

## Successfully Launching The Clinical Trials Network of Tennessee

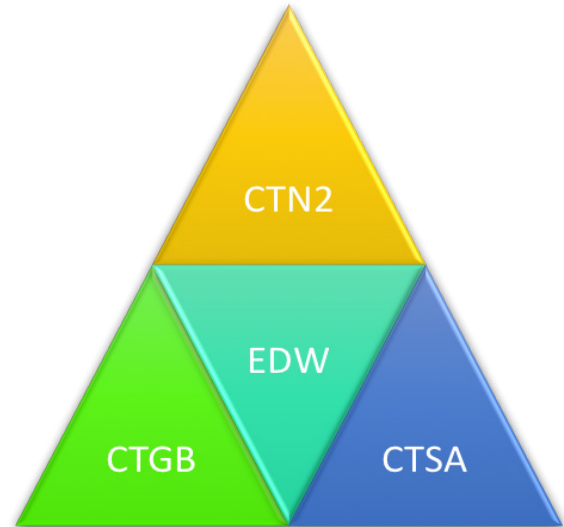
*“Tennessee’s state-wide multi-site clinical trial facilitator – Hospital operated, academically supported, powered by a robust research enterprise data warehouse, for superior performance and increased sponsor engagement.”*

The Clinical Trials Network of Tennessee (CTN2) has been activated. It will operate as a separate 501(c)(3) subsidiary of the University of Tennessee Research Foundation (UTRF), the non-profit 501(c)(3) organization whose mission is to promote the commercialization of UT intellectual property, encourage an entrepreneurial culture, contribute to state and regional economic development and promote research and education to benefit the people of Tennessee and beyond. CTN2 was created to enable the University of Tennessee Health Science Center (UTHSC) clinical research faculty to design, solicit, and conduct robust statewide clinical trials with the overarching goal of providing new therapeutics and medical devices aimed at improving the health of all Tennesseans.



From left to Right: Richard Magid, Phil Cestaro, Karen Johnson, Chancellor Steve Schwab, Steven Goodman, Robert Davis, Bill Mason, and Ari VanderWalde.

The Clinical Trials Network of Tennessee was the vision of Steven R. Goodman, PhD, vice chancellor for Research at UTHSC. “CTN2 will provide robust statewide clinical trials that will improve medical treatments, while providing UTHSC credit for the clinical trial contracts being performed by its faculty who are located at participating hospitals throughout the State,” Dr. Goodman, who has been elected to serve as the interim president and CEO of CTN2, said.



C3: A model of the integrated vision for the future of UTHSC clinical trials

Dr. Goodman and his CTN2 team presented the idea to create a 501(c)(3) organization as a wholly-owned subsidiary of the University of Tennessee Research Foundation to the UTRF Board of Directors on December 5, 2017 and it received unanimous approval. Having a separate clearinghouse for clinical trials at UT decreases administrative functions and permits a more streamlined budgeting and contracting process for this cross-institutional initiative. CTN2 will allow UTHSC faculty to respond to opportunities for clinical trials at the speed of industry. The UT Board of Trustees has agreed to provide \$3 million in funding to UTRF to support CTN2’s first three years of operation.

Dr. Goodman enlisted several key players to help establish CTN2 including members of UTHSC and UTRF’s upper administration; Phil Cestaro, president and CEO of TriMetis Life Sciences and UTHSC’s new associate vice chancellor for Research and Business Development; Robert Davis, PhD, Governor’s Chair in the UTHSC-Oak Ridge National Laboratory Center in Biomedical Informatics and professor in the Department of Pediatrics; Ari VanderWalde, MD, MBioeth, associate vice chancellor for Clinical Research; and Karen Johnson, MD, MPH, Endowed Professor of Women’s Health in the Department of Preventive Medicine. Stacey Patterson, PhD, president of UTRF; Richard Magid, vice

## 2 The Research Rainmaker

### The Clinical Trials Network of Tennessee Continued...

president of UTRF at UTHSC; and Bill Mason, JD, secretary and General Counsel for UTRF were all key consultants in the development of CTN2.

The university's partner hospitals include Methodist University Hospital, Le Bonheur Children's Hospital, Regional One Health, West Cancer Center, Saint Thomas Health in Nashville, the University of Tennessee Medical Center in Knoxville, and Erlanger Health System in Chattanooga. CTN2 has incentivized buy-in from these partner hospitals by providing its services without charge, including their representatives on the CTN2 Board of Directors, and providing personnel to support clinical trials at the hospitals.

