



Biomedical & Healthcare Task Force Recommendations

Virginia Beach Bio Task Force | January 2015

Acknowledgements

This report was prepared by the Virginia Beach Biomedical and Healthcare Task Force, which is led by Mr. Thomas Frantz and Mr. Rony Thomas, with support from the City of Virginia Beach Department of Economic Development. A complete list of Task Force Members can be found in Appendix A.

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Introduction

On March 13, 2014, Virginia Beach Mayor William D. Sessoms, Jr. announced the creation of a Biomedical and Healthcare Task Force at his 2014 State of the City Address. The Mayor noted that the diversification of our economy is critical to ensure Virginia Beach's continued economic success and pointed to the biomedical and healthcare sector as the way to achieve this goal. In outlining his vision, the Mayor stated the following:

“It’s time to establish Virginia Beach as a destination for groundbreaking research and development, and headquarters of some of the world’s leading innovators in healthcare, bio-technology, pharmaceutical development and healthcare delivery systems. Partnering with Tidewater Community College, Old Dominion University, Eastern Virginia Medical School, Hampton University, Regent University, Virginia Wesleyan College, the College of William and Mary, Sentara Healthcare, Bon Secours Health System, LifeNet Health, and WellPoint’s Amerigroup, we will attract the best minds, and establish a healthcare and pharmaceuticals research and policy center... where ideas of the future are generated and incubated — ideas that lead to new inventions, new alliances, and new frontiers in healthcare. This will be the newest sector in our economy! By doing so, we can create more jobs, we can strengthen and diversify our economy, and we can enhance our quality of life. And students who go to college and concentrate in STEM fields will be able to come home to the best jobs — right here in Virginia Beach and Coastal Virginia.” – Mayor William D. Sessoms, Jr.

Mayor Sessoms appointed Tom Frantz, CEO and Chairman of Williams Mullen, as Chairman. Mr. Frantz asked Rony Thomas, President & CEO of LifeNet Health, to serve as Vice Chairman.

The mission of the Bio Task Force is to develop a plan for a bio-medical and healthcare hub in the Princess Anne Commons area of Virginia Beach. In order to maximize the benefit to the region, it was decided that industry assets and leaders should be utilized from Richmond to Virginia Beach. The Task Force is comprised of industry leaders from biomedical and life science companies, universities, leading research and development institutions, and private equity firms, including:

- Bon Secours
- Children’s Hospital of the King’s Daughters
- College of William & Mary
- Eden Capital
- Eastern Virginia Medical School
- Hampton University Proton Therapy Institute
- Jefferson Lab
- MCV Hospitals
- Norfolk State University
- Old Dominion University
- Operation Smile

- Riverside Health System
- Sentara Healthcare
- Tidewater Community College
- Virginia Biotech Park (Richmond)

Due to overwhelming interest, a second group of industry leaders were asked to serve in an advisory capacity and provide additional support and input when needed. The complete list of Task Force and Advisory Committee Members can be found in Appendix A.

Under Tom Frantz's leadership, the Task Force met once a month beginning in June of 2014 and began developing a plan, which included the hiring of a consultant to assist.

Consultant – Facility Logix

At the direction of the Task Force, an RFP was issued in the spring of 2014 for a consultant to perform a market analysis and to assist the task force in creating a list of recommendations for a plan to strengthen and, in some cases, create a biomedical and healthcare cluster in the region. After review of all submitted proposals, a consultant out of Maryland, Facility Logix, was selected to perform the in-depth analysis of our existing market and determine what strengths the region could leverage in order to gain a larger and more critical mass of biomedical and life science companies.

The consultant performed extensive research and conducted stakeholder interviews with all of the major players in the region. This report provided not only recommendations for areas of focus and the region that should be covered, but also detailed potential financial commitments that will be necessary from the city, state, and private sector in order to succeed.

The complete market assessment and report from Facility Logix will be made available in late February 2015.

Context

The Bio Task Force was tasked with creating a structure onto which the recommendations of Facility Logix could be attached. Thus, the Task Force created a set of guiding principles that should determine the region and areas of focus, along with a set of goals that should be achieved by successfully implementing the defined recommendations.

