

BEYOND THE MILLION VETERANS PROGRAM: BARRIERS TO PRECISION MEDICINE

HEARING

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BEYOND THE MILLION VETERANS PROGRAM: BARRIERS TO PRECISION MEDICINE

Wednesday, June 26, 2019

COMMITTEE ON VETERANS' AFFAIRS,
U. S. HOUSE OF REPRESENTATIVES,
Washington, D.C.

The Subcommittee met, pursuant to notice, at 3:15 p.m., in Room 210, House Visitors Center, Hon. Julia Brownley [Chairwoman of the Subcommittee] presiding.

Present: Representatives Brownley, Lamb, Dunn, Radewagen, and Barr.

OPENING STATEMENT OF JULIA BROWNLEY, CHAIRWOMAN

Ms. BROWNLEY. Thank you all for being here today to discuss the current state of VA's pursuit of precision medicine. Precision medicine has been described as an innovative approach that takes into account individual differences in people's genes, environments, and lifestyles. Not only is VA uniquely designed to pursue this cutting-edge research, its patient population would benefit most from its development.

According to VA's National Center for Veterans Analysis and Statistics, veterans of color are predicted to increase from 23.2 percent to 32.8 percent by 3037, while women veterans continue to be the fastest growing population of veterans and are projected to be the only group of veterans that will continue to grow through 2037.

The manner in which veterans receive health care should reflect their increasing diversity. In the past, VA conducted studies using only white men and some methods of treatment were approved based on these heavily skewed trials. This was not unique to VA; the medical research field as a whole has operated in this manner.

However, what is unique to VA is its ability and willingness to regain its position as the Nation's best research institution, a research institution that attracts the Nation's most talented physicians and investigators, and delivers the most progressive and effective treatments available.

In an effort to facilitate this transformation, VA launched the Million Veterans Program in 2011 to pursue its goal of collecting genetic material from 1 million veterans. Currently, with 750,000 veterans enrolled, it is the largest collection of its kind. Because of this rich database of information and VA's access to millions of veterans' health records, VA is becoming an increasingly attractive option as private industry determines where to focus its research dollars.

VA has limited resources, a stagnant budget, and the Administration has sought to slowly gut the National Institutes of Health, which is one of VA's biggest interagency partners. That is why it is increasingly important that VA's Office of Research and Development remain a competitive contender for private funds. It must also retain access to the technology and research infrastructure that private research partners can provide.

This is not to say that VA's Research Department under the guidance of Dr. Ramoni has not thrived. The work of VA employees to facilitate partnerships with private foundations such as Cohen Veterans Bioscience and other Government agencies like the Department of Energy to fill gaps in resources should be commended.

Today's hearing should serve as an opportunity for the agency to tout those achievements, but also for the Members of this Subcommittee to learn more information on ways in which Congress may assist. Not only will VA's increasingly diverse patient population benefit from advances in precision medicine, but some aspects of precision medicine could transform the way in which VA treats those veterans suffering from what have traditionally been thought of as invisible wounds.

Advancements in the understanding and discovery of biomarkers leads many to believe that the trauma leading to a TBI or PTSD can affect a person's genetic sequencing in a way that could assist physicians as they diagnose veteran patients.

Additionally, Dr. Haas has suggested that there may be hundreds of types of PTSD. If these variations can be identified, then veterans could receive effective treatment on the first try as opposed to the trial-and-error treatments the VA is currently forced to offer.

And, as chair of the Women Veterans Task Force, I am eager for VA investigators to identify diagnostic biomarkers for TBIs. Traumatic brain injuries are disproportionately misdiagnosed in women veterans as depression, thus denying much-needed treatment to this growing population.

Due to the incredible impact precision medicine could have on veterans' health care, I am thankful for each of our witnesses' willingness to join us in today's discussion. I am hopeful that at the end of this hearing we can better understand exactly what barriers VA's Office of Research is up against as it continues to modernize its processes and pursue increasingly important partnerships.

I will now yield 5 minutes to Ranking Member Dunn for his opening comments.

OPENING STATEMENT OF NEAL P. DUNN, RANKING MEMBER

Mr. DUNN. Thank you very much, Chairwoman Brownley.

A little over a year ago, I chaired my first VA Research meeting and at that meeting three basic concerns were raised about the VA's research program. The first concern was that the VA Research was not sufficiently focused on veteran-specific conditions and concerns. The second was that the VA medical facilities weren't complying with the VA's policy by administering grants from outside entities, as Chairwoman Brownley mentioned, through VA non-profit research and education corporations, to the extent that is possible. And the third concern was that the VA is not efficiently

translating bench discoveries to bedside in order to advance the treatment of veterans.

There have been a number of changes made to the VA's research program since that hearing and perhaps the single most significant change is the appointment of Dr. Carolyn Clancy as the Deputy Under Secretary for Discovery, Education, and Affiliated Networks, with the oversight responsibility to the Office of Research and Development.

Dr. Clancy will be testifying for the VA today and was recently named one of Modern Health Care's 50 Most Influential Clinical Executives, an honor recognizing leaders who work in health care industries, deemed by their peers and an expert panel to be one of the most influential leaders in research today. So, congratulations to you for that, Dr. Clancy.

I do wish to point out that our three primary concerns still have to be met, so we will address those. Another one of our witnesses this afternoon is Mr. Matt Kuntz, the Executive Director of the National Alliance on Mental Illness from Montana. Mr. Kuntz's written statement powerfully lays out the very real stakes for this issue, which is veterans' lives.

Research is an important tool at the VA's disposal to improve and save lives for veterans and for all Americans, and it is incumbent on us to make sure that the VA is using that tool to its highest potential. During this afternoon's hearing, we will discuss several recommendations for how we can do that and, with our collective work, I am confident that the VA's best breakthroughs are still ahead, and that those breakthroughs will be able to make a difference in the quality and longevity of veterans' lives and all Americans.

And at that point, I now yield back, Chairwoman Brownley.

Ms. BROWNLEY. Thank you, Dr. Dunn.

On today's panel we have Dr. Carolyn Clancy, Deputy Under Secretary for Health for Discovery, Education, and Affiliated Networks at the Department of Veterans Affairs. Dr. Clancy is accompanied by VA's Chief Research and Development Officer, Dr. Rachel Ramoni, and the Director of the Million Veterans Program, Dr. Sumitra Muralidhar.