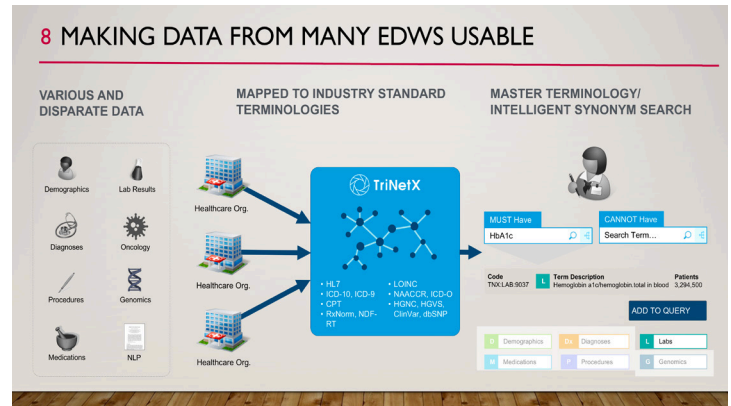
"Based on UTRF's experiences supporting other projects across UT, we've established CTN2 as a nonprofit UTRF subsidiary and set up the bylaws to ensure that its governing Board represents all of the stakeholders," Dr. Magid, who has also been elected to serve as the UTRF board representative for CTN2, said.

### INTEGRATING BIOMEDICAL INFORMATICS

Intricately linked to CTN2 is the development of a HIPAA-compliant Enterprise Data Warehouse (EDW) for all CTN2 partnering medical center patients. The network platform that UTHSC and CTN2 will use belongs to TriNetX, a global provider with data on nearly 100 million patients in over 10 countries, whose state-of-the-art security and privacy procedures, including HIPAA compliance, have been verified by independent experts specialized in big health data analytics and infrastructure.

Dr. Robert Davis serves as the lead curator for the research Enterprise Data Warehouse and said work on the EDW and the biorepository is already underway.

"It's very difficult to get enough sample subjects from one health center for a good clinical trial," Dr. Davis said. "Through the EDW, UT researchers will have access to more patient data than ever before, allowing for project collaboration and the develop-



An example of how the EDW will work. Information Source: TriNetX

ment of products and solutions for patients and our community no matter their physical location."

### SUPPORTING THE INFRASTRUCTURE

In addition to the Enterprise Data Warehouse, CTN2 will provide clinical trials budgeting and contracting, site management, site quality assurance, sponsor relationship management, central IRB management, and other resources. Phil Cestaro will serve as CTN2's executive director responsible for the overall leadership of CTN2, including but not limited, to overseeing the budget, services provided, procurement of new clinical trial projects, and other activities as assigned by the CTN2 board of directors.

"CTN2 will provide pharmaceutical and medical device companies access to the talent in academia and a diverse patient population throughout the state of Tennessee via streamlined start up and contracting processes," Cestaro said. "CTN2's unique combination of centralized business resources, incorporation of an EDW, and the resources available through the UT Board of Trustees differentiate it from other clinical trials programs."

Additionally, CTN2 will have Dr. VanderWalde serve as its Medical Director. As the Medical Director, Dr. VanderWalde understands the clinical aspects of the research protocol and has the ability to have discussions with study sponsors on the pros and cons of different protocols and pipeline activities.

#### Have a story we should include?

Submissions and ideas can be sent to Sarah Bloch at [sabloch@uthsc.edu](mailto:sabloch@uthsc.edu)

## THE CLINICAL TRIALS GOVERNANCE BOARD

The UTHSC Clinical Trials Governance Board (CTGB), the university's fully integrated Federated Model for developing and sharing best practices for clinical research through institution-wide offerings, has also been created by Vice Chancellor for Research Goodman. Heading the CTGB are Drs. VanderWalde and Johnson. UTHSC Chancellor Steve J. Schwab, MD, has provided a \$3 million "boots-on-the-ground budget" to the CTGB so that it will be able to successfully provide the necessary clinical trials staff needed to support the level of clinical trials CTN2 will attract.

"Currently, there are a number of clinical research offices that exist at UTHSC each with specific expertise, focus, and infrastructure," Dr. VanderWalde said. "Through the CTGB we are beginning to integrate these offices and share best practices across Clinical Research Offices as well as encourage a staffing model that takes advantage of resources across groups."

Dr. Johnson adds that the CTGB aims to facilitate clinical research and promote collaborations within and across departments, colleges, and campuses as well as within the UT System and beyond. Dr. Johnson has been designated to lead the UTHSC effort as it works to become a Clinical and Translational Science Award (CTSA) site.

"CTN2, CTGB, and the Enterprise Data Warehouse will be central to our ability to obtain a CTSA designation," Dr. Johnson said.

With the Clinical Trials Governance Board already working to better support clinical research faculty, and the successful creation of The Clinical Trials Network of Tennessee and the Enterprise Data Warehouse, Dr. Goodman's vision to enhance clinical research activity is becoming a reality. UTHSC is positioning itself "to contest for competitive grants and contracts and attract and retain outstanding faculty members with the ultimate goal of stimu-



lating research initiatives and growing its research footprint," Dr. Goodman said.

Chancellor Schwab echoes Dr. Goodman's excitement. "CTN2 will accelerate our faculty's ability to conduct patient-based investigation," Chancellor Schwab said. "This final step in the bench-to-bedside pathway of improving patient care through new medicines and new techniques is essential to bringing health care advances to the people of Tennessee."

CTN2 Memorandums of understandings and articulation agreements are being signed with each partner hospital location. Dr. Goodman anticipates CTN2 will be accepting clinical trials by May or June 2018.



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## 4 The Research Rainmaker

### Welcoming the new Senior Director of Development for Regional and Research Philanthropy Greg Harris



In 2016, the University of Tennessee Health Science Center (UTHSC) set a goal of doubling its research footprint over the next ten years. This investment required a renewed investment of resources. This fiscal year, UTHSC's investment was augmented with a commitment by the University of Tennessee Foundation (UTFI). UTFI's Love Collins, III, vice chancellor of development

and alumni affairs at UTHSC, announced that he was dedicating a position on his expanding team to research philanthropy.

In January 2018, Love hired Greg Harris to head the new initiative. As senior director of development for regional and research philanthropy, Greg will work closely with VCR Goodman, the Office of Research and its entities offering his expertise when it comes to philanthropic funding for research that crosses all colleges, campuses and institutions.

"Greg will play a key role in helping drive UTHSC towards being a top-tier health science center," said Dr. Goodman. "By aligning investments and initiatives that are vital to the expansion of the institutional research footprint with the capabilities and resources of UTFI, we are setting ourselves on the path to success."

Dr. Goodman's initial top research priorities are: (A) the Memphis Institute for Regenerative Medicine, which will bring together the expertise of UTHSC, the University of Memphis, St. Jude Children's Research Hospital and Industry Leaders (Revotek, Medtronic, and FedEx) to perform basic, clinical and translational research in the areas of stem cell biology, 3D bioprinting and tissue engineering for organ repair and replacement therapies; (B) the Memphis Consortium for Sickle Cell Disease and Classical Hematology Research, which aims to be a consortium without walls designed to develop collaborative sickle cell research among all participating Memphis institutions and create standardized evidenced-based clinical care across participating institutions that will support clinical and translational research; (C)

infrastructure build, equipment and Institutional Research Core Labs; and (D) other initiatives including the VCR Distinguished Lecture series, CORNET Awards, and the Clinical Trials Governance Board.

"While Dr. Goodman's research priorities represent grand-scale initiatives, I am most excited about the clinical trial platform he and his team are building," said Greg. "Potentially a model other state universities will duplicate in the future; the system offers clinical trial sponsors a cadre of seven in-state partners providing a statewide reach of an incredibly diverse population of patients. I'm building a strategy that should attract research philanthropy from companies interested in seeing this platform excel."

Prior to working for UTFI, Greg was employed with several universities and nonprofits over a 30-plus year career in the Advancement profession. Immediately before taking on his new position at UTHSC, Greg served as Life University's vice president for university advancement in Atlanta where he led the development, alumni relations, postgraduate education, community investment and government relations. Greg has held vice president positions at several nonprofits and his experience and expertise includes the areas of fundraising, alumni and membership relations, event planning, data management, strategic planning, and government and community relations.

Greg is married to Lindsey Fore Harris and they have two children. In addition to enjoying family activities, he is an avid college football fan and an investor in new technologies. Greg is a seeker of life changing experiences and has enjoyed hang gliding in several states; leading safaris in Africa; tubing over waterfalls; and performing music on the national stage.

## UT Collaboration Examines How Natural Chemicals in Green Tea Work

Green tea has been known to have beneficial health effects, but how these effects come about has been a mystery. Now, a team collaborating across the University of Tennessee System has discovered the molecular mechanisms through which key chemicals in green tea work to benefit the human body.

The research teams of L. Darryl Quarles, MD, (pictured left) of the University of Tennessee Health Science Center (UTHSC), Jeremy C. Smith, PhD, (pictured right) of the University of Tennessee, Knoxville (UTK) and Oak Ridge National Laboratory (ORNL), and Jerome Baudry, PhD (who was at UTK, but has since moved to the University of Alabama in Huntsville) have discovered which body receptor key chemicals in green tea



interact with, according to work published in the article, "GPCR6A is a Molecular Target for the Natural Products Gallate and EGCG in Green Tea," in the journal *Molecular Nutrition and Food Research*, a peer-reviewed scientific journal that covers the latest research in nutrition and food science.

Dr. Quarles, the primary investigator of this research, states that the work is important for a number of reasons.

"First, it provides a molecular mechanism to explain the medicinal effects of green tea on energy metabolism and why consumption of green tea may impact a wide range of clinical disorders," Dr. Quarles said. The clinical disorders that green tea consumption has been reported to impact include metabolic syndrome, type 2 diabetes, and prostate cancer. "Second, the publication of this research is another example of the unique computational bi-

ology expertise at UTK/ORNL."

For Dr. Smith at UTK/ORNL, the discovery of the molecular mechanism by which green tea becomes beneficial to the human body signals a

continuation of a fruitful collaboration between the UTK/ORNL and UTHSC laboratories.

"With the help of the computational power at ORNL and experiments performed in Dr. Quarles' lab, we have identified that gallates, which are key natural chemicals in green tea, bind to a specific receptor named GPCR6a," Dr. Smith said. "Imagine the chemicals as the keys, and the receptors as the locks. What the computing allowed us to do is find the key that fits into the lock. By computing different chemical shapes into these receptors, we were able to make a great step forward in the direction of understanding the molecular mechanism of green tea action."

Interestingly, the green tea story has a twist in its tail; two of the more prominent gallates in green tea — epigallocatechin 3-gallate (EGCG) and gallic acid — have opposite effects when they bind to the receptor. Whereas EGCG inhibits the progression of prostate cancer, gallic acid may advance the disease. The team has also now found an explanation for this in how the chemicals bind differently to the receptor.

"It's important that we seem to have identified how these essential players in green tea's nutritional function might be working in the human body," Dr. Smith said.



### Subscribe to the UTHSC Researchers Listserv!

The Office of Research has established a new e-mailing list specifically geared toward all research Faculty, Post Docs, and Graduate Students at UTHSC. We use this platform to let the UTHSC research community know of important events, workshops, opportunities, news, etc. that specifically pertains to them.

To subscribe to the Researchers e-mailing list, please visit [listserv.uthsc.edu/mailman/listinfo/researchers](http://listserv.uthsc.edu/mailman/listinfo/researchers) and follow the subscription instructions.

## 6 The Research Rainmaker

### Improving the Research Infrastructure and Lessening the Administrative Burden on Faculty

As written in the Operational Strategic Plan for Research: “At a time of diminishing grant dollars and increasing competition, it is essential now, more than ever before, that investigators are provided with an outstanding research infrastructure that will enhance their productivity and the research enterprise. Moreover, there is a pressing need to foster an environment in which all investigators - whether working within UTHSC or collaboratively on a local, regional, national, or multi-national scientific initiative - have access to efficient support services and infrastructure, regardless of their physical location.”



Photo by Brandon Dill/Brandon Dill Photography

The OSPR identified three specific infrastructure challenges that directly threatened the productivity of researchers at UTHSC and, as such, required specific attention by the Office of Research. These three challenges were: (A) the quality of the Laboratory Animal Care Unit (LACU), a critical “Institutional Core” serving the majority of campus investigators; (B) the need to expand and strengthen the Office of Grants and Research Agreements (GRA) in order to provide an integrated support center that facilitates the pace of research; and (C) review the activities and policies related to compliance (e.g., IACUC, IRB, IBC, etc.), with the goal of streamlining processes and reducing unnecessary burdens on investigators.

As you’ve read in past editions of *The Research Rainmaker*, the unification of all existing pre- and

post-award functions under the Office of Research, as well as additional activities directly related to the research enterprise, is already underway. In May 2017, the Office of Sponsored Programs opened with Sarah White now serving as its Associate Vice Chancellor for Research. The unification has created an economy of scale by using a team-based approach. The unified model has also improved effective communication among personnel, thereby increasing efficiency. We estimate that the changes thus far have resulted in OSP turnaround times that are approximately 3X faster and faculty satisfaction has improved. Additional steps are continually being implemented to improve processes.

But what of the other two areas? As outlined below, significant progress has been made in the Laboratory Animal Care Unit (LACU) and the Institutional Animal Care and Use Committee (IACUC).

#### Laboratory Animal Care Unit (LACU)

Beginning in January 2017, the LACU underwent a complete reorganization of its staffing and leadership, as well as a re-derivation of all standard operating procedures, policies and staff training practices. Fundamental to the reorganization process was the new requirement that all husbandry staff achieve a minimum level of American Association for Laboratory Animals Science (AALAS) certification appropriate for their position. These industry standard training certifications are now a routine part of the continual proficiency training for LACU staff. In this respect, the reorganization of the LACU included the creation and hire of a Director of Operations, an Assistant Operations/Quality Assurance Manager, and a Training/Quality Assurance Coordinator. These positions are responsible for the ongoing implementation and assessment of both initial and continued staff training, as well as facility quality assurance monitoring. These enhancements to the program recently led to a three-year re-accreditation of the facility by AAALACi (Association for Assessment and Accreditation of Laboratory Animal Care International) with no mandatory findings for correction. As noted by one reviewer during the AAALACi site visit, “you have an excellent program that is headed in the right direction.”



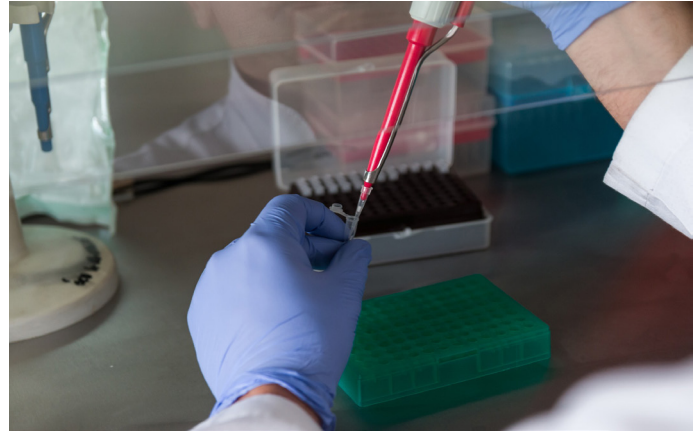
## Institutional Animal Care and Use Committee (IACUC)

In order to promote research, while at the same time enhancing regulatory compliance, the IACUC has made a number of critically needed policy-related and operational changes. First, the IACUC completed an extensive review of all current policies related to animal research activities at UTHSC, as well as developed new ones.

“This activity served two main purposes, namely, to ensure that IACUC policies do not create unnecessary self-imposed burdens on the research community, and to provide researchers with clear regulatory guidance related to their animal research activities,” said Steve Youngentob, PhD, senior associate vice chancellor for Research.

In addition, the IACUC initiated major procedural changes in the submission and review process of animal use protocols. The goal: decrease the IACUC protocol approval timeline while at the same time streamlining the submission and review process. All newly proposed animal-related activities are now required to undergo mandatory pre-review, prior to submission. Essential to this pre-review process, assigned reviewers and subject matter experts now interact collaboratively with investigators in order to foster the development of a quality protocol prior to submission. Further, the IACUC implemented the use of two IACUC meetings per month, and added the use of Designated Member Review (DMR) (i.e., two assigned reviewers who act on behalf of the committee), as a possible mechanism for protocol review. Two meetings per month (i.e., every two weeks) coupled with mandatory pre-review, has created what amounts to a rolling review process.

“The use of the DMR process for appropriate protocols has also permitted the IACUC to review and approve protocols outside a normally scheduled meeting and, thus, at a faster pace than those requiring Full Committee Review (FCR),” said Dr. Youngentob. “The result of these cultural and functional changes has exceeded expectations, reducing the average time of protocol approval from 9.3 weeks to ~ 21 days.



According to Francesca-Fang Liao, PhD, professor in the Department of Pharmacology, the recent changes to the IACUC protocol review process is “good news” and has drastically improved the faculty experience.

“Much less pain than in the past,” said Dr. Francesca-Fang Liao.

Weikuan Gu, PhD, professor in the Department of Orthopaedic Surgery and Assistant Vice Chancellor for Global Partnerships echoes Dr. Liao’s thoughts.

“Thanks so much for the work efficiency,” said Dr. Gu. “This is a great improvement in the IACUC protocol committee. I appreciate it very much.”

To become a premier research institution requires not only highly qualified researchers and considerable resources, but also proficient administration and supporting units. Successful refining of these key research infrastructure areas will propel us towards this common goal.

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## 8 The Research Rainmaker

### A Message from the Vice Chancellor for Research



photosource: BOB DYLAN. Digital Image. 7 May 2018 <<http://simon-godfrey.com/simon-godfrey-3/2013/10/02/blowin-in-the-wind-when-is-harmonica-appropriate>>

“And I’ll tell it and think it and speak it and breathe it

And reflect it from the mountain so all souls can see it” -Bob Dylan, *A Hard Rain’s Gonna Fall*

I came to UTHSC to find several clinical trial offices: Office of Clinical Research, Clinical Research Center, Office of Preventive Medicine Clinical Research, Pediatric Clinical Research Unit, Dental Clinical Research Center, Nephrology Clinical Outcomes and Clinical Trials Program, and Clinical Trials Offices on our Knoxville, Chattanooga and Nashville campuses. They were functioning independently, but with little communication or collaboration. I created the Clinical Trials Governance Board (CTGB) as a Federated Model with representation from each Clinical Trials Unit. Dr. Ari VanderWalde was appointed as Chair, and Dr. Karen Johnson as Vice-Chair, and now the Clinical Trial Offices are working together collaboratively to create a robust environment for all types of clinical trials.

I arrived at UTHSC with the intent of creating a State-wide Clinical Trials Network, as I had done as part of SUNY REACH. It was more complex as SUNY owned their hospitals while UTHSC did not, but supplies the clinical faculty. I met Dr. Bob Davis who was hard at work on an Enterprise Data Warehouse (EDW). I shared the concept of a state-wide clinical trials network with an expanded EDW covering our partner hospitals at all locations. Bob was onboard, and we were off and running. Chancellor Steve Schwab and Executive Vice Chancellor Ken Brown came to me independently asking me to think about an old problem at UTHSC: getting credit for clinical trials conducted by UTHSC faculty at hospital sites that we did not own. As these clinical trial contracts were being executed outside of UTHSC we were not getting any annual credit, thus hurting our standing when we were compared to other academic health centers. The problem was challenging, but discussions with Dr. Stacey Patterson (now UT Vice President for Research and UTRF President) led to a solution. By cre-

ating the Clinical Trials Network of Tennessee (CTN2) as a 501(c)(3) wholly-owned subsidiary of UTRF, any clinical trial contract money that passed through this non-profit, even though it all ended up at the hospital sites where our UTHSC faculty were conducting the trials, would be accounted for via the HERD survey as part of UTHSC’s annual Grants and Contracts reporting. This leads to UTHSC rising in the annual rankings and the ripple effects that occur with a higher level of prestige. The UT Board of Trustees supported the concept with \$3 million, over three years, given to UTRF which then transfers the money annually to CTN2. Meanwhile, Chancellor Steve Schwab understanding that the large number of statewide clinical trials would require a clinical trial “boots on the ground” workforce, supplied \$3 million over three years to the CTGB to hire the necessary staff. We will be running clinical trials through CTN2 beginning in May or June 2018. Phil Cestaro is the CTN2 executive director, Dr. Ari VanderWalde the medical director, Bill Mason, Esq., is the legal counsel and I will be the interim president and CEO. All have played important roles in CTN2 development.

When I joined UTHSC, a CTSA application was being prepared that received a reasonable score but was not funded. I provided the UTHSC Research Council an alternative approach which they approved unanimously. The idea was to create a Delta Consortium CTSA application focused on our common patient demographics. We now have a Delta Consortium CTSA group composed of UTHSC, University of Mississippi Medical Center and Tulane Medical Center. This will be a multi-PI application with Drs. Karen Johnson and Michelle Martin being the PIs representing UTHSC. The focus of the grant will be health disparities. The application will involve all six UTHSC Colleges, all four campuses, CTN2 and the EDW. Karen and Michelle will be assisted by the CTGB, and many others, in the writing of the application.

I have now explained the integrated vision for future clinical trial research at UTHSC involving the 3Cs (CTGB, CTN2 and CTSA) plus the EDW. I predict that based on this vision and the dedicated leaders that are involved, we will experience a Hard Rain and “I’m a-goin’ back out ‘fore the rain starts a-fallin’...But I’ll know my song well before I start singin’”-Bob Dylan, Nobel Laureate in Literature

-Steven R. Goodman, PhD  
Vice Chancellor for Research