Guiding Principles

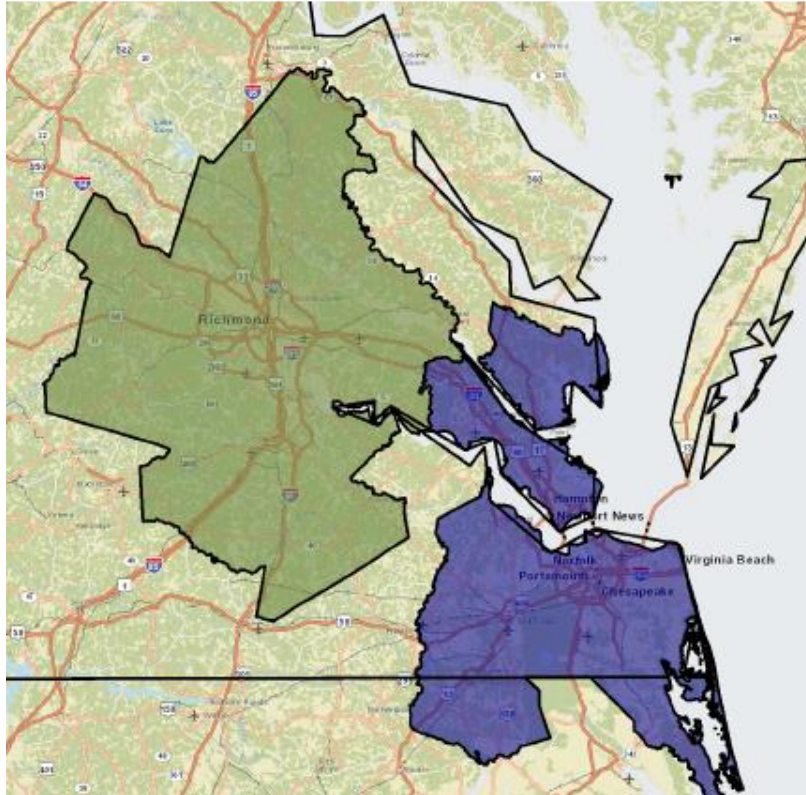
- Establish our region & city as the center for advanced bio-tech and healthcare research and industry "on the East Coast"
 - Establish a hub in Virginia Beach's Princess Anne Commons.
 - Physical location of hub participants will be region-wide.
- Must be an economic driver for the regional economy.
- Must drive substantial job creation in the region (focus on higher-income jobs).
- Progress should be measurable and reportable annually.
- Use existing regional assets and resources in hub development when appropriate.
- All institutions of higher education, hospitals and large healthcare enterprises in the region will be asked to partner in achieving the mission.
- Regional governmental authorities and private entities will work together.
 - Obtain state and federal funding for hub development and attract required private equity investment.

Goals

- Capitalize on our areas of expertise (which should be affirmed and defined by Facility Logix)
- Attract companies from the following sectors:
 - Big Data
 - Analytics
 - Healthcare Population Management, Analysis, & Informatics
 - Centers of Excellence in Treatment and Research
 - Life Sciences
 - Bio-Medical and Advanced Healthcare Manufacturing
- Attract public funding and private equity to assist in the process.

Region Covered

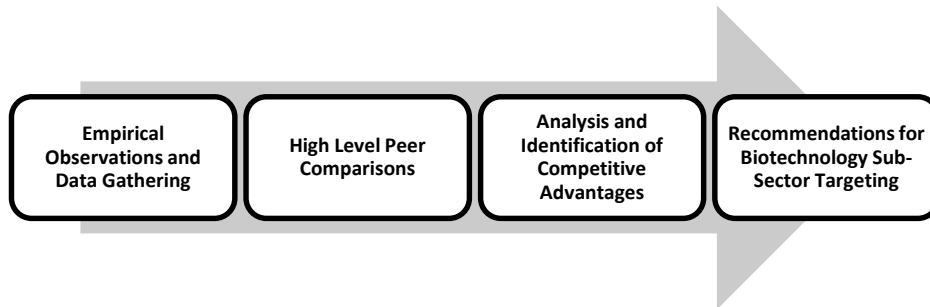
In order to leverage all of the assets in the eastern Virginia region, it was concluded that the Virginia Beach-Norfolk-Newport News Metropolitan Statistical Area, also known as “Hampton Roads”, (in blue) should be combined with the Richmond Metropolitan Statistical Area (in green). For the purposes of the Task Force’s report, these combined MSAs shall be referred to as “the region.”



This regional definition was affirmed by Facility Logix, which stated that this combined region “is an effective way to include a critical mass of universities, research activities, diverse and educated workforce along with a myriad of healthcare professionals, and to deliberately augment the Virginia Veteran’s Administration Region 5.”

Areas of Focus

The consultant, with assistance from the Biomedical and Healthcare Task Force, evaluated the regional market to determine the strengths, weaknesses, opportunities, and threats (SWOT) to the creation and enhancement of a biomedical cluster (or clusters) in the region. The methodology for evaluation is illustrated in the graphic below.



Graphic Source: Facility Logix

Strengths were discovered across the region, in areas such as the Eastern Virginia Medical School Streilitz Center for Diabetes, the Sentara Heart Hospital, and the Virginia Commonwealth University Brain Injury Rehabilitation Program. Leading diabetes researcher Dr. Jerry Nadler wrote a white paper on the importance of diabetes research and the unique assets that exist not only in the patient population but also in available data from healthcare providers. This white paper can be found in Appendix B.

Based upon the strengths of the market the consultant recommended, and the Task Force affirmed, that the areas of focus for the region should be as follows:

- Diabetes
- Cardiovascular Disease
- Neuroscience
- Traumatic Brain Injury/Wounded Warrior-Related Injuries

The in-depth market assessment and SWOT analysis will be made available in the report from the consultant.

Recommendations

According to the Brookings Institution, the healthcare sector will represent approximately 25% of the nation's gross domestic product in 20 years. This presents a unique opportunity for the region to grow a vital sector of the economy and further diversify and lessen the strong reliance on military and defense-related industries, which currently comprises a large portion of the region's gross domestic product.

After completion of the market assessment and consultation with Task Force leaders, Facility Logix developed the following recommendations designed to:

- Capitalize on current strengths and promote future benefits
- Diminish weaknesses and prevent potential problems
- Spur economic development and create high-paying, sustainable jobs

Recommendation One: Enhance the Vertical Entrepreneurial Support Ecosystem

The region should focus on enhancing efforts to grow indigenous companies, which could result in long-term, sustainable benefits including diversifying and growing the overall economy and creating high-paying jobs. The horizon for implementation and subsequent realization of success based on this recommendation will be long-term. This is particularly important due to the fact that the region has had limited success recruiting large life science and biomedical companies to the region.

Actions

- Create a Virginia Impact Grant that offers small awards to start-up companies for a variety of uses such as business plan analysis, market analysis, product development, etc.
- Determine sources of funding that could be used to address the high cost of laboratory fit-out for poorly capitalized life science firms. This could take the form of lease guarantees; fit-out laboratory suites; or capital improvement funding grants or loans.
- Create a sector-specific seed fund to invest in early stage ventures.
- Provide life science and biomedical specific resources such as Mentors and Coaches at existing co-work, incubation, and accelerator facilities. Build a roster of advisors and mentors from outside the academic community.
- Offer programs such as Small Business Innovation Research Grant (SBIR) workshops to educate the region's higher education researchers on how to obtain SBIR grants and/or other funding opportunities. If programs are offered currently through any of these institutions, open the enrollment to include faculty from other schools. Partner as appropriate to align and better leverage resources.

Suggested Timeline and Budget

Six months to ongoing. Needs to be provided and funded for a minimum of five (5) – ten (10) years. Significant effort and financial requirement. Funding will likely be needed on an annual basis and be split among private participants, as well as federal, state, and local governments.

Desired Outcome

Enhanced entrepreneurial activity leading to economic diversification and job creation.

Measuring Success

- Increased number of sector-focused new company formations
- Increased angel investment in regional companies

Recommendation Two: Enhance Translational Research & Commercialization Competitiveness

Bolster the translational research competitiveness from among the region's core focus areas, which include diabetes, cardiovascular disease, neuroscience, and traumatic brain injury/wounded warrior-related injuries. This enhanced focus on research will serve to create a "deeper bench" of entrepreneurial researchers who generate commercializable discoveries.

Actions

- Help a newly established regional organization secure funding to support the recruitment of at least two star research hires. This effort will likely extend across a seven to ten year time frame.
- Establish Co-Principal Investigator relationships between higher education institutions. Collaborative arrangements are more likely to meet with success in securing grants and would allow the region's investigators to co-label and co-market their expertise with well-regarded global researchers such as Dr. David Cifu at VCU.
- Leverage experts in the region, such as Dr. Jerry Nadler and his reputation and expertise in the field of diabetes research.
- Explore campus wide approaches to sector-specific entrepreneurship by working with regional institutions and the military.
- Streamline and enhance the technology licensing process at the region's institutions.
- Support efforts to enhance regional broadband connectivity, allowing researchers to perform more in depth analysis in fields including bioinformatics and data analytics.
- Hold networking events, first under the leadership of the Task Force and then under the direction of the new regional organization, that will allow discussion to occur both intentionally and spontaneously. These events and the discussions that will take place will result in continually growing collaborations and expanded business and personal partnerships and serve to break down silos of expertise across the region.

Suggested Timeline and Budget

Mid-term and ongoing. Needs to be provided and funded for a minimum of five (5) – ten (10) years. Significant effort and financial requirement from multiple partners. Some funding will likely be required annually and be split among private sector stakeholders and federal, state, and local government entities.

Desired Outcome

Increase in technology licensing and commercialization activity.

Measuring Success

- Increased translational research and commercialization of discoveries

- Enhanced research competitiveness within the Commonwealth of Virginia as measured by the ability to compete for and secure Commonwealth funded opportunities as available

Recommendation Three: Develop and Launch an Organizational Entity to Support Bold Development Plan

Establish a public-private organizational entity that would lead efforts to secure the funding and support needed to “prime the pump” and grow the region’s life science and biomedical cluster. This organization will assist economic development efforts in guiding and implementing an economic gardening strategy to exploit regional expertise in the targeted life science and biomedical sector.

Actions

- Hold meetings with the leadership of similarly successful organizations from around the country, such as BioHealth Innovation (BHI) and Cortex, to evaluate pro’s and con’s and discuss lessons learned.
 - BHI is a 501 (c) 3 non-profit regional innovation intermediary active in Maryland and specific to the life science and biomedical sector.
 - Cortex Innovation Community in St. Louis, also a 501 (c) 3 non-profit regional entity.
 - Funding for each of the above suggested models came from corporate and community stakeholders.
- Develop a plan and annual and capital budgets for the organization
- Solicit financial contributions from stakeholders and partners to underwrite establishment of the selected model
- Select and implement model
- Recruit an industry-seasoned veteran with private sector commercialization experience to lead new organization
- Develop a memorandum of understanding or partnership agreement that includes all of the region’s municipalities and counties, as well as institutions of higher education, and aligns their interests and strategic plans with that of the new organization.

Next Steps

The Biomedical and Healthcare Task Force will remain in place until this new organizational entity is formed and a CEO/Executive Director is hired. The Task Force, a list of whose members can be found in Appendix A, will also solicit input from life science and biomedical business development specialists from all regional municipalities and counties. Their mission will be to define the criteria for membership and to create a job description for the new organization’s first leader.

Once a leader is selected, he/she will craft strategic plan which should fall in line with those of all member institutions and organizations. The CEO/Executive Director will also bring a plan for

funding back to the state legislature before the end of 2015. After the organizations' structure and financial needs are outlined, the work of the Task Force will be folded into the new organizational entity.

Suggested Timeline and Budget

Six months to one year. Significant effort and financial requirement from multiple partners. Funding will be required on an annual basis and be split among the organization's members/participants as well as federal, state, and local government entities.

Desired Outcome

A single, regional entity that becomes the home for this sector-focused regional economic development effort.

Measuring Success

- Formation of a public-private entity
- Entity leadership in place
- Funding support for entity secured

Ask

In order to successfully implement these recommendations, the Biomedical and Healthcare Task Force requests \$500,000 from the Commonwealth of Virginia for the purposes of standing up the regional organization described in recommendation three and hiring its first CEO/Executive Director. That individual will be responsible, based upon input from regional organizations and municipalities, for crafting a financial request from the Commonwealth for future budget cycles. The funds will also be utilized to develop a plan and budget for the organization.

Appendix

Appendix A – Bio Task Force & Advisory Committee Membership Lists

Bio Task Force Members

Prefix	First Name	Last Name	Company	Title
Mr.	Thomas	Frantz	Williams Mullen	CEO and Chairman
Mr.	Rony	Thomas	LifeNet Health	President and CEO
Mr.	Paul	Hirschbiel	Eden Capital	President
Dr.	Jerry	Nadler	Eastern Virginia Medical School	Director, Strelitz Diabetes Center
Dr.	Richard	Homan	Eastern Virginia Medical School	Provost and Dean
Mr.	David	Bernd	Sentara Healthcare	Chief Executive Officer
Mr.	James	Dahling	Children's Hospital of the King's Daughters of Hampton Roads	President and Chief Executive Officer
Dr.	John	Broderick	Old Dominion University	President
Mr.	John	Duval	MCV Hospitals	Chief Executive Officer
Mrs.	Carrie	Roth	VA Biotech Park	President & Chief Executive Officer
Mr.	Drew	Weisenberger	Jefferson Lab	Phd. Group Leader, Radiation Detector and Imaging
Mr.	Eddie	Moore, Jr.	Norfolk State University	Interim President & Chief Executive Officer
Mr.	Keith	Gregory	Hampton University Proton Therapy Institute	Executive Director

Mr.	Michael	Kerner	Bon Secours	Chief Executive Officer
Dr.	Bill	Magee	Operation Smile	Executive Director
Dr.	Edna	Baehre-Kolovani	Tidewater Community College	President
Mr.	Taylor	Reveley	College of William & Mary	President
Mr.	William	Downey	Riverside Health System	President and Chief Executive Officer (CEO)
Mr.	Joseph	Butz	Sentara Healthcare	Senior Vice President, Cardiac and Transplant Services (Sentara Heart Hospital)
Dr.	Carl	Hartman	Sentara Healthcare	Medical Director, Cardiac Services
Mr.	Karl	Thorpe	Sentara Healthcare	Strategic Expansion Manager

Bio Task Force Advisory Committee Members

Mr.	Bob	Armstrong	National Center for Collaboration in Medical Modeling and Simulation	Director of Research and Business Development
Mr.	Gordon	Berkstresser	LifeNet Health	Chief Financial Officer
Mr.	Robert	Bohannon	Health Diagnostic Laboratory, Inc.	Director of Corporate & Government Affairs
Ms.	Linda	Bright	Linda Bright Consulting	President & CEO
Mr.	Robert	Broermann	Sentara Healthcare	Vice President/CFO
Ms.	Ann	Crenshaw	Kaufman & Canoles	Attorney
Dr.	Morris	Foster	Old Dominion University	Vice President of Research

Mr.	Jeffrey	Gallagher	Virginia Biotechnology Association	Chief Executive Officer
Mr.	Mike	Grisham	Virginia Biosciences Health Research Corporation	President and Chief Executive Officer
Dr.	William	Harvey	Hampton University	President
Mr.	Pat	Hogan	University of Virginia	Executive Vice President and Chief Operating Officer
Mr.	John	Littel	GR Healthcare Solutions	Partner
Ms.	Tonya	Mallory	Health Diagnostic Laboratory, Inc.	President and Chief Executive Officer
Mrs.	Anna	McKean	Health Diagnostic Laboratory, Inc.	Chief Commercial Officer
Dr.	Robert D.	McKeown	Jefferson Lab	Deputy Director of Science
Dr.	Mike	Rao	Virginia Commonwealth University	President
Mr.	Richard	Severinghaus	The Aegis Technologies Group, Inc.	Director Life Science Programs
Dr.	Thomas	Skalak	University of Virginia	Vice President for Research
Dr.	John	Sokolowski	Virginia Modeling, Analysis & Simulation Center (VMASC)	Executive Director
Ms.	Julie	Summs	College of William & Mary	Director of Economic Development and Business Innovation
Dr.	Thomas	Thames	Sentara Princess Anne	President/Administrator
Rear Admiral	Elaine	Wagner	Naval Medical Center Portsmouth	Commander
Dr.	William	Wasilenko	Eastern Virginia Medical School	Associate Dean for Research

Summary

12.3% of Americans 20 years and older have diabetes, and almost 40% have pre-diabetes! Within the Commonwealth of Virginia, diabetes is a major health issue. The Eastern Virginia Medical School (EVMS) Strelitz Diabetes Center (SDC) is the only established diabetes center available to patients in Virginia, and indeed for much of the mid-Atlantic region. EVMS has established collaborations with other academic institutions in Virginia and beyond and has received major recognition from the NIH and other diabetes funding agencies.

There are clearly unmet medical needs within the scope of diabetes care that can lead to useful commercial products, including products that target prevention, early diagnosis, and treatments. Several opportunities exist for integrated clinical programs with academic-industry-government collaboration using new technology and to attract Industry to the region. These include (1) data mining and analysis as a tool for discovering improved individualized treatment guidelines, (2) a cardiovascular diabetes and biomarker program, (3) targeting inflammatory complications of diabetes, including the growing unmet medical need of non-alcoholic steatohepatitis (NASH). (4) New uses of innovative technology including sensors and new developments in biologic and small molecules. Our region has great assets that can complement expertise and resources in other parts of the Commonwealth to advance commercialization and reputation in Diabetes and Metabolism Technology, clinical care and research.

The Diabetes and Obesity Epidemic

Diabetes rates have reached epidemic proportions. The International Diabetes Federation (IDF) Diabetes Atlas, 6th edition, was recently released; it provides the latest astounding data that 382 million people currently have diabetes worldwide, with a rise predicted to almost 600 million within a generation. Both forms of diabetes are caused by loss of functional pancreatic beta islet cells, and this leads to reduced insulin production. This serious disease leads to increased mortality and large health costs due to serious complications, such as kidney failure, blindness, amputations, and cardiovascular disease. In 2013, roughly half of all deaths due to diabetes were in people under the age of 60; by the end of the year, diabetes caused 5.1 million deaths and cost \$548 billion dollars in healthcare spending throughout the world. A very high percentage of people with diabetes and pre-diabetes develop cardiovascular disease or other disorders such as liver disease or certain forms of cancer. It is predicted that up to one third of the US population will have diabetes given the current trends.

Within the Commonwealth of Virginia, diabetes is a major health issue. Many locations in Virginia lie within the National Diabetes Belt, reflecting the highest rates of diabetes in the US. In addition, several areas within the Hampton Roads region show a disproportionate mortality rate due to diabetes. Additionally, due in large part to the ongoing obesity epidemic, there continues to be a projected increase in the rate of diabetes growth for years to come. The health risks of diabetes span all age groups due to the significant morbidity and mortality due to complications of eyes, nerves, liver, kidneys and cardiovascular system (CVD).

The diabetes and obesity epidemic has now led to non-alcoholic fatty liver disease (NAFLD) becoming the most common cause of chronic liver disease in Western countries. Non-alcoholic steatohepatitis (NASH) is an especially dangerous form of the disease which can lead to liver cirrhosis and hepatocellular carcinoma (HCC). There are no reliable biomarkers or approved treatments for NASH or other major complications of diabetes. The prevalence of NAFLD is much higher than previously believed in overweight patients with Type 2 diabetes. In diabetes, fatty liver can rapidly progress to a dangerous form of liver disease called non-alcoholic steatohepatitis (NASH), cirrhosis and even HCC. HCC is one of the most common cancers in the world and prevalence is rapidly increasing in the US due to the epidemic of obesity, metabolic syndrome and Type 2 diabetes.

There are clearly unmet medical needs within the scope of diabetes care and NASH that can lead to useful commercial products. This includes products which target:

- Prevention,
- Early diagnosis, and
- Treatment.

The Eastern Virginia Medical School (EVMS) Strelitz Diabetes Center (SDC) is the only established diabetes center available to patients in Virginia, and indeed for much of the mid-Atlantic region. EVMS has just been selected as the only program in Virginia to be part of a multimillion-dollar translational research consortium funded by the National Institutes of Health (NIH) to understand ways to identify and prevent pancreatic Beta cell damage in Diabetes. This presents us a major opportunity to develop a nationally recognized program in Diabetes and Cardiovascular Disease in our region and throughout the Commonwealth. It is expected that the combined clinical and research programs will become a regional and national destination of choice.

History of Diabetes Research and Care in the Region

Eastern Virginia Medical School leads the region in the field of diabetes care and research. A renowned team of experts, which includes clinical care personal, research scientists and educators, make up the EVMS SDC in Norfolk, Virginia. Together EVMS works with local health care partners at Sentara and Bon Secours and regional institutions and engages in research that advances the medical field's knowledge of prevention, early diagnosis, and treatment of diabetes and its complications.

Grant support at the SDC comes from various esteemed organizations such as the NIH, the American Diabetes Association and the Juvenile Diabetes Research Foundation. Although excellent basic laboratory and clinical research facilities are located on campus, EVMS also collaborates with experts from other institutions. Within Virginia, these include The Medical College of Virginia/Virginia Commonwealth University School of Medicine, The University of Virginia, Virginia Tech, Old Dominion University, College of William and Mary, Norfolk State University and Hampton University. Beyond Virginia, EVMS works with several major university centers in various parts of the US and World.

Historically, The EVMS SDC has been successful in securing intellectual property and patents surrounding diabetes and diabetic complications. In addition, several technologies have been translated from preclinical work into clinical studies and start-up biotech companies. Investigators at

EVMS have also developed a quality of life tool that is in widespread clinical trials all over the world for testing new treatments for neuropathy.

In Virginia, we have a great opportunity to develop advances in the diagnosis, prevention and treatment of diabetes and metabolic complications given the expertise in our academic institutions. We also have opportunities to partner with companies such as Health Diagnostic Laboratory and Global Genomics Group, LifeNet Health and other innovative companies developing sensor technology. Seed (Angel) fund support and targeted recruitment of thought leaders in the field to our region will greatly accelerate progress and opportunities to spin out new companies and attract other established companies to the region. We have a great opportunity to benefit economically by using our regional academic institutions to increase the workforce for high paying jobs. We are also in an excellent position to develop a Nationally-recognized program to treat and improve outcomes of cardiovascular disease and NASH due to diabetes and pre-diabetes. Sentara has the only nationally ranked heart program in Virginia, and the Strelitz Diabetes Center has great expertise in treating and preventing diabetes complications. Dr. Arun Sanyal at VCU runs the major US Network for testing new treatments for NAFL and NASH.

The improvement in quality of care and safety metrics also provides for a significant financial benefit to our hospital systems and population in the Commonwealth. This program will also form the platform for attracting companies to the region to provide advanced technology and development of new products.

Examples of Opportunities for the Biotechnology and Life Sciences Business

A: Advances Using “Data Mining Technology” to Enhance Care of Diabetes Patients with Cardiovascular Disease

As one goal of this new initiative, we propose development of an integrated clinical program with academic-industry-government collaboration using new technology for data mining and analysis and as a tool for discovering new targets and treatment pathways. This “Big Data” program will facilitate a robust best practice approach that will be a model for other programs and be competitive for additional federal funding.

Diabetic patients, particularly type 2 diabetics (T2D) are at significantly high risk for cardiovascular events and mortality after suffering a *myocardial infarction* (MI) or developing congestive heart failure. A recent, large-scale study examined the prevalence of undiagnosed diabetes or pre-diabetes and associations with ischemic outcomes in patients with acute coronary syndrome (ACS). Undiagnosed diabetes was associated with greater 30 day death or MI. One year mortality was greater among known diabetics. These results are similar to other studies indicating that undiagnosed diabetics presenting with an acute coronary event have increased morbidity and mortality. T2D patients older than 75 have an increased risk of readmission and also have higher risks of hypoglycemic events. Also compared to younger diabetics, those 80 years or older are 2.5 times more likely to present to the emergency department (ED) with an insulin adverse event and 5 times more likely to be emergently hospitalized for an event. However, diabetic patients aged 65-79 had the highest total overall proportion of hospitalization (33%).

We are in an excellent position in the Commonwealth to develop a nationally recognized program in Virginia to treat and improve outcomes of cardiovascular disease due to diabetes and pre-diabetes. We have outstanding health systems with the only nationally ranked heart program and a well-connected leading diabetes center with great expertise in treating and preventing diabetes complications. From 1997 to 2011, the number of people aged 35 years or older with diabetes and (self-reported) heart disease or stroke increased from 4.2 million to 7.6 million. In 2011, among people with diabetes aged 35 years and older, 5.0 million reported having coronary heart disease; 3.7 million reported having other heart disease or conditions. The diabetic statistics at Sentara Heart Hospital mirror the national pattern. Cardiac surgical statistics show that 67% of this population have diabetes. Of the 67% with diabetes, 38% are classified as "new onset." Sentara Heart Hospital has an opportunity to partner with EVMS and other Industry-academic partners to develop a nationally recognized program in Diabetes and Cardiovascular disease.

Combined use of "best practices" and new technology will also have a major impact in improving quality of life and reducing health care costs due to diabetes. The translation of best practices and improvement in diabetes outcomes has been challenging, with close to half of patients in the USA failing to achieve the currently recommended goals for glycemic, blood pressure or lipid control.

In Virginia, we have an excellent opportunity to utilize new technology to mine large sets of electronic data and apply this information to improved outcomes and reduced healthcare costs for patients with diabetes. Biomedical research is increasingly data driven with researchers and clinicians routinely generating and using large diverse datasets. However, the ability to manage, analyze, and integrate the data is limited due to lack of access to tools able to utilize "unstructured" big data sets. While individual labs and research consortium generate diverse quantities of data, an even greater source is clinical data in electronic medical records (EMR) whose value can be enormously useful if data can be integrated and interrogated using modern data mining technology.

Current EMR systems are not designed to capture unstructured, nonstandard data such as narrative discussions, dictations, or radiologic imaging. In addition, EMR systems do not adhere to a cross system interoperability standard, which isolates patient information and hinders sharing between caregivers or sites of patient care. Technologies are available that could be adapted for EMR system data mining as well as non-electronic medical data. These powerful analytic tools could be utilized in several innovative processes for real-time and predictive models in selected populations to be studied. Several examples are included below to illustrate how EMR data can be utilized with innovative Big Data mining technology.

1. Use the EMR data for synthesis of disparate information to look at the impact of known traditional risk factors (e.g., hemoglobin a1c, lipids, tobacco use, body mass index) for cardiovascular (CV) disease, thereby generating a pool of patients who would benefit from intensive risk factor (RF) reduction.
2. Take advantage of the database to learn something new. For example, using the same criteria as above, generate a cohort of patients with multiple CV RF who DO NOT develop complications.
 - a. This research would be an opportunity to identify distinct biochemical, genetic, or chemical substances which are naturally occurring and protecting them.
 - b. Take this commonality among patients with diabetes but who do not develop complications, and translate it to new therapies.

3. Use the EMR database to look at events associated with hospital admission for patients with diabetes.
 - a. This could encompass anything from missed appointments, prescription refills (indirect measurement of compliance), prior hospitalization, etc.
 - b. This may provide insights to caring for high risk patients more effectively and with less cost.
4. Use the EMR database to provide best practice predictions of diabetic patients' highest risk to go on to develop microvascular complications such as nephropathy.
 - a. To date, despite similar blood sugars, the factors leading one patient to develop complications as compared to others remains unclear.
 - b. Databases also provide a springboard for investigators to be competitive for NIH grant funding ("Big Data" initiatives).

In order to accomplish these goals, computer scientists, statisticians, and laboratory scientists will need to be recruited. EVMS in partnership with Sentara Health System will be applying to the State Eminent Scholar Program for funds to recruit a well-respected leader in Outcome Health Analytics Research.

B. Biomarker Development Using Advanced Technologies and Clinical Resources in the Region

Powerful techniques, including highly sensitive proteomics and lipidomics as well as access to unique human samples, offer an unprecedented opportunity for disease and complication prediction using biomarkers. Partnerships fostered by the consortium can help rapidly bring forward novel targeted therapeutic treatments.

Armed with this new information and potential targets, new methods of diagnoses and therapies can be developed. As stated in Section 1 of this White Paper, "The Diabetes and Obesity Epidemic", there exist unmet medical needs within the scope of diabetes care that can lead to useful commercial products, including medical products which target prevention, early diagnosis, and/or treatment of diabetes and related metabolic disorders.

- a. *Prevention.* The opportunities to develop diagnostic tests to prevent diabetes by detecting the loss of insulin-producing cells or beta cells in both type 1 and type 2 diabetes would represent a major advance for the field. Loss of beta cells is a key biomarker in diabetes; research may enable detection of 'at risk' individuals, such as the sibling of a child with type 1 diabetes. State-of-the-art technologies that would be needed to develop these early tests include various "Omics" methods and sensor technology. Development of such tests benefit from access to unique patient samples, highly trained scientists, and state-of-the-art laboratory facilities. At Sentara Heart Hospital, there exists the most advanced cardiac imaging technology available to help validate new biomarkers and targets for therapy. Also, in our region today are imaging resources at both Old Dominion University and Jefferson Lab that would be important in the validation of diagnostic technology. EVMS is developing a highly developed bio-repository of tissue and fluid samples, and EVMS health care partners can incorporate these advanced technologies to develop personalized medicine and wellness programs to both improve healthcare across our region and attract regional and national referrals. Additionally, there is a company in Northern Virginia that has developed unique biosensor technology that could greatly advance diabetes care and prevention. This

company is excited to partner with the Strelitz Diabetes Center and other healthcare organizations in our region and may potentially relocate to the new Research Park.

- b. *Early Diagnosis and Treatment.* As beta cell loss may occur over a period of a few months to years, these diagnostic tests would serve as useful tools for early diagnosis and may allow for early therapeutic intervention and better control of the disease. There is also a unique opportunity to utilize advanced technologies to predict risk of complications so early treatment can be initiated. EVMS has an advanced Proteomics and Lipidomics Core that has the most up-to-date equipment including novel “Imaging Proteomics” capabilities. These technologies are now being applied to identify novel biomarkers in the pancreas that are unique to Type 1 or Type 2 diabetes. These analyses could lead to identification of new treatment targets to prevent complications of diabetes or progression of Beta cell failure. EVMS is the only program in the Mid-Atlantic States to be invited to participate in two major international consortia to identify biomarkers of beta cell damage.

C. Development of Treatments for Inflammatory Complications of Diabetes and Obesity including NASH.

Another major set of objectives for the Diabetes Academic – Industry Consortium will be to foster development of innovative treatments to prevent, treat, and reverse diabetes or NASH and related inflammatory complications. NASH treatment and mitigation represents a major growing unmet medical need. Our region has the expertise and clinical population - including a leader of the US Consortium to test new treatments for NASH - to address this major disorder. Outstanding talent resides in academic and industry sites within the Commonwealth in areas including, but not limited, to drug development, technology for improving wound healing, and technology-enhanced diagnostic sensors. Related to NASH treatment, there also exists an unmet medical need for small molecule or biologics approaches to prevent or treat the core defects seen in type 1 and type 2 diabetes. Again, developing these therapies would require not only seed funds, state of the art technologies and laboratory facilities, but also experts in medicinal chemistry, statistics, and drug development. EVMS has developed expertise in the area of small molecules and biologics for targeting pathways leading to inflammatory complication of diabetes. A large and growing portfolio of companies across our region are interested in developing new devices to enhance treatment and monitoring of patients with diabetes and related complications; these outstanding health care industry partners provide the ideal opportunity to test new treatments.

Current Assets and Partnering Opportunities

Our region has many key elements for successful technology development, work force development, and robust partnership with industry. These include:

- Outstanding patient base for clinical investigation – help develop statewide clinical trial network,
- Latest technology in proteomics for biomarker development,
- Excellent small and large animal facilities,
- Highly integrated health systems with strong EMR and database capabilities,
- The Heart Hospital ranked in the top tier in Virginia,
- Several universities and community college systems to provide training and work force development,
- Faculty with entrepreneurial spirit and experience in translating their findings to the clinic,
- A Major Center of Bioelectronics research,

- Highly integrated Diabetes Center with strong tradition of basic and translational research with ongoing collaboration at most universities in the Commonwealth,
- Establishment of only accredited biorepository in the Commonwealth,
- Major leaders and opportunities in NASH and other inflammatory complications of diabetes including CVD, wound care, neuropathy and nephropathy.

Summary and Impact

Translation of this research and relevant technology to improve care in diabetes or associated complications will have a direct beneficial impact for the people of the Commonwealth. Development of a therapy that can help to halt or reverse diabetes will have a significant positive influence on diabetes healthcare, currently impacting over 2.6 million (diagnosed plus undiagnosed pre-diabetes) adult individuals in Virginia.

It is reasonable to expect that a demonstration of proof-of-concept efficacy for a new therapeutic or diagnostic strategy applicable to diabetes or NASH will place us in a competitive position to attract significant research and commercial funding. This would be expected to come from both conventional research applications and public/private partnerships such as the SBIR/STTR programs, as well as newer programs in Virginia such as the Virginia Bioscience Health Research Corporation (“The Catalyst”), Commonwealth Commercialization Fund, and Eminent Scholar Matching Funds. These sources would be complemented by established pharmaceutical or device company interest. Quantifiable large pharmaceutical interest is apparent in prior awarded research-grant-based funding. Clear investments are needed to develop the infrastructure and financial support to foster early stage discoveries moving from academia to early stage companies and to provide incentives to recruit established companies to the area.

In summary, diabetes mellitus and NASH remain an enormous healthcare challenge in the Commonwealth, given the rapid growth in patient numbers and large costs to the patient and healthcare system due to the many complications. This opportunity can lead to major economic benefits through new jobs with pharmaceutical and manufacturing partnerships. There is an outstanding opportunity for this new Consortium to address best practices today and treatments for tomorrow. Resources for key elements of success will be needed and developed in collaboration with external consultants. These resources include space, personnel, and early stage funding. This initiative fully aligns with the Governor’s new initiative to advance Biomedical Research and Technology in Virginia.