are decreasing, keeping the state at the forefront of research nationally. Key trends include:

- **FY 2011-2012 funding from outside sources that is directly attributable to the UCRF totaled $88.0 million in annual total cost dollars.**
    - This amount is based on a snapshot of active attributable extramural funding held by faculty in the first quarter of FY 2012-2013. The dollars represent one year of funding. A complete list of the awards is included in the Appendix.
    - The attributable extramural funding has risen from $5 million in FY 2007-2008 as the positive effects of faculty recruitment and retention, technology enhancement, and developmental projects has accumulated. Many of the currently active awards will continue for several more years, and we fully expect new awards to add to the total.

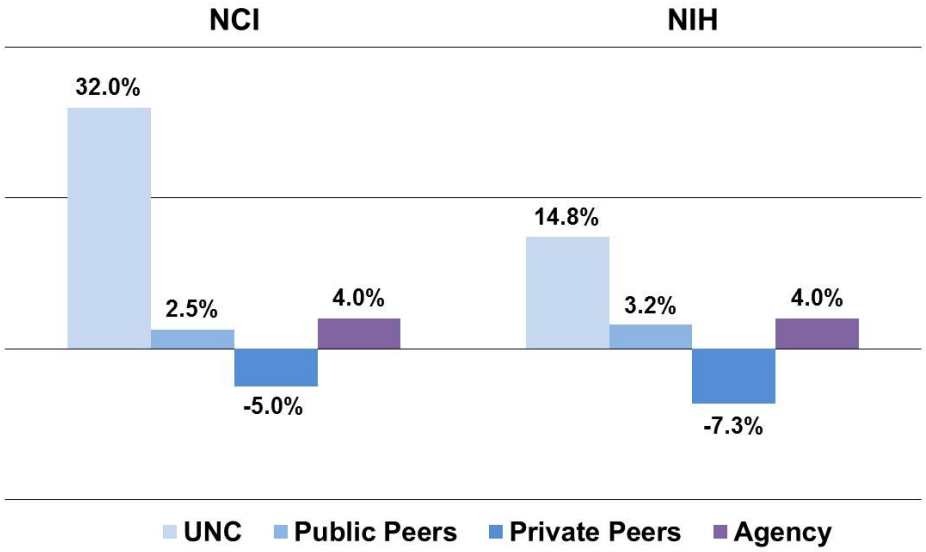
- **Between 2007 and 2012, extramural support to the members of UNC Lineberger Comprehensive Cancer Center increased from $163.6 million to $233.5 million; support from all National Cancer Institute sources grew from $48.5 million to $71.1 million.**

Growth in UNC Lineberger Extramural Funds ($ Millions)



- **Despite declining to flat federal funding, the National Institutes of Health (NIH) increased awards to UNC Chapel Hill faculty members between 2007 and 2012, while awards to many comparable institutions decreased during that time period.**
  - Overall, NIH awards to UNC Chapel Hill increased by almost 15 percent, significantly ahead of both public peer institutions (3.2% increase) and private peer (7.3% decrease).
  - National Cancer Institute awards to UNC Chapel Hill increased 32%, significantly ahead of both public peers (2.5% increase) and private peers (5.0% decrease).

NCI and NIH Funding Trends 2007-2012: UNC vs. Peers and Agencies



Intellectual Property, Innovation, and Entrepreneurship

The UCRF's focus on innovation has helped researchers create inventions, licenses, and patents.

- **Reports of Invention and Licensing Agreements have increased.** In the five years before UCRF was established, UNC Lineberger members reported 46 inventions and made 18 licensing agreements. In FY 2011-2012 alone, UNC Lineberger members and UCRF-assisted faculty were associated with 58 Reports of Invention and 25 licenses.

UCRF support also has promoted entrepreneurship that has created jobs and spinoff companies:

- **NC Kickstart:** The University Cancer Research Fund, in collaboration with UNC's TraCS Institute, is developing an entrepreneurial mindset at UNC. UCRF supports specialized staff that help faculty develop these start-up companies and maximize the use of intellectual property. In the past five years, 10 startup companies whose progress is directly attributable to UCRF-funded research have been launched, creating private-sector jobs.

Spinoff Companies Helped by UCRF	
Coordination Therapeutics	Enci Therapeutics, Inc.
Exigent Pharmaceuticals	Qualiber
G1 Therapeutics	XinRay
GeneCentric Diagnostics	XinNano Material, Inc.
Liquidia Technologies	Xintek

SUCCESS STORY: UNC-based company has exclusive licenses for cancer diagnostics

GeneCentric Diagnostics, Inc., a company co-founded by two UNC cancer researchers, has two new license agreements with UNC-Chapel Hill for promising technologies that target a tumor's molecular details to improve the way doctors diagnose different types of cancer and to allow oncologists and patients to make better informed treatment decisions.

Charles Perou, PhD, and Neil Hayes, MD, MPH, both UNC Lineberger members who are leading UNC's efforts in the $20 million Cancer Genome Atlas project, founded GeneCentric in 2011 with partners from Hatteras Venture. The company holds the license to the Lung Subtype Platform (LSP) technology, which can distinguish multiple subtypes of lung cancer based on a genetic "fingerprint" from a tumor sample.

Drs. Perou and Hayes also hold exclusive commercial rights to a 13-gene biomarker called "Hypoxia Signature" that is associated with cancer spreading to other organs and lymph nodes as well as poor outcomes for patients. Certain molecules promote angiogenesis, or the formation of new blood cells, which plays a key role in cancer as tumors need blood vessels to grow and spread, and it's believed that Hypoxia Signature could help doctors identify likely responders to drugs that would inhibit the growth of new blood vessels, thus reducing a tumor's ability to grow and spread.

SUCCESS STORY: Rachel Roper's pancreatic cancer vaccine work earns patent

East Carolina University-based UNC Lineberger member Rachel Roper, PhD, received a patent this year for her discovery of a poxvirus gene called A35R that suppresses the immune system. Poxviruses are commonly used to develop vaccines, but viruses' natural tendency to exploit vulnerabilities in human immune systems has been a roadblock in cancer vaccine development. Roper found that deleting A35R from the poxvirus weakens that tendency and, in turn, strengthens immune response to the vaccine.

Roper, Associate Professor of Microbiology and Immunology at East Carolina University's Brody School of Medicine, and UNC Lineberger member Emmanuel E. Zervos, ECU Professor of Surgery, received a UCRF Innovation Award in 2008 to help develop a pancreatic cancer vaccine based on a virus with the A35R poxvirus gene deleted. Roper also believes that A35R's role in suppressing the immune system could be beneficial in certain cases such as organ transplants, where transplanted organs are often rejected by a body's immune system.

RESEARCH OUTCOMES

The National Cancer Institute has given the UNC Lineberger Cancer Center an "exceptional" rating – its top rating for cancer centers – explicitly citing UCRF as a significant reason for the center's high rank. The "exceptional" rating has only been given to five of the nation's 40 recently reviewed NCI-designated cancer centers.

When full funding for the University Cancer Research Fund was reached in 2009, the Cancer Research Fund Committee, the oversight committee established by law, adopted a Strategic Plan to guide the most effective and responsible use of the state's landmark investment.

The Strategic Plan is composed of three primary tiers: Research Priorities, the Opportunity Fund, and Critical Infrastructure. This section of our report highlights noteworthy successes in each of these tiers.

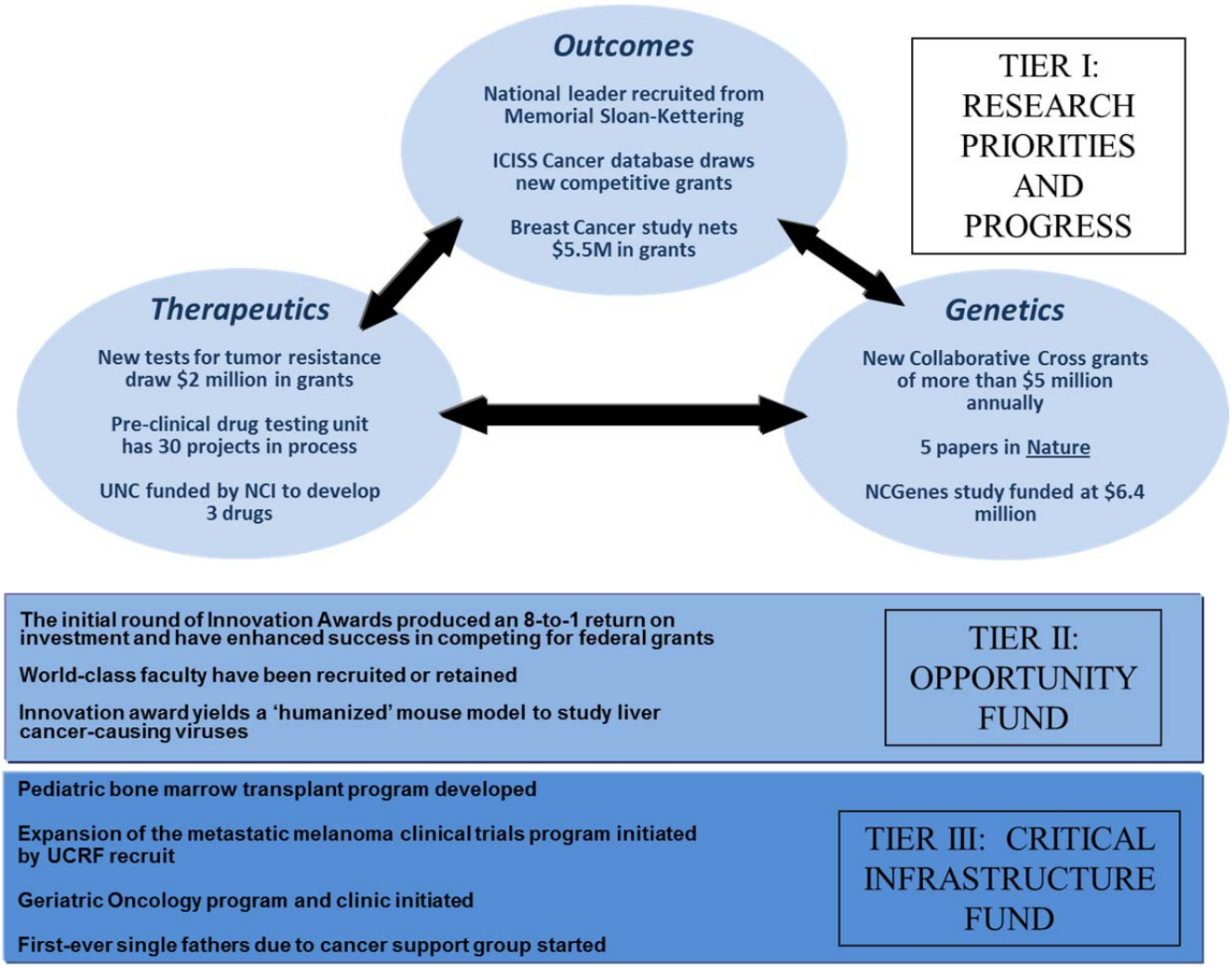
1) **Research Priorities:** A targeted number of initiatives where with focused investment in major scientific programs, disease-based initiatives, or cutting-edge research platforms, UNC could have substantial impact and become a world leader. The three research priority areas are as follows.

   - ***Understanding the Role of Genetics in Cancer Causation and Treatment*** : to discover the genes that predispose families to cancer and that predispose cancer patients to poor treatment outcomes – particularly by looking for the mutant genes in specific cancer subtypes that lead to cancer therapy failure.
   - ***Developing Novel Therapeutics:*** to devise new therapies targeted to the specific vulnerabilities of treatment-resistant cancers, and to develop new ways of delivering drugs and therapies to reduce toxic side effects for patients. This research priority relates to the genetics initiative, making key observations that will be turned into clinical applications as quickly as possible.
   - ***Optimizing NC Cancer Outcomes***: to build population-based data to track the occurrence and treatment of cancer across North Carolina in order to initiate research aimed at improving community prevention and early detection of cancer, and to enhance the quality of oncology and survivor care across the state. Our goal is to understand North Carolina's cancer problem at a level unprecedented in the nation and to design research interventions to rectify these problems at the community, health system, and practice levels.

2) **Opportunity Fund:** Allows UCRF to remain nimble, seizing research or clinical opportunities as they arise and providing the top minds in the field with the resources they need. Examples include competitive, innovative pilot projects; seed funds to recruit top researchers; support of leading-edge technology and equipment for use by multiple faculty members; and the development of shared research resources.

3) **Critical Infrastructure Fund:** Provides critical resources for cancer research that are not readily obtainable by outside funding but upon which future progress relies. Investing in imaging, informatics and fundamental research techniques ultimately provides clinician scientists with the tools to change patient outcomes. To do this requires enhancement of multidisciplinary excellence in cancer care and the development of a statewide infrastructure to help bring leading-edge clinical research and applications into community practices.

Progress Toward Strategic Goals



Research Priority 1: The Role of Genetics

The presence of certain genes could affect how much risk a person and their family members have of developing cancer and, in some instances, how well a patient responds to cancer treatments. The gene mutations in a patient's tumor give us information to predict the course of his or her disease and may help us choose the correct therapy. That's why cancer genetics – or the study of the genetic changes that determine how and why cancer develops – plays such a critical role in early detection, treatment, prevention and prognosis. UCRF investments are helping UNC emerge as a national leader in this fast-growing field of study.

UNC Leadership of National Collaboration yields important genetic discoveries that will change cancer care: UCRF invested in genomic technology that helped UNC become one of just 12 cancer centers in an unprecedented, large-scale collaboration by the National Cancer Institute and the National Human Genome Research Institute to categorize the genomic changes that occur in cancer. More recent investment by UCRF has permitted UNC to vault into a leadership role in this consortium. The Cancer Genome Atlas grant (TCGA) is a five-year award, bringing a total of $20 million in outside

funding to UNC. The project – which also includes Harvard University, Johns Hopkins University, Memorial Sloan-Kettering, and MD Anderson – is fueling rapid advances in cancer research including categorizing tumors in new ways, identifying new therapeutic targets, and allowing clinical trials to focus on patients who are most likely to respond to specific treatments.

Led by Chuck Perou, PhD, and Neil Hayes, MD, MPH, our group has performed the RNA sequencing and analysis for all the major TCGA reports. These include the research group in colon and rectal cancer, which published this summer that these two cancers are, genetically speaking, nearly indistinguishable. Researchers also found that colorectal tumors with high levels of genetic errors were more aggressive. The study is allowing doctors to identify new signaling pathways, which control gene activity during cell development, to improve the development of therapies that target colorectal cancer, the fourth most common type of cancer in both men and women.

Another TGCA study discovered potential therapeutic targets in a common type of lung cancer (lung squamous cell carcinoma) after comprehensively characterizing the squamous cell's genome. Dr. Hayes hosted the 30-person analysis group at the UNC Lineberger building and was a major author on the lung cancer report. The group found that a large number and variety of DNA mutations that appear to have important effects on the initiation and progression of lung cancer. Three families of enzymes, along with several signaling pathways, were identified as potential therapeutic targets. These findings should stimulate new clinical trials for patients with this type of lung cancer.

As noted in the highlights section, Dr. Perou and Katie Hoadley, PhD, hosted the National Breast Cancer TCGA Group Meeting and primarily authored this September's *Nature* paper providing the breast cancer data set. The impact was reported in the New York Times and Dr. Perou appeared on CBS News. The findings define in a genetic sense the different types of breast cancer and the presumed new targets in each.

UNCseq aims to create individualized patient cancer care: UNCseq (said like U-N-seek) is a new genetic sequencing protocol (LCCC 1108) designed to create a cancer treatment plan based on an individual patient's tumor. This protocol will be especially important for situations where standard therapeutic options are not effective or applicable. Under UNCseq, researchers will analyze tumor samples obtained from a biopsy or surgery, using next-generation sequencing to identify the molecular (genetic) changes that may influence outcomes or choice of therapy. If researchers find and validate a molecular alteration that can be treated with a drug targeted to that change, UNC oncologists will provide this information to the patient and their doctor so that they can discuss this treatment option. Findings may also provide patients with information leading to their enrollment in a clinical trial of a targeted therapy directed toward that molecular change. For scientists, the UNCseq protocol will help provide the genetic data needed to pursue new treatments and to test the effects of clinical therapies

currently being investigated. The launch of UNCseq will put UNC Lineberger at the national cutting edge of using genetic information in cancer therapy.

ENCODE project examines functions of DNA, proteins: Completed 10 years ago, the Human Genome Project identified tens of thousands of genes, and determined the sequences of three billion chemical pairs, in human DNA. Over the past five years, ENCODE – a collaboration of more than 400 researchers worldwide, including UNC scientists – has taken genomic research a major step further by working to understand not just what DNA is made of, but how DNA actually works. Jason Lieb, PhD, and his collaborators found that so-called "junk" DNA – those genes for which scientists haven't found a specific function – in fact serves a critical regulatory purpose, controlling which genes are active in the right cells at the right time. If the wrong genes are active in the wrong type of cell, diseases such as cancer can occur. Dr. Lieb noted in the *Nature* paper that he co-authored that there are 2.9 million pieces of regulatory DNA. Further study will aim to determine how these sites are involved in controlling gene activity.

UNC mouse genetics library fuels worldwide research: The most ambitious mouse genetics program ever devised, the Collaborative Cross is a UCRF-supported "library" of genetic material available to researchers worldwide. By enhancing scientists' ability to conduct systematic genetic mapping and analysis, the Collaborative Cross provides a fast track for testing new treatment and prevention approaches for cancer and other diseases.

Since 95 percent of the genetic material in mice is the same as in people, test results on mice are proving in many instances to be applicable to humans. But traditional lab mice have a very narrow range of genetic variation, so that test results can be efficiently translated to humans. The Collaborative Cross holds 450 strains of genetically manipulated mice and is nearly equivalent to human genetic diversity.

The power of the Collaborative Cross will be enhanced even more greatly by tools being developed by William Valdar, PhD, assistant professor of genetics. Dr. Valdar, who was recruited to UNC using UCRF funds, has received a 5-year, $1.4 million grant from the National Institute of General Medical Sciences (part of the National Institutes of Health) to strengthen statistical analysis of Collaborative Cross experiments. He will develop statistical methods so scientists can conduct complex trait analysis of genetically diverse populations, and will create a statistical framework so those diverse populations can be compared and contrasted more easily.

Research Priority 2: Drug Development and Delivery

The University Cancer Research Fund is helping UNC scientists develop therapies and delivery methods that effectively target vulnerabilities in cancer cells with less toxic effects on patients. It takes more than a decade to go through comprehensive testing of a new drug, and the US Food and Drug Administration approves only about 5 percent of drugs that make it through this process. With UCRF support, UNC is becoming a leader in finding a shorter path from lab to market – and to helping patients on a larger scale.

Drug discovery center promotes national collaboration: UCRF funds and funding from the UNC Eshelman School of Pharmacy led to the creation of the Center for Integrative Chemical Biology and Drug Discovery (CICBDD) at UNC-Chapel Hill. The CICBDD was established to bring medicinal chemistry expertise to bear on biological targets of therapies being developed. Director Stephen Frye, PhD, is the lead principal investigator for the North Carolina Comprehensive Chemical Biology Center, a UNC-based, NCI-designated center that engages in oncology drug discovery. The National Cancer

Institute has awarded the Center more than $6 million in the past two years to support research on small molecule inhibitors and therapies to fight childhood leukemia, kidney cancer and brain tumors. Housed in the Genetic Medicine Building with plans to move into the Imaging Research Building upon its completion in early 2014, the Center is co-founding a national academic drug discovery consortium with Johns Hopkins, Harvard and others. Patents and the first publications of UNC-developed drugs were submitted in the last 18 months.

Mouse models improve understanding of drug responses: UCRF enabled the creation of the Mouse Phase I Unit, which has established multiple models of human cancer that can be bred in genetically identical mice. These mice can develop breast cancer, pancreatic cancer, lung cancer, ovarian cancer, melanoma, and other types of cancer with 100 percent incidence at defined times – providing researchers with a way to test innovative therapies quickly and accurately. For example, these mouse models have enabled scientists to gain a better understanding of cancer's response to 55 anti-cancer drugs in the past year alone. Since 2011, MP1U has grown significantly, with a standing mouse colony producing three models of breast cancer, three models of melanoma and two models of lymphoma/leukemia. Additional models of melanoma, breast, bladder, ovarian and lung cancer are in development. MP1U has projects with 47 collaborators, including Merck, GSK, Pfizer and other private-sector companies.

SUCCESS STORY: V Foundation awards $600,000 Translational Grant combining genetics and drug development

W. Kimryn Rathmell, MD, PhD, Jason Lieb, PhD, and Ian Davis, MD, PhD, were awarded a 2012 Translational Grant from The V Foundation. Each one of them was awarded a V Scholar grant earlier in their careers. Dr. Lieb is a scientist who has made important fundamental discoveries about how genes are regulated and was retained with the help of UCRF; Dr. Rathmell is a disease focused physician-scientist who studies the genetics of kidney cancer; and Dr. Davis, also a physician-scientist, bridges those two with a lab focused on understanding broadly how DNA packaging impacts cancer.

The team hopes that the grant will help them find new approaches to renal cancer treatment by applying the entire spectrum of medical science. They want to start with fundamental questions about gene packaging and how gene regulation plays a role in the development of cancer, and to understand what goes wrong with genes that can lead to cancer.

UNC-linked company teams with venture partners to advance drug pipeline: G1 Therapeutics, Inc., (formerly GZero) has partnered with Hatteras Venture Partners to advance their drug discovery pipeline. Co-founded by Norman Sharpless, MD, Associate Director for Translational Research at UNC Lineberger, G1 is working on several new small-molecule inhibitors aimed at protecting organs against toxic side effects of radiation. The company was created based on Sharpless' UCRF-funded research at UNC that aimed to create a way to protect patients from cellular damage caused by radiation or chemotherapy, cancer treatments whose side effects can be devastating to patients. Hatteras' seed funding, along with support G1 has received from UCRF and other funding sources, will help G1 accelerate preclinical programs so that these drugs can be available to cancer patients.

New kinase test could boost therapeutic success: Agents that can block the activity of kinases that drive cancers are now entering human therapy. For example, Gleevec® has been extraordinarily successful turning a form of chronic leukemia into a treatable disease, while other molecules have shown great success in a small portion of lung cancers and melanomas. Unfortunately, however, in the case of lung cancer and melanoma, resistance develops and the tumors recur. To make advances in understanding resistance, UNC researcher Gary Johnson, PhD, and his colleagues have developed a method to test up to 70 percent of protein kinases simultaneously, giving investigators a glimpse of how cancers resist treatment so they can develop strategies to block that resistance. Of the 518 known human kinases – which are proteins expressed in human tissues that play a key role in cell growth – about 400 are expressed in cancers, but which ones and how many are actually active in tumors has been difficult to measure. This new technology uses kinase inhibitors to allow investigators to see how cancers evade treatment. The team hopes to use the new test to identify combinations of drugs to overcome therapy resistance and continue to effectively treat cancer. A patent application has been filed for the testing technology, and the team was recently awarded two grants totaling almost $2 million to research clinical applications of the test to examine the treatment responses for aggressive types of breast cancer. The first human clinical trial using the new diagnostic potential has received IRB approval and is enrolling patients.

UNC team reports evidence for using nanoparticles to improve chemotherapy: Combining chemotherapy and radiation is an approach used to treat many types of cancer because it makes a tumor more sensitive to radiation, but it subjects patients to the unwanted and often painful side effects of chemotherapy. A team of UNC researchers led by Andrew Wang, MD, who was recruited to UNC with UCRF support, have shown the potential of using nanoparticles to target cancer at the molecular level, making chemoradiotherapy treatment more effective and avoiding damage to normal cells. Docetaxel is a proven drug for head and neck cancers that leads to unwanted side effects. Scientists developed a biodegradable nanoparticle version of docetaxel that targets the folate receptor, which is overexpressed in head and neck and other tumors. They found in pre-clinical studies that the folate-targeted docetaxel is more effective than the traditional drug, and also more effective than a non-targeted nanoparticle version. The novel particles had fewer side effects. Dr. Wang is also leading efforts to develop nanoparticle "carriers" to deliver drugs previously thought to be too toxic for humans. These carriers show promise in developing new strategies to fight cancer, and safely and effectively reviving the use of drugs that have been previously abandoned because of side effects or other problems.

SUCCESS STORY: UNC nanotechnology expert Joseph DeSimone nets major funding, national honor

UNC scientist Joseph DeSimone, PhD, a pioneer in using nanotechnology to improve the diagnosis and treatment of cancer, this year received one of the highest honors that a US scientist or engineer can receive: election into the National Academy of Sciences.

The Academy recognized DeSimone's groundbreaking work in nanomedicine. He and his students invented a technology called PRINT (Particle Replication in Non-wetting Templates) to become the first to manufacture precisely engineered nanoparticles to make advances in medicine. His research led to the formation of Liquidia Technologies, a Triangle-based nanotechnology company created to further develop PRINT and UCRF support stimulated the cancer applications of PRINT. Liquidia received a $10 million investment last year from the Bill & Melinda Gates Foundation to support the development and commercialization of safer and more effective vaccines and therapeutics. Its first product – a nanoparticle flu vaccine – is in clinical trials.

With Joel Tepper, MD, DeSimone also co-leads UNC's Carolina Center of Cancer Nanotechnology Excellence (C-CCNE), received a five-year, $13.6 million NCI grant last year to support multidisciplinary nanotechnology research. This is the second phase of the NCI's Alliance for Nanotechnology in Cancer; UNC also received funding in the first phase. X-ray technology developed at UNC by Otto Zhou, PhD, and colleagues holds great promise in fighting cancer and will also be part of this research effort.

DeSimone, Director of the Kenan Institute of Private Enterprise, Chancellor's Eminent Professor of Chemistry in the College of Arts and Sciences at UNC and the William R. Kenan Jr. Professor of Chemical Engineering at N.C. State University, has more than 280 publications and more than 130 patents. UCRF investments have successfully retained him at UNC and have continued to support collaborative nanotechnology research.

SUCCESS STORY: Carey Anders, MD, and William Kim, MD, honored with Damon Runyon Cancer Research Foundation Clinical Investigator awards.

Dr. Anders received a 2012 Clinical Investigator Award and Dr. Kim received a continuation of his 2011 Clinical Investigator Award. Both are assistant professors of medicine and members of UNC Lineberger Comprehensive Cancer Center.

Dr. Anders' award is one of six made by the Damon Runyon Cancer Research Foundation. She will receive a three-year $450,000 grant to support the development of her cancer research program. Her work is focused on improving survival for women with breast cancer brain metastases. Her goals are to provide a novel therapy for women, who, at present, have few therapeutic options, while laying the foundation for future clinical trials incorporating biomarkers to enhance therapeutic response and survival for women with HER-2-positive breast cancer brain metastases.

Dr. Kim will receive an additional two years of funding totaling $300,000 to complete a promising avenue of research. His grant is made possible through the William K. Bowes, Jr. Foundation, and Connie and Robert Lurie. His work is focused on renal cell carcinoma, a type of kidney cancer that has poor prognosis when diagnosed at later stages. He will use the continuation grant to identify new drug combinations by applying novel proteomic technologies in collaboration with Gary Johnson, PhD, with a goal of rapidly moving these findings to the clinical setting for improved treatment of renal cell carcinoma. Dr. Johnson is professor and chair of the department of pharmacology and co-leader of UNC Lineberger's Molecular Therapeutics program.

Research Priority 3: Improving Cancer Outcomes

Population-based, data-rich resources will help researchers better understand our state's cancer problems so that interventions can be developed to rectify these problems. UCRF has been instrumental in developing these tools to improve community prevention and early detection of cancer, and enhance the quality of oncology and survivor care across North Carolina.

Integrated database provides foundation for research: UCRF funding has helped build and support the Integrated Cancer Information and Surveillance System (ICISS), a system built on North

Carolina data that will provide a model for the nation. The database provides a rich informatics resource for scientists. ICISS already links multiple population, clinical, and other data sources including health care claims data, Medicare, Medicaid, State Employees, and Blue Cross Blue Shield of North Carolina. It is beginning to be used to measure outcomes of cancer control activities, especially among vulnerable subgroups and communities that have been traditionally under-represented. Projects will eventually include other academic centers in North Carolina and there are already two projects formed in collaboration with Duke University outcomes researchers. ICISS claims data are expected to cover about 80 percent of the North Carolina population with cancer. This will enable scientists to examine what treatments are most effective, what parts of the state need more access to cutting-edge cancer care, what environmental or economic factors affect prognosis, and other important issues that will better our understanding of cancer – and enhance our efforts to improve cancer outcomes.

SAS collaboration uses data analytics to assess outcomes: A partnership forged in 2011 with SAS Institute will allow doctors to evaluate the effectiveness of cancer care by harnessing deep pools of data about patients' risk factors, the characteristics of their cancer, and treatment results. UNC Hospitals' patients who choose to enroll in the study will be tracked intensively from diagnosis through survivorship, integrating data about the patient's genetic inheritance, their tumors' genetic mutations, clinical experience and treatment. Two thousand patients have already given their consent to participate in the Cancer Survivorship Cohort with a target population of 10,000 over the next five years. This will be one of the nation's largest data-rich, survivorship cohorts, enabling our academic-SAS partnership to create important new analytical approaches. Doctors will be able to analyze what worked and what didn't work for the patient's care, specifically following patient response, toxicity issues, and patient quality of life post-treatment. This large, long-term study will use data analytics to look for ways to initiate new, improved patterns of cancer care for better short and long-term outcomes.

Comparative effectiveness studies offer real-world insights: The tightly controlled lab and clinical studies of new therapies are needed to test their safety and effectiveness, but this testing does not often reflect the reality of how therapies are being used on a more diverse population of patients and in a less controlled environment. Comparative effectiveness research is emerging as a more practical way to evaluate the effects – both positive and negative – of health care interventions, by examining how they work in a more general population. UNC is conducting collaborative research with Harvard University to examine comparative effectiveness for cancer treatments, providing real-world context to the use of drug therapies. Ronald Chen, MD, did a large-scale observational study that entailed a review of Medicare records on more than 12,000 men treated for early-stage prostate cancers from 2002 to 2007, as well as follow-up information on recurrences and side effects. Dr. Chen compared conventional conformal radiation therapy (CRT) to intensity modulated radiation therapy (IMRT), finding that IMRT is better at reducing prostate cancer recurrence and lessening side effects than the more traditional CRT. But he also found that proton therapy – which is growing in popularity as a prostate treatment but costs at least twice as much as other prostate treatments – was no more effective than IMRT and, in fact, caused more complications. His findings suggest that despite the newfound popularity (and expense) of proton therapy, IRMT better controls prostate cancer and results in fewer side effects and thus should continue to be the therapy of choice in most cases.

Breast cancer study seeks reasons for health disparity: The Carolina Breast Cancer Study, now in Phase III, has been a groundbreaking longitudinal study of breast cancer incidences in African-American and Caucasian women. The study has found that black women under the age of 45 are more likely to be diagnosed with aggressive types of breast cancer than are women of European ancestry. The Phase III NCI program grant will result in a better understanding of this significant health disparity by collecting information on more than 3,000 North Carolina breast cancer patients to explore biological, environmental and epidemiologic reasons for the difference in cancer incidence. Collection of detailed treatment data across a population such as North Carolina's is difficult, but CBCS III will do it. This will provide an opportunity to analyze the impact of health services access and delivery on the survival of breast cancer patients, with a particular emphasis on race and socioeconomic status.

This groundbreaking study was led by Robert Millikan, DVM, PhD, Barbara Sorenson Hulka Distinguished Professor of Cancer Epidemiology, who passed away in October 2012. He was a tremendous advocate for breast cancer patients and a brilliant scientist, and his loss is profound. His leadership in this research area led to a $19.3 million grant in 2011 from the National Cancer Institute, a member institute of the National Institutes of Health, to support the Phase III breast cancer study. Dr. Millikan was also a lead investigator on the UNC Specialized Program of Research Excellence (SPORE) in Breast Cancer, which was recently renewed by NCI for $10 million over the next five years. A team consisting of Andrew Olshan, PhD, Melissa Troester, PhD, Jeanette Benson, PhD, and Shelley Earp, MD, are taking over Dr. Millikan's multiple roles so that CBCS III and Dr. Millikan's legacy will be fully realized.

Health-e-NC focuses on community-based pilot projects: A community-based partnership for statewide cancer prevention called Health-e-NC (Health for Everyone in North Carolina), aims to reduce risk factors, increase cancer screenings and referrals, help people make more informed decisions about their care options, and improve prevention efforts across the state. Working with the UNC Gillings School of Public Health, UNC Lineberger members are involved in community-based pilot programs in tobacco prevention, exercise programs for cancer survivors, and strategies to improve cancer screenings in underserved areas. This spring, Health-e-NC partnered with eight cancer clinics across the state to hold *Cancer Transitions* workshops that provide survivors with individualized advice and information on issues such as exercise, nutrition, emotional health, quality of life, and medical concerns after treatment ends. Another pilot program of preventive strategies, delivered by minimal in-person and maximal social media avenues, has been implemented with a test group in Kannapolis.

Tier 2: Opportunity Fund

Although UCRF investment has focused on the three Tier 1 Research Priorities, research and knowledge continue to evolve and opportunities for new areas of strategically important cancer research will develop outside the initial priorities. UCRF investments have strengthened and broadened UNC's cancer research capabilities and, through highly competitive internal seed grant funding, have stimulated new research and attracted extramural grant funding.

UCRF Innovation Awards – Developing the Next Generation of Cancer Research. UCRF promotes innovation at UNC, with a highly competitive internal award process that has stimulated cancer research across the public health, clinical and basic science spectrum as well as providing data with which to seek new external funding.

- From 2007 to 2012, UCRF conducted seven rounds of competition and received 416 applications.
- Rigorous peer reviews led to 69 awards, a funding rate of about one in six, for a total of $11.3 million.
- Follow-up results from the initial round in 2007 found that the $2.4 million in awards resulted in more than 20 extramural grant awards with projected total funding (all years) of $20.4 million. The awards directly or indirectly contributed to one clinical trial, two patent filings, and two startup companies. Follow-up from subsequent rounds is ongoing.

SUCCESS STORY: Basch joins UNC Lineberger faculty to lead cancer outcomes research program

Ethan Basch, MD, MSc, has joined UNC Lineberger as associate professor of medicine and Director of Cancer Outcomes Research. UCRF funding helped to successfully recruit Basch from Memorial Sloan-Kettering Cancer Center in New York.

Dr. Basch is a nationally recognized medical oncologist and health services researcher whose expertise is in patient-reported outcomes, clinical informatics, and drug regulatory policy. His work focuses on developing ways to better evaluate patient symptoms and adverse events, with a goal toward improving patient safety and outcomes through more availability of information during drug development, stronger doctor-patient communication, and better practice of cancer care. He also leads an ongoing NCI initiative to develop a patient-reported adverse event monitoring system for use in clinical research and oversees multiple large trials using patient-reported endpoints.

SUCCESS STORY: Matthew Milowsky recruited to co-lead urologic oncology team

Matthew I. Milowsky, MD, associate professor of medicine, has been appointed co-director of UNC's urologic oncology program. Prior to his recruitment he led the translational research program for urologic cancers at Memorial Sloan-Kettering Cancer Center, where he focused on the development of novel therapies for patients with advanced bladder and other urothelial cancers. As director of genitourinary oncology research at Cornell University, Dr. Milowsky received a Department of Defense Award to develop anti-prostate specific membrane antigen (PSMA) targeted therapy in patients with advanced prostate cancer.

Dr. Milowsky was principal investigator for the Bladder Cancer Oncogenome Project, which aimed to identify molecular changes in bladder tumors that could serve as targets for individualized treatment strategies. He joined UNC this year thanks to recruitment funds from the UCRF.

Tier 3: Infrastructure

Nurse navigators help patients find their way: Six oncology nurse navigators have provided care for more than 3,000 patients residing in over 40 counties in North Carolina. Over 31,000 individuals across the state have been reached through community outreach and educational events. These programs show that Oncology Nurse Navigators improve communication between patients, doctors, and caregivers by helping patients and family members connect with community resources, and collaborate across their medical team on all aspects of cancer care from screening to diagnosis, treatment and survivorship.

Telemedicine cites expand reach of tumor expertise: The University Cancer Research Fund's investment in telemedicine has extended the reach of UNC's experts to 28 sites in more than a dozen communities across the state. Affiliated physicians videoconference with a team of UNC experts from a wide variety of specialties who meet and discuss treatment plans for patients during weekly Multidisciplinary Oncology Tumor Boards. Doctors at Wilson Medical Center, Rex Hospitals, Moses Cone, Marion L. Shepard Cancer Center, and Mission Hospitals participate in Tumor Board conferences as patient cases warrant. Cancer research conferences between East Carolina University and UNC occur on a bi-monthly basis. The videoconferencing system is also used to facilitate the distribution of Lunch and Learn lectures. In selected specialties lacking in rural communities, physician-to-patient consultations also are provided via telemedicine. The Comprehensive Cancer Support Program provides mental health support for cancer patients. In addition, the Clinical Genetics Program offers genetics counseling to patients via telemedicine.

Clinical Excellence and Outreach: The objective of this component of UCRF is to assemble an outstanding group of specialist oncologists so that the North Carolina Cancer Hospital can offer nationally competitive consultative care to patients. Under the best of circumstances, 30 to 35 percent of patients diagnosed with cancer will die from the disease. It is the objective of UNC's Cancer Center to create the knowledge that changes those outcomes. This means that we need to have a faculty that keeps up with the best tenets of current cancer care, and, through our outreach programs, makes those available to patients across the state. Our faculty is intimately engaged in clinical and translational research. Several examples of research launched this year by UCRF-supported faculty and infrastructures, including technological tools that will keep us at the forefront of cancer research, include the following.

The use of imaging research to analyze cancer care: The UNC Biomedical Research Imaging Center (BRIC), which is supported in its cancer aspects by UCRF, has just taken delivery of the fourth MRI/PET scanner in the United States. The advent of combining computerized tomography and PET scanning a decade ago created numerous opportunities for following cancer patients. This next generation of technology allows simultaneous acquisition of MRI images and the functional information provided by PET scanning. UNC Lineberger and the BRIC combined hold a competition for proposals of how to use this technology, and several clinical translational research projects have already been launched. The technology will probably be particularly useful in the abdomen and pelvis, and therefore our gastrointestinal, genitourinary, and GYN oncologists have developed pilot projects.

The renal cancer group has a remarkable project in which they will perform MRI/PET scans prior to surgery for the removal of renal masses. The renal cancers will then be subject to genomic sequencing by our UNCseq team. Various regions of the kidney tumor will be sequenced, and the mutational spectrum will be compared to the MRI and PET scanning images. This unique project will link the characteristics of the images with specific mutational analysis.

The GYN Oncology pilot project will attempt to guide the extent of surgery by assessing MRI/ PET scanning prior to an operation. The extent and specific mode of surgery (whether open surgery or robotic surgery) are often difficult to decide before the surgeon has been able to see the operative field. It will be tested whether this new machine enables the surgeon to assess the anatomy and spread of the tumor before actually seeing it. It is our hope that the combination of MRI and PET scanning will enable more accurate pre-planning of the surgical approach. A similar project has been planned by the team that cares for rectal cancer patients. The rectum is a particularly difficult place to operate, and the decision about whether to perform an operation that allows the patients to continue to have normal bowel function, again, is difficult without open visualization of the operative field. This project will test whether MRI/PET can accurately determine the extent of the disease and, therefore, help doctors decide the most appropriate operative approach.

Using molecular markers in the clinic: The ability to predict the course of any individual's cancer outcome would be extraordinarily valuable in planning therapy while paying attention to that patient's quality of life. If current therapy will not work on a subset of patients, it is important to *not* subject them to toxic therapies that will be ineffective. We would also like to quickly advance patients into appropriate clinical trials offering better care options. Finally, if it is clear that therapeutic options

are not going to work, we need to help the patient plan for comfortable, high-quality end-of-life care. Predicting outcomes using standard pathologic and radiologic examinations is imperfect and outdated. As we have described in the genetics section, it is our faculty's strongly held opinion that genomic testing of the tumor will be more effective in the long run.

Virtually every disease type has projects ongoing in this area. We have achieved an international reputation for prognostic and predictive genomic tests in breast cancer, and we are evolving genomic signatures in lung cancer, which are in the process of being validated. The progress in breast cancer has resulted in UNC intellectual property licensed to an international company, which has already obtained approval for marketing in Europe. This company is entering negotiations with the FDA for approval in the United States. UNC intellectual property in this arena has been used to launch a Research Triangle located start-up, GeneCentric.

A number of our clinicians who treat specific cancers are creating these types of prognostic and predictive models based upon genomic data. One interesting project, led by Jen Jen Yeh, MD, is an attempt to understand the possibility of surgical cure of pancreatic cancer. This devastating disease is operable in less than 20 percent of the patients, and yet only 5 percent of these patients have successful surgery that allows a 5-year survival. The surgical procedure is extensive, and both patients and clinicians would benefit from a better understanding of who will have a successful surgical intervention. Dr. Yeh has performed genomic analysis on pancreatic cancer patients and created a six-gene signature that is better than any other prognostic indicator at determining who will have long-term survival. She has published on this work during the last year. The cooperative effort between our clinicians, geneticists, and biostatisticians in the School of Public Health indicates the important collaborative and team science nature of UNC Lineberger research.

Geriatric Oncology: It is clear from demographic analysis that the population of the United States is aging, and the incidence of cancer rises after the age of 65. With the baby boomers now reaching this age, and given their projected life span into their late 70s and 80s, the incidence of cancer in the elderly is becoming a much greater issue. In the past, doctors and oncologists have tended to not treat people over the age of 75, yet with appropriate treatment this group may well live a decade or more. There is a dearth of geriatricians in this country, and there's particularly a lack of oncologists trained in understanding cancer in this age group. With UCRF, we were extremely fortunate to recruit Hyman Muss, MD, an acknowledged leader in breast cancer research and the winner of multiple national awards for his work in geriatric oncology. Through his recruitment, UNC is having and will continue to have a profound impact on geriatric oncology. First, Dr. Muss has set up a joint training program with the geriatrics division in the Department of Medicine to train geriatric oncologists. Second, with UCRF support, he is creating one of the nation's largest databases of elderly cancer patients, monitoring their treatment, outcomes, and quality of life. The database will soon reach 1,000 participants, and he is beginning to accrue patients at other sites around the state of North Carolina. Third, in concert with UNC Lineberger Associate Director for Translational Research, Norman Sharpless, MD, Dr. Muss is validating a biomarker of health and aging, which we believe will be predictive of who will do well with appropriate therapies. Doctors are prone to believe that they can, by looking at a patient, determine whether that person is an "old" 75-year-old, or a "young" 75-year-old. Using patients' white blood cells, Drs. Muss

and Sharpless have devised a test that can actually quantify this relative age. They are testing it to determine whether they can predict which patient will do well (respond to therapy with low toxicity), as opposed to those in whom our therapy is doing more harm than good. They are soon to publish about this exciting program.

Understanding and reversing the toxicity inherent in allogeneic bone marrow transplantation (BMT): Stefanie Sarantopoulos, MD, PhD, a UCRF recruit from Harvard, has set up a program to understand and hopefully devise a therapy for complications of bone marrow transplantation.

There are two types of marrow transplantation. The first involves harvesting the patient's marrow, followed by high-dose chemotherapy in an attempt to eliminate the leukemia or myeloma in the patient. That therapy results in obliteration of the patient's stem cells that play a key role in creating blood cells. Infusion of the harvested autologous (i.e., the patient's own) bone marrow restores the ability to make red and white blood cells. A more dramatic form of BMT involves harvesting and then transplanting bone marrow from another person. The advantage of this allogeneic (i.e., another person's) bone marrow is that the new immune system can attack the patient's leukemia if it recurs. However, a substantial group of patients end up with a devastating complication in which the new bone marrow attacks the patients themselves, referred to as graft vs. host disease. Dr. Sarantopoulos is a world expert in understanding how B lymphocytes – white blood cells involved in the immune system – can drive graft vs. host disease. Her extensive studies using human patient materials have been facilitated by UCRF funding for tissue procurement, as well as her own research start-up funds. She has published her first paper from this research, indicating that a specific B cell growth factor is potentially involved in triggering graft vs. host disease. She has obtained federal funding to continue this research, which will be aimed at a developing a therapy that will ameliorate this condition.

BUDGET AND EXPENDITURE INFORMATION

UCRF Funding Sources

The 2007 law establishing the UCRF states that North Carolina should provide a minimum of $50 million annually for cancer research under UNC Hospitals, the UNC Lineberger Cancer Center, or both. The Fund initially received $25 million in 2007 and $40 million in 2008 before reaching its full funding amount of $50 million in 2009.

The UCRF is supported by three funding sources: tobacco settlement funds, taxes on other (non-cigarette) tobacco products such as snuff, and state appropriations. The Fund receives $8 million per year in tobacco settlement funds, according to the law. Approximately $16 million in state appropriations is allocated annually. Since 2009, however, total funding has fallen short of the $50 million objective stated in law due to lower than expected receipts from the tax on other tobacco products**.**

FY 11-12 Anticipated and Actual Fund Revenue	$ Amount *
Anticipated	
State Appropriation	16,020,000
Tobacco Trust Fund Transfer	8,000,000
Projected OTP Tax Receipts	25,980,000
Total	50,000,000
Actual	
State Appropriation	16,020,000
Tobacco Settlement Fund Transfer	8,000,000
Actual OTP Tax Receipts	23,820,819
Total	47,840,819
Shortfall Due to OTP Tax Receipts	**(2,159,181)**

*** Rounded to the nearest dollar**

Fund Balance

For the third year in a row, receipts from the tax on other tobacco products (OTP) were less than projected. The FY11-12 shortfall was more than $2.1 million. In FY 10-11 the shortfall was $1.8 million; in FY 09-10, it was $1.0 million.

This year the UCRF had a negative carryover of $3.3 million due to past shortfalls in collections, making the 2012 actual budget roughly $44.5 million. The UCRF year-end fund balance is $39,881.63.

FY 11-12 Budget and Expenditures	Amount $
Anticipated Budget	
Revenue	50,000,000
Carryover from FY11	(1,513,206)
Carryover from unrealized FY11 OTP tax receipts	(1,830,350)
Total	**46,656,444**
Actual Budget	
Revenue	47,840,819
Carryover from FY11	(1,513,206)
Carryover from unrealized FY11 OTP tax	(1,830,350)
Total	**44,497,263**
Expenditures	**44,457,381**
Balance	**39,881**

*** Rounded to the nearest dollar**

Restrictions on the Use of UCRF Monies

The General Assembly created the University Cancer Research Fund as part of the 2007 budget. G.S. 116-29.1, by which the Fund was created, established the Fund as a special revenue fund in the Office of the President of the University of North Carolina. This law, included as an appendix to this report, explicitly states that allocations from the fund "shall be made in the discretion of the Cancer Research Fund Committee and shall be used only for the purpose of cancer research under UNC Hospitals, the Lineberger Comprehensive Cancer Center, or both."

As the Cancer Research Fund Committee developed the UCRF Strategic Plan in 2009, each potential use of UCRF resources was evaluated according to the following questions:

- Will it address the needs of North Carolina, in terms of the goal of reducing the cancer burden in the state?
- Can we be world class at it? (Does it build on existing strengths, and is there an opportunity to lead?)
- Is there a strong economic model/justification for UCRF investment?

Guided by these questions, a clear set of ground rules was developed to determine how UCRF funds would be best spent. Planners, including then-UNC President Erskine Bowles, agreed that UCRF funds should focus major resources on a limited set of opportunities to have the greatest impact; fund

initiatives where UNC has the opportunity to establish a leadership position; be self-sustaining and provide leverage for additional extramural funding; build fundamental cancer-related research capabilities that benefit UNC research programs; and enhance North Carolina's economy by creating jobs, intellectual property, and startup companies.

To maximize the effectiveness of the state's cancer investment and to ensure wise and responsible use of the funding, the Strategic Plan also imposed additional restrictions on the use of these funds. It was determined that UCRF funds *should not*:

- Invest broadly in an effort to make incremental improvements everywhere;
- Provide funding that would limit future flexibility;
- Undermine faculty innovation and competitiveness by eliminating the need for extramural grant funding;
- Substitute for existing university or health system funding or new philanthropy;
- Make expenditures based upon institutional or other needs outside cancer research; or
- Negatively impact other research on campus, for example by appropriating shared research infrastructure or resources.

Expenditures of State Funds related to UCRF

As required by G.S. 116-29.1(g), the table below provides an accounting of expenditures of state funding related to the University Cancer Research Fund. Additional details regarding these expenditures can be found as appendices to this report.

More than half the funding from UCRF has been to recruit world-class researchers to North Carolina. Only 1.2 percent of the total UCRF budget is used for ongoing administrative expenses.

Categories	YTD Actual
Strategic Plan Categories	
Tier 1: Research Priorities	
Understanding Genetics	6,796,152.29
Developing Novel Therapies	8,731,321.44
Optimizing Outcomes	5,907,400.66
Tier 2: Opportunity Fund	7,027,248.47
Tier 3: Critical Infrastructure	
Clinical Excellence – Research & Outreach	8,124,384.57
Research & Tech Development and Training	7,870,874.06
Total	**44,457,381.47**

CONCLUSION

The University Cancer Research Fund has been a remarkable investment for our state. It is fueling innovative research that will significantly advance cancer care, and is connecting communities all across our state with better resources for care. Economically, it is leveraging unprecedented amounts of outside funding and this year produced a 5 to 1 return on investment. We appreciate the legislature's continued investment in UCRF and we utilize these funds responsibly and strategically. While we are already seeing results from this investment, we believe the Fund's biggest and most important impact will be in the years to come – when we change the odds in the fight against our state's most lethal disease and significantly reduce the burden of cancer on North Carolina's population.