Dr. Magali Haas will offer testimony on behalf of the Coalition to Heal Invisible Wounds. And also Mr. Matt Kuntz joins us today on behalf of the National Alliance on Mental Illness.

I appreciate all of you and your willingness to join us today and look forward to receiving your testimony. And, to that end, Dr. Clancy, you are now recognized for 5 minutes.

STATEMENT OF CAROLYN CLANCY

Dr. CLANCY. Thank you. Good afternoon, Chairwoman Brownley, Ranking Member Dunn, and distinguished Members of the Subcommittee. As you noted, I am accompanied by Drs. Ramoni and Muralidhar.

As Deputy Under Secretary for Health for Discovery, Education, and Affiliated Networks, I am pleased to be here to share our vision and deliverables in the field of precision medicine.

My office was created precisely because Secretary Wilkie and Dr. Stone recognized that aligning and elevating our academic missions

is absolute vital to making sure that all veterans, irrespective of background, get cutting-edge care, and there are studies to support that in the academic arena. So we are very excited about that. And we are committed to ensuring that veterans are among the first to benefit from cutting-edge care.

And I am sure that you know that Secretary Wilkie, as a result of his prior position at the Department of Defense, is probably more attuned to the growing diversity of the veteran population now and in the future than most would be, and is usually the first to come out with statistics like the ones that you cited.

Since its inception, VA Research has measured its success based upon real-world impact. The pacemaker and liver transplantation are well-known examples of early VA research advances that transformed health care. Fewer people know that the Gleason grading system, which is used worldwide to predict the prognosis of a man with prostate cancer, was created by Dr. Donald Gleason, a VA pathologist.

More recently, VA conducted the foundational trial that established active surveillance as a safe, long-term alternative to prostatectomy in men with low-risk prostate cancer.

By continuing to advance the precision of medical care, we can go beyond, way beyond general predictions like low, medium, and high-risk prostate cancer, to specific predictions that will guide an individual veteran's care. One of the ways we are making this vision a reality for veterans is through our partnership with the Prostate Cancer Foundation. Our first milestone is to ensure that men with metastatic prostate cancer receive DNA sequencing, and already this effort has identified men who based on their genetic variations are benefitting from precision therapies.

New precision medicine treatments are first made available through clinical trials and in February of 2018 we began the Access to Clinical Trials, or ACT for Veterans Initiative, in collaboration with the National Association of Veterans Research and Education Foundations. Through this effort, we have set a goal to start up industry-sponsored clinical trials 100 days faster than our current average by the end of fiscal year 2021.

In October of last year, the Office of Research and Development welcomed a new Director of the Office of Research Protections, Policy, and Education, she and her team immediately began working towards that goal in a fairly relentless fashion, including opening the door to relying on commercial institutional review boards, which are used by many industry-sponsored clinical trials.

Precision medicine treatments are grounded in the discovery of the relationship between genetic variations and disease. One of VA's major investments, of course, is the Million Veterans Program that you referenced, and today, 8 years after it began, it is the largest mega-bio bank in the world. Over 750,000 veterans from all 50 states, Guam, and Puerto Rico have enrolled, and we also have their clinical electronic data, which makes it literally a unique resource in the world.

Because of the richness of the data, VA researchers have begun to shed light on the genetics of a range of conditions that impact veterans' health, including alcohol use disorder and post-traumatic stress disorder, or PTSD. It is a source of hope to veterans living

with the invisible wounds of war and it is our job to turn that hope into treatments.

For example, on one end of the spectrum, we are partnering with the Department of Defense to follow thousands of veterans with mild traumatic brain injury experienced in combat. Each of these participants undergoes intensive bio sampling and imaging, enabling us to identify biomarkers associated with brain injury and comorbidities like PTSD.

On the clinical end of the spectrum, we now have a study in progress, the Prime Care Study, a trial which is determining whether matching veterans with depression to medications based on their genetic variation leads to improved outcomes.

These studies exist because our veteran partners are willing to continue to serve our Nation through participation and research. And an essential step to realize our promise to participants to advance precision medicine is to establish a modern computational infrastructure that can scale to support hundreds of analyses occurring in parallel.

To that end, we are working with the University of Chicago on the Open Commons Consortium to pilot a VA Data Commons where de-identified data from MVP and electronic health record data will be broadly available to approved VA and non-VA researchers. Our goal is to have the infrastructure and services to support a minimum of 100 parallel projects in the VA Data Commons by the end of fiscal year 2021.

On behalf of ORD, the many VA researchers, and the veterans who participate in VA Research, I thank you for your attention. My colleagues and I look forward to answering your questions.

[THE PREPARED STATEMENT OF CAROLYN CLANCY APPEARS IN THE APPENDIX]

Ms. BROWNLEY. Thank you, Dr. Clancy.

Dr. Haas, you are now recognized for 5 minutes.

STATEMENT OF MAGALI HAAS

Dr. HAAS. Good afternoon, Chairwoman Brownley, Ranking Member Dunn, and distinguished Members of the Subcommittee. I am Dr. Magali Haas, CEO and President of Cohen Veterans Bioscience. I am the wife of a veteran and I am representing the Coalition to Heal Invisible Wounds.

It is an honor to testify before the Subcommittee on the topic of advancing precision therapies for veterans alongside Dr. Clancy and my fellow Coalition Member Matt Kuntz.

Cohen Veterans Bioscience is a national, nonpartisan 501(c)(3) public charity that operates as a translational research organization. We are dedicated to fast-tracking the development of diagnostic tests and personalized therapeutics for the millions of veterans and civilians who suffer the devastating effects of trauma-related and other brain disorders. We partner closely with the Department of Defense, the VA, the NIH, FDA, and other agencies, as well as academia, foundations, and industry partners, to advance this mission.

We share this mission, because today more military servicemembers are dying after they come home by suicide than on

the battlefield, and many more are suffering the chronic effects of post-traumatic stress and traumatic brain injury. For these invisible wounds, we have inadequate treatment options for far too many.

In an effort to close this gap, we are partnering with the Department of Defense to fund and operate an ambitious program to conduct a multi-center, adaptive platform trial to test multiple therapies in parallel under a design approach that is cutting-edge. The VA is a critical partner in this effort, and we need VA Research sites to participate in the program starting this fall.

I am testifying today on behalf of the Coalition to Heal Invisible Wounds, which advocates for policy reforms to widen and expedite the pipeline for new therapies and diagnostics for PTSD and TBI, and suicide prevention.

The Coalition's focus since its founding in 2017 has been to empower the Veterans Health Administration, the largest integrated health care system in the United States, and one that is home to an established scientific enterprise that conducts more than \$1 billion of research each year, to be positioned as a leading clinical research partner.

We ask today that the Subcommittee bolster the VA's efforts to overhaul its clinical trial start-up practices. According to industry data, VA sites take an average of 265 days to activate a site, versus 141 days for non-VA sites. Because of these lengthy delays, many clinical research sponsors do not even attempt to bring clinical research to the VA and have not done so for decades. Sponsors that do engage face a non-streamlined decisions and protocol-review process and significant wait times for site initiations that can cost overruns.

When sponsors are unable or unwilling to conduct studies at VA sites, it means that veterans lack access to the frontier of medicine for many disease conditions, particularly oncological research. For many individuals with cancer, investigational therapies are the only last, best hope for a patient. What happens when a cancer study does not open in a VA facility, a veteran suffering from that form of cancer is denied this path and is more likely to die sooner.

And if we can't launch the PTSD adaptive platform trial in a timely fashion within VA sites this year, we stand to fail in establishing scientific evidence that supports the proper utilization of existing and new therapeutics for these conditions. Without better treatments for PTSD and TBI, we cannot effectively combat the suicide and opioid epidemics.

We believe that with targeted reforms the VA can become 100 days faster on average at clinical trial startup by 2021. The Coalition calls this the 100 Days Faster Initiative; for us, faster is shorthand for efficiency, improved quality, performance metrics, and adoption of cutting-edge technologies and best-in-class solutions.

A hundred days matter. These reforms will require systemwide engagement and implementation, and will extend throughout numerous functions within the VA. It is thereby imperative that Congress provide the VA statutory guidance to achieve the 100-days-faster objective to ensure prioritization around this focus.

We recommend that guidance focus on four reforms, some of which are partially underway at the VA already: allow the use of

commercial institutional review boards, or IRBs, in sponsored clinical research; create and make permanent research-specific capacities within both the Office of Information Technology and the Office of Privacy and Records Management, and refocus the role of the Research and Development Committee.

In conclusion, the Coalition thanks the Subcommittee for its work to strengthen the VA's capacity to support the development of precision medicine. Veterans have earned the right to world-class health care and we strongly believe that the VA has the potential to be a world-class research partner, enabling better health care for servicemembers and veterans.

Thank you.

[THE PREPARED STATEMENT OF MAGALI HAAS APPEARS IN THE APPENDIX]

Ms. BROWNLEY. Thank you, Dr. Haas.

Mr. Kuntz, you are now recognized for 5 minutes.

STATEMENT OF MATT KUNTZ

Mr. KUNTZ. Chairwoman Brownley, Ranking Member Dunn, and distinguished Members of the Subcommittee, on behalf of NAMI, the National Alliance on Mental Illness, I would like to extend our gratitude for the opportunity to share with you our views and recommendations regarding "Beyond the Million Veterans Program: Barriers to Precision Medicine." The entire NAMI community applauds the Committee's dedication in addressing the critical issues around veterans' brain health.

NAMI is the Nation's largest grassroots mental health organization dedicated to building better lives for millions of Americans affected by mental illness. NAMI advocates for access to services, treatment, support, and research, and is steadfast in its commitment to raising awareness and building a community of hope for all of those in need.

To start out with the scientific justification, the VA serves over 1.8 million veterans in a treatment system based upon mental health diagnostic categorization that the former Director of the National Institute of Mental Health has deemed not to be predictive of treatment response. This is not the VA's fault; this is the state of the science. But it is incumbent on Congress and VA to push the state of the science forward to take better care of America's heroes.

From the ground, how it looks, is like my stepbrother, Specialist Chris Dana. We lost him to PTSD after serving in Iraq. And I will tell you flat out, the Montana National Guard, who he served with, and our family did not understand the extent of his injury until after we lost him.

And for another example, my friend Commander John Scott Hannon, 23 years in the Navy Seals, retired to come back home to Montana to live one gulch over from me in the woods. And he battled with a number of brain conditions and got treatment for years, but what lost him was the final diagnosis, was the bipolar disorder. And I sat down with his sister a few months after his death and she said, if we had just known about the bipolar disorder earlier—he addressed, he worked on everything else, but we didn't even know this was the case. And that is what I see day in and day out.

Or like my friend Mike Franklin. He was a fellow West Pointer and Army infantryman, a Navy chaplain, and then a college counselor. And just as interesting as that goofy resume would suggest, but he suffered from treatment-resistant depression, which affects about 30 percent of the people that depression, and none of the standardized treatments would work for him, and the treatments would just fail and fail. And my last conversation with him was, "Mike, please keep trying. We will find research; we will find something." But he could not keep going.

And that is the reality on the ground while we wait for precision medicine to catch up.

There has been scientific progress in the past 10 years, as discussed, and especially the emergence of transdiagnostic biomarkers for brain health conditions. For me, that has kind of changed the paradigm for how we think about this. It shows that the traditional diagnostic categories aren't going to line up exactly with the biosignatures; we should not expect them to.

And there are some really good examples of precision mental health care happening in research around the country. Dr. Amit Etkin's work at the Palo Alto VA on treatment-resistant PTSD was an amazing study, Dr. Madhukar Trivedi and his work at the University of Texas Southwestern on finding biosignatures to better treat depression, is real steps forward.

Some of the recommendations that we have. NAMI Montana and NAMI National were real good partners in helping write the Precision Mental Health Initiative and the Commander John Scott Hannon Act, and that is on the Senate side. And we really like that model for moving forward.

On a local level, we would like to ensure that the Veterans Equitable Resource Allocation model supports precision mental health initiatives. If local VA administrators are not incentivized to do this, this will fail. So ensuring that VERA reflects that reality.

And on a really simplistic note, using machine learning to take some of the pain of the article-drafting process off of VA researchers, I have toured around the country with the COVER Commission looking at VA researchers and clinicians, and some of them cannot publish because they don't have time. They have the data that we paid for, that we are ready for, and they can't publish because it takes too much time, and using machine learning to help ease some of that.

And, in conclusion, I just want to say this means so much to me personally. When we lost my stepbrother Chris, there was just no hope, and to see Committees like this looking to improve the brain health treatment system for our veterans is incredibly important.

Thank you.

[THE PREPARED STATEMENT OF MATT KUNTZ APPEARS IN THE APPENDIX]

Ms. BROWNLEY. Thank you, Mr. Kuntz. And this Committee offers its condolences to you for the loss of your stepbrother Chris. Thank you for being here today.

Mr. KUNTZ. Thank you, ma'am.

Ms. BROWNLEY. I now recognize myself for 5 minutes. And the first question I had was really to Dr. Haas. In my opening com-

ments, we talked a little bit about your summation that there could be lots of different variations of post-traumatic stress. So where are we in that research? I mean, if there are possibly a hundred versions of these, is there—can you just kind of describe where we are? Is this a hypothesis? Is this science-based that you know this already or you believe through my research we can determine whether this is true or not?

Dr. HAAS. So we believe that there are multiple forms or underlying mechanisms that can lead to a presentation that we call PTSD, post-traumatic stress disorder, and the science is essentially still in its nascency on some fronts. If we are looking at this in terms of what do we understand about the molecular basis and circuit basis of disease, that science is still in its discovery form.

We have the earliest findings now for genetics that are emerging out of both the Million Veterans Project and also from the Psychiatric Genetics Consortium. The first date were just published last year on this, showing genome-wide significant findings that there is a genetic underpinning PTSD. And so, with different genes, we can expect them. There are different pathways and therefore different mechanisms, that different people have vulnerability to PTSD in the wake of trauma. That is the tip of the iceberg.

Matt Kuntz mentioned the data from Palo Alto, Dr. Etkin's work. He has been working on a biomarker that is identifying a subset of patients that have a different underlying circuit and they all have the same diagnosis of PTSD. They look the same in terms of symptoms, but you can differentiate them based on their circuit using resting-state fMRI.

So that is suggesting to us, and that work needs to be validated, that there are subsets and subtypes within PTSD. That is the type of emerging evidence that suggests that we are going to see more. But if you look across other brain disorders and diseases, we see this as a systematic principle of science and health care and disease. We are seeing that in cancer already. We no longer just talk about lung cancer, we talk about lung cancer subtypes, we do the same in cardiovascular disease. We do this in every other field of biology except in brain disorders.

Ms. BROWNLEY. So when you talk about identifying the circuit, does that mean that the man or woman when they sign up to serve, that circuit exists before they have actually served our country?

Dr. HAAS. So at this time we don't know whether this is a pre-existing circuit or one that—

Ms. BROWNLEY. I see.

Dr. HAAS [continued]. —becomes emergent in the course of exposures. Also, even with your genetics, it is vulnerability, it is a probability, but it doesn't mean that you are going to get a given condition.

Ms. BROWNLEY. Thank you.

Dr. Clancy, I wanted to ask you, as Chair of the Women Veterans Task Force, when I read through your testimony and the others, you know, the first thing that came to mind was the inclusion of women and minorities into clinical trials, but even in terms of broadening the database that we have currently.

And so I guess my question is twofold. One, you know, how do we sort of incentivize inclusion of clinical trials for women and minorities? And then, certainly in terms of women veterans, infertility is a big issue and many women are often diagnosed with an unexplained infertility, and that seems to be a higher diagnosis rate than for men. And I was just in a hearing this morning where I was told that ALS, which is very—seems to be more prominent in the veteran community than the civilian community, I was told that we don't know why that is true.

So I guess my question is inclusion, infertility, and are we looking at things like ALS. And I have no more time left, but I will give you a few minutes.

Dr. CLANCY. So some of this we would like to take for the record to give you a complete accounting of what is known. As you know, all federally-funded research has to be inclusive of women and minorities. I believe that the diversity of the veteran population is precisely why the Prostate Cancer Foundation came to us for the collaboration that we undertaking now, which has been underway for a couple of years. And it is hard for me to convey the energy and excitement around this right up to Dr. Stone and the Secretary, which I think is phenomenal.

I would need to learn a little bit more, but we would be happy to get you information about infertility.

ALS, in my mind, represents a very large question mark. I do know that it is a presumption for some veterans as a condition of military exposure, but we still have a lot to learn, because that disease itself—I can tell you that I personally have a relative who has ALS, a woman, who she has not quite been in the same territory as Stephen Hawking, but has had a pattern of disease which is very, very different, and I think that underscores all of the points that Dr. Haas is making that understanding—and that Matt made as well about shifting how precision medicine and understanding more about genetic variation is going to help us redefine how we think about diagnoses and disease. That we will probably look back on this time in the not-too-distant future as kind of, you know, the Ice Age or something, because all of our diagnoses, particularly in mental health, are based—and much of a neurological diseases are based on careful categorization of symptoms and signs, but we didn't have the imaging and biomarkers that we needed.

Ms. BROWNLEY. Thank you, Dr. Clancy.

Dr. Dunn.

Mr. DUNN. Thank you very much. I appreciate your comments on that, I think you are right too.

Dr. Clancy, I am going to sort of do a lot of rapid-fire questions here, if I can, because I have so many. Have we started doing the sequencing on all these bio-bank?

Dr. CLANCY. Yes, we have started that sequencing.

Mr. DUNN. Where is that being done?

Dr. CLANCY. I am going to turn to Suma for specifics here.

Dr. MURALIDHAR. Contracted vendor—

Mr. DUNN. I couldn't hear.

Dr. MURALIDHAR. Sorry. Contracted vendor Personalist is out in California.

Mr. DUNN. All right. And what is the status of the VA, Department of Veterans Affairs partnership on the computing? This is the quantum computing; we were going to start comparing the data in the records to the sequencing.

Dr. MURALIDHAR. So we have just completed the IRB approvals for the three projects. Our first three projects are—

Mr. DUNN. This is the national single IRB?

Dr. MURALIDHAR. Yes, this is the VA central IRB.

Mr. DUNN. So it is done?

Dr. MURALIDHAR. The projects have completed central IRB approval.

Mr. DUNN. Good.

Dr. MURALIDHAR. And the computing environment is tested and ready in the Department of Energy oak Ridge National Laboratory. And the first three projects are focused on assessing suicide risk, especially acute suicide risk, which is of the great relevance for us. The second is on prostate cancer, to distinguish between lethal and nonlethal.

Mr. DUNN. We have got a lot of that.

Dr. MURALIDHAR. Yes. And then the third one is on the total cardiovascular disease burden.

Mr. DUNN. Outstanding, good. We look forward—one—are there interim updates on this or are we just sort of waiting for the research papers?

Dr. MURALIDHAR. We are just waiting to get the work started.

Mr. DUNN. Okay. So, Dr. Clancy, why does the Office of Research and Development have to enter into a partnership with the VA National Clinical Oncology Program given they are both VA entities? I mean, I thought the partnership existed ipso facto.

Dr. CLANCY. So this is interesting, because it gets to your earlier point in your opening statement about getting to rapid translation and impact on veterans' lives.

Traditionally—and, I mean, this is true everywhere—you know, first we do the research and then we make the publications, then the word gets out and it is incorporated into textbooks. And, in my former life, we documented that that time lag is about 17 years. That was not VA-specific, but in general scientifically.

Mr. DUNN. I agree.

Dr. CLANCY. The important part about this collaboration with the Prostate Cancer Foundation is that we are really pushing the boundaries of that history, right? So where we have got researchers working along—

Mr. DUNN. So let me interrupt you, just because in the interest of time. I am very, very familiar with the Prostate Cancer Foundation, I have been working with them for years. Great translation work, much, much faster, very, very accelerated. I couldn't agree with you more. Let's do more along that line.

Dr. Haas, and perhaps Mr. Kuntz as well, what do you think is the single greatest barrier to VA researchers? What is the biggest barrier they are facing, researchers in the VA?

Dr. HAAS. Having time carved out for their research is the—

Mr. DUNN. So are clinical duties interfering with research?

Dr. HAAS. Yes, other duties in general. Yes, they have reported that repeatedly to us that they don't have the ability to focus—

Mr. DUNN. Mr. Kuntz, do you agree with that?

Mr. KUNTZ. Yes, sir, and that is why I highlighted the Veterans Equitable Resource Allocation, so those clinician researchers are on the ground.

Mr. DUNN. I am concerned, I will tell you. It is not intuitive to me that following this equitable research distribution across the VISNs is going to speed up the research or make more time available to the researchers. We will consider that, but not in the next minute and a half.

Dr. Clancy, can you quantify the impact that your research program has on your department's ability to recruit and retain clinician researchers?

Dr. CLANCY. It is phenomenal. I will tell you why, because frankly a young physician emerging from training today from residency, surgery, whatever, if they want a terrific career in research, their best shot is to come to VA, and I think many of them know that, because we value and put a very high premium on physicians who both see patients and actually do research. So it is a tremendous recruiting tool for us.

I will say that we—you have probably just highlighted some issues about the tension between clinical productivity and appropriate documentation—

Mr. DUNN. Yeah, I am familiar with that.

Dr. CLANCY [continued]. —as well—yes, as well as carving out time for research, but we are happy to take that and get back with you.

Mr. DUNN. So a hot-button issue is one we hear about frequently, is service dogs for veterans with PTSD. Could you give us an update on that study and when we are going to hear some recommendations?

Dr. CLANCY. The final data collection was completing this month and we should have results for you in a year.

Mr. DUNN. We would love that; we would love that.

Dr. CLANCY. Yes.

Mr. DUNN. Oh, gosh, I have got so many questions here, Chairwoman, and I have 7 seconds. Which one is the best one? Based on the Shepherd Therapeutics statement for the record, over 60 cancers disproportionately affect veterans and servicemembers, 25 of those are rare cancers. What specifically is the VA doing to identify treatment options for cancers that tend to be associated more with veterans? And this sounds like a great use of the Million Veterans Project, frankly.

Dr. RAMONI. So I would say that that is something that our Post-Deployment Health Group is looking at very closely in terms of which truly are disproportionately affecting veterans. And then that is one of the reasons why NCI wanted to partner with us, National Cancer Institute wanted to partner with us is our ability to find rare cancers because we have such a large database.

Now, whether they will be represented in the Million Veterans Program, they may be so rare that they are small in number in MVP, but throughout our system, I agree, we have a great opportunity to shed light on those conditions.

Mr. DUNN. Let me say that I think Chairwoman Brownley and I would love to help in any way we can, removing regulatory bar-

riers or underscoring things that you need underscored in order to make progress.

Thank you very much, Madam Chair.

Dr. RAMONI. Thank you.

Ms. BROWNLEY. Thank you, Dr. Dunn.

Mr. Lamb?

Mr. LAMB. Thank you, Madam Chairwoman. If I could just pick right, there where Dr. Dunn left off. Is VA starting any sort of database to track the specific types of cancer that patients are diagnosed with and possibly collect tissue samples for further research and integration with the genetic information, is that sort of collection going on of the tissue samples in particular?

Dr. CLANCY. So all veterans with cancer are entered into cancer registries locally, as are patients everywhere. I don't know that we have yet made that connection with MVP, but I actually think it is a terrific idea. There are technical issues related to creating the kind of repository of tissue samples that frankly have been a big challenge for our colleagues at NIH and others as well, but I think it is a fabulous idea.

Mr. LAMB. What are the—is there a way you could briefly summarize the obstacles to doing that?

Dr. CLANCY. I would have to take that for the record. I am familiar with it only because it really came up when I was running a research agency at HHS, but it has been very tricky to figure out how we would store them and guarantee safety. I am sure you have read stories where issues with samples that have been lost have been sort of a hot-button issue. But do you want to add?

Dr. RAMONI. Yes. So one of the challenges is, for example just in cancer, there are about 400,000 cases a year, so the size of a biobank that you would need to have at the ready and to be able to fund in perpetuity is one of the barriers. So to ensure that you can fund that kind of bio-bank forever, essentially, is one of the barriers.

One of the options—

Mr. LAMB. Sorry to interrupt—

Dr. RAMONI. Yes.

Mr. LAMB [continued]. —does that type of thing exist anywhere else or would the VA be the first to do something like that?

Dr. RAMONI. I would have to come back to you with that, but I don't believe that such a database with that many cancers exists anywhere.

Mr. LAMB. But you are saying 400,000 per year just within the VA patient population?

Dr. RAMONI. Yes. So VA has 8 percent of the cancers in the country, so when you think about that, that is just an enormous number. So that is one of the challenges and that is only talking about cancers and not other conditions, for instance, invisible wounds of war.

So the alternative that I think we should explore is the fact that many of these individuals do have pathology samples already extant in the VA in various repositories across the country. So while they wouldn't be specifically collected for research, we could have essentially a virtual biobank of pathology stores, and that is the direction that we are looking for, in addition to capturing some of

those images, like slide images, and the radiological images to pair with, for instance, MVP data.

Mr. LAMB. Okay, thank you. Yeah, that is—we are looking sort of to the future with a whole generation of veterans now exposed to burn pits especially, that is kind of what is motivating my question here. So—

Dr. RAMONI. Yes.

Mr. LAMB [continued]. —we will stay in touch with you about that.

Dr. RAMONI. Thank you.

Mr. LAMB. Dr. Clancy, I also just wanted to say, I am very happy to hear about the research at the Philadelphia Medical Center on opioids and genetic predictors there. So if there is anything, we can ever do to help accelerate that program or if you have results to share at any point, please let us know.

Dr. CLANCY. Absolutely.

Mr. LAMB. The last thing I just wanted to ask is, I see there being an IT side to this whole thing as well. Obviously, we are in the process now of building this new health record system for the VA. When and if the science advances enough from the Million Veterans Program or otherwise, I could see a future in which clinicians are using their electronic health record system to look at maybe genetic information about the patient who is in front of them and whether they would reject certain drugs or not, you know, to help them speed through that appointment. Is that something that is being talked about at your level with Cerner to make sure there is room for that in the system that is being built, do you know?

Dr. CLANCY. So we are actively working with Cerner to make sure that the system will be able to accommodate our research needs.

Mr. LAMB. Okay.

Dr. CLANCY. I think it is safe to say that they probably don't have a customer with the extent and depth of the research that we support, at least on paper. And in person, they are excited about it, but we do have people who are getting way down into the technical weeds to make sure that that happens.

Some piece of that that we are excited about, although we have not found the perfect solution yet, nor has anyone else, is the notion of trial matching. So that, you know, today any patient's entry into a clinical trial depends on a light bulb going on over a doctor's head and then needing to go look things up. If you think about how Amazon and other companies work, we could be pushing that information to the encounter to at least lift some of the burden and, frankly, to make the information, how would I say, more patient-friendly—

Mr. LAMB. Uh-huh.

Dr. CLANCY [continued]. —but that is exactly the kind of thing that we need to be doing and, you know, an electronic record that supports our needs has to have those needs as well.

Mr. LAMB. Okay. Well, I am sure you know we have the separate Subcommittee on IT—

Dr. CLANCY. Yes.

Mr. LAMB [continued]. —and are frequently in dialogue with all the players. So if you run into any roadblocks there or there is a

way, we can help the conversation with Cerner or otherwise, please let us know.

Dr. CLANCY. Thank you.

Mr. LAMB. Thank you, Madam Chairwoman. I yield back.

Ms. BROWNLEY. Thank you, Mr. Lamb.

And I now recognize Mrs. Radewagen for 5 minutes.

Mrs. RADEWAGEN. Thank you, Madam Chair.

Dr. Haas, why does it take VA sites so much longer to activate a clinical trial than non-VA sites? And what are the barriers to using commercial IRBs?

Dr. HAAS. It takes longer because the current system doesn't allow the utilization of commercial IRBs, among other factors. So when a sponsor goes to the VA to conduct a trial, they have to go through multiple reviews, and the current centralized process is significantly slower than the commercial IRB process is.

Why—the second question was why the central IRB—

Mrs. RADEWAGEN. What are the barriers to using commercial IRBs?

Dr. HAAS. As far as I understand, both Drs. Clancy and Dr. Ramoni are committed to utilizing a central IRB, a commercial central IRB process, but they continue to run into major challenges. And, at a minimum, we believe that Secretary Wilkie should facilitate the successful and timely implementation of this reform, it is actionable, and the enactment of legislation may also be necessary, but there are no overt reasons why it cannot be implemented.

Mrs. RADEWAGEN. And, Dr. Clancy, do you agree with that assessment? And do you support the 100-days-faster initiative and why?

Dr. CLANCY. Absolutely. And, not only that, I am pleased to say that we have got work in progress to make that happen. The finalizing of the new common rule for research that affects all participants in research and so forth, which has to be in place this fall, next fall, or early 2020?

Dr. RAMONI. Early 2020.

Dr. CLANCY. Early calendar year 2020, for a system our size is one big, heavy lift. And so the leader whom Dr. Ramoni recruited hit the ground running like I can't even describe, and I think we will get that done.

When I worked at HHS, we used a commercial IRB in a different manifestation, but nonetheless had very good luck with it, and there is no reason we can't do this here.

Mrs. RADEWAGEN. Thank you, Madam Chair. I yield back the balance of my time.

Ms. BROWNLEY. Thank you, Mrs. Radewagen.

Mr. Barr, I recognize you for 5 minutes.

Mr. BARR. Thank you, Madam Chairwoman.

My grandfather served on a destroyer in Navy in World War II and he was diagnosed with cancer as a young veteran, and he received treatment and was in remission, and then at age 59 he was diagnosed with multiple myeloma and passed. This was in 1977 when I was a young child. And of course we have had a lot of advances in the diagnosis of cancer and the treatment of cancer, and obviously servicemembers in eras since World War II have, you know, better treatment outcomes and hopefully better diagnostics.

But we think that my grandfather was exposed to radiation on that destroyer—we don't know for sure, but we think that was probably what caused his cancer. In Vietnam, obviously, Agent Orange is something that we think is a cause and then now, in the post-911 generation, burn pits, but radiation throughout the eras.

My question to you all is, what advances in precision medicine are helping with diagnosis? And how is the VA doing in terms of—in conjunction with DoD, how are they doing in terms of, you know, identifying risk factors for cancers with servicemembers, and how is the VA trying to detect these cancers earlier because of servicemembers' exposures to these various risks.

And I will start with Dr. Clancy.

Dr. CLANCY. Sure, and I will start off and then turn to Dr. Ramoni.

So at baseline, as a foundational element of course, veterans receive the, you know, current state of the science, recommended screening tests for cancers, which sounds fairly basic, but it is surprising because not all Americans do for one reason or another, so that is colorectal cancer screening, breast cancer and lung cancer and so forth, all of which is good stuff.

Linking that back to exposures as a result of service is trickier for sure. A lot of our ability to do that is obviously dependent on the precision of the records of where people served. Now, depending on their job classification, those records may be more available or not, but that is why it is very important that we have a research collaboration as part of our Health Executive Committee where VA and DoD come together on a regular basis to explore those very issues.

For some conflicts, the first Gulf War is a good example, there is very, very little information about where people served because of the short-term nature of the deployment and we just don't have very good information. For other issues, it is a matter of our records available and so forth.

But obviously, as you pointed out with burn pit exposure, people are very, very worried about that, which is why we are trying to beef up the registry and encourage people to come in for exams and so forth.

Do you want to add anything?

Mr. BARR. Dr. Ramoni?

Dr. RAMONI. So I would agree with Dr. Clancy that getting accurate records of exposures is key to our ability to understand the impacts of those exposures. There are well-known associations with Agent Orange and cancer and prostate cancer, have more severe cancer if you are exposed to it, to Agent Orange, Camp Lejeune exposures. But for the multiplicity of things people were exposed to in their deployments to Iraq and Afghanistan, we need to understand much more.

And we are committing to—you know, we are in the process of putting together 2021 priorities and we are committing to better understand the effects of military exposures, and, in particular, there is a dearth of information on the clinical side. So we have a lot of epidemiologic research, we have basic science research, but there is an enormous gap for the clinical research that will lead to translation much more quickly.

Mr. BARR. Thank you. And in my remaining time, of course, with precision medicine, there is tremendous opportunity, and what we are told is that oncology in particular there is potential with the use of molecular diagnostics at the time of diagnosis to help establish genetic characteristics of cancer. Is the VA performing this type of molecular testing for cancer patients at the moment of diagnosis?

Yes. And what is the promise of that? Explain that to us.

Dr. CLANCY. So it is unknown what the promise is right at this moment. There are some diagnostics that are well recognized, for example, there are certain types of lung tumor variants that have turned out to be very important, and we are working actively with several organizations that are facilitating access to industry funding for additional research in this area, which is terrific. At the moment for lung cancer, those appear to be a small minority of patients, although it is amazing to meet people who tell you they were diagnosed with stage 4 lung cancer 7, 8 years ago and, you know, here they are just doing fine now, which still blows my mind.

For other areas, we are still in a much more exploratory phase. So I am thinking about relatives who have shared their results of testing with me. When I say to them, gosh, this is like a lot of markers and tests, and did you ask what they are for? And they all said, well, yes, but they are not sure yet, but they are testing just in case. And we haven't quite advanced to that level yet, but the number of tests that are actually approved and recommended in terms of the evidence that we have got that it makes a difference is still a fairly short list.

We do have a partnership with the Sanford Health System actually looking at a cancer survivorship cohort, which may have helped the situation you described with your grandfather, but that was just launched about a year ago. So we will have more to report on that as it progresses.

Mr. BARR. Thank you. I yield back.

Ms. BROWNLEY. Thank you, Mr. Barr.

And, Dr. Dunn, do you have some words—

Mr. DUNN. I confess, I do.

Ms. BROWNLEY. Good.

Mr. DUNN. Thank you so much, Chairwoman Brownley.

Ms. BROWNLEY. Absolutely.

Mr. DUNN. So one of the things, we talk about translation and speeding up the translation to bedside, and I think that a lot of that is about the system, how we work as clinicians with researchers. And you made a point earlier that it used to be 10 to 15 years, you know, somebody would do work away in a lab, a dusty, old lab, you know, find some facts out, write a paper, add a chapter to a textbook, and then some young, brilliant scientist comes along, reads it, and applies it to patients. Now it is much quicker. We actually—you know, we bring a sick patient to the scientist and say, what do you know, what do you have. And then I think that the Million Veteran Project is an ideal resource for that kind of translational research that quickly gets in there and really hits the literature very quickly.

And I think, by the way, you have partnered well with PCF on that. And there is a similar group, by the way, that does breast

cancer research in the same way, translational very fast, and that is another group that I think you could find very easily.

So one thing that I was reading in your memo about the three principal lines of science that we were talking about, researching with—you know, the 31 alpha, beta, and gamma research projects, then the three exemplar projects with the DOE, which you mentioned earlier, and the MVP project itself, how are we doing on those three—generally on those three lines of research? And I am not sure who to ask that question to.

Dr. MURALIDHAR. Sure. So from the 31 alpha, beta, and gamma projects, we have about five or six projects that are pretty mature and already yielding results. And, for example, there was one project on the genetics of cholesterol and we found—

Mr. DUNN. Genetics of what?

Dr. MURALIDHAR. Cholesterol, lipids—

Mr. DUNN. Okay.

Dr. MURALIDHAR [continued]. —high cholesterol. And—

Mr. DUNN. I guess I will need to read that paper.

Dr. MURALIDHAR. Yes, it has some very interesting findings. First of all, that they have discovered some new genetic variants in the subgroup of African-Americans and Hispanics, so it is different from what is seen in the Caucasian population.

Mr. DUNN. Have you published that paper?

Dr. MURALIDHAR. Yes, it came out in Nature Genetics last November. We can send you a link.

Mr. DUNN. I would love that.

Dr. MURALIDHAR. Yes, we will. And what they found very interesting in that is there are genetic variations in three genes, which could be potential therapeutic targets, and then there are drugs out there already in the market that could be applied to these. And so we are now investigating how we can translate that discovery pretty quickly into the clinic.

And another example is one where we are also piloting returning genetic results to men with metastatic prostate cancer, where knowing specific variants in their DNA repair genes, for example, can then direct them to a particular treatment that would work better with them.

And so that is—

Mr. DUNN. I am familiar with that, that is great.

Dr. MURALIDHAR. And also in familial hypercholesterolemia, FH, an inherited form of high cholesterol, where you can begin, you know, intensive treatment earlier on if you knew that you have the genes for that. So we are also piloting that with MVP.

So there are two projects that can see immediate translation from MVP.

The three exemplar projects with DOE that I mentioned, with the Department of Energy, are just about to begin. So we are going to have milestones within the first year. Within a year we hope to report back to you some of the findings on the predictive algorithms for suicide risk or prostate cancer.

Mr. DUNN. That would be exciting. You know, it is great to see that kind of progress happening and happening in short timeframes, relatively speaking.

What mechanisms do we have to inform the patients at the VA, the veterans in the VA health system, that we have some of these research projects available? That maybe they want to participate in the research, or maybe they just want to benefit from the very cutting-edge work that you are doing. Is there an information portal saying the VA is studying this, we have expertise maybe in the VA in Miami in this and the VA in LA on a different subject?

Dr. CLANCY. So what I am less clear about, but very hot on finding out, so I will be meeting with all of our chiefs of staff, I guess the second week in July, just to ask that very question, is how much local facilities tout what they are doing, because there is nothing like home team pride, right? Right here at the Philadelphia or whatever VA we are doing something really amazing. I happened to meet a couple of researchers from the amazing Philadelphia VA last week at our research day here over in the Rayburn Building.

We certainly—VSO conventions are a very big place for us to share a lot of these findings and also, by the way, to enroll people in MVP. But I think that we could exploit other opportunities as well. We also have a blog that goes out to a lot of veterans, although I am told, since we don't make the printed copy anymore, we may not be reaching everyone. That is a different topic.

But, in any case, I think there are other venues that we could explore for that, because I do think it is a point of pride.

Mr. DUNN. Yeah, getting the word out is almost as important as actually, you know, making the great discovery.

And I will make one request of you and then I yield back, and the request is, next time you have a research day here on the Hill, let me know. All right? I would love to come.

Dr. CLANCY. Absolutely, you can count on it.

Mr. DUNN. Thanks so very much. I yield back.

Ms. BROWNLEY. Don't just let Dr. Dunn know exclusively, but—yeah, I am going to yield myself a little bit more time too.

And so I want to know exactly how we can tear down the barriers and what Congress barriers are to enhancing, hastening the research that the VA is doing. So I know we have talked about the commercial review boards moving to that. I honestly don't understand why the VA can't just mimic a commercial review board, why we have to make it so complicated. That, you know, it goes back to this idea of every head of a medical center has full decision-making power and authority over so many programs that we are trying to kind of standardize, you know, across the board.

So that is one, if that is what we have to do, let's do it. I think there were probably some mention of some other important—I think, Dr. Haas, you talked about some targeted reforms that are needed. And I am not sure I have that in my head, but if there is—if we are only talking about changing statutory guidance, that is one thing, but if we need legislation, that is another thing. And certainly I think I do, and I think the Committee does, has a big interest in if we can move forward legislation to tear down some of these barriers, it doesn't seem to be there are costs really associated with that, if we can do that, I think we need to start rolling up our sleeves and getting that work done.

So, Dr. Clancy, I am just looking to you as our resource, so that we can begin that work.

Dr. CLANCY. So, thank you for that. And I cannot overstate how much your interest in having this hearing and, frankly, just the level of questions and the depth of interest will be for our efforts for sure.

I think we will just move ahead with commercial IRBs. I see one—or commercial IRB—I see one little wrinkle, but I think that is easy, it feels easy now to more or less adjudicate, which is what is their relationship between commercial IRB and our internal office of oversight and review, but if that is an issue I will bring that back to you. I am just not sure that I am seeing that need of legislative guidance and so forth. But we will certainly bring back the intensity of interest here, which means more to me than I can tell you.

Ms. BROWNLEY. Well, and I think—I mean, I don't know—I believe I know where you stand on this, but I think we are also interested in opening up more opportunities with private industry—

Dr. CLANCY. Yes.

Ms. BROWNLEY [continued]. —and the research that they are doing that, you know, I think together collectively we can make more progress and perhaps make faster progress.

Dr. CLANCY. Well, that is a very, very important signal for us and we will certainly make the most of it.

Ms. BROWNLEY. Okay. But in terms of what we need to do, you know, to include that particular area too I think is really important.

And I wanted to go back to Mr. Lamb's questioning with the electronic health record. So it seems to me in reading the testimony that one of the things needed is that the Department of Energy's computer structure, whatever, to manage the data that we have so far—I am not a computer scientist, nor am I a doctor, nor am I a researcher, so forgive me for not having the right terminology, but that if that is the case and if we are using the Department of Energy to help to manipulate that data, if the electronic health record is going to be, you know, sort of finalized in the next 7, 8, 9 years it is going to be to finalize it, I guess the question that I am trying to ask without being a technical expert here is, if the VA were to change or to do their own in-house computer system to manage this data, or they are going to continue to use the Department of Energy or the Department of Energy changes their process, does that have to be compatible and interactive with an electronic health record to get to where we want to go?

Dr. CLANCY. Well, certainly for speeding up ease of identifying relevant patients, being interactive is absolutely necessary. And I would say it is also necessary to make sure that we can translate rapidly.

I will say that the computational needs for research writ large are pretty immense, so even NIH is exploring lots of different venues from investing in their own—you know, the Cancer Institute has had like a very robust investment in bio-informatics for quite a few years, but they are working with Google too. And we are having conversations with Google and a number of other companies. And, you know, frankly, they are delighted to have them,

because they don't have access to specific patient data. Obviously, that needs to be negotiated to make sure all the Ts are crossed and Is are dotted and so forth, and privacy is protected, but nonetheless I think there is just immense opportunity.

Ms. BROWNLEY. Just the concern I have is if there are different entities that you are working with and we ultimately want that to be compatible with our health records, if that is changing constantly, the health record to be interoperable between DoD and VA right now is complicated enough, that really adds, at least it seems to me, another very complicated level that will take some level of sophistication to make all that happen.

Now, I am just expressing that concern.

Dr. CLANCY. I think Dr. Ramoni had something to add.

Dr. RAMONI. So, you know, we have all highlighted how rich VA data are and currently those data are held in a VistA system. One of the key factors in ensuring that we continue to derive value from that data for our veterans is that that historical data be maintained and that it not simply be mapped to the new system, because you lose information when you kind of map it to a new system. So, for research to continue, it is important that we maintain those historical data well before—you know, for people even who have passed on, it is still important that we have that information.

So it may exceed the clinical needs for that information at this point, but we still need it for research.

Ms. BROWNLEY. Very good, very good. And then I guess the last question that I had is just—you know, just to help me understand how this fits into the larger research arena is, you know, how does the VA's research budget compare to the National Institutes of Health, the Food and Drug Administration, other governmental agencies, do you have any idea?

Dr. CLANCY. Well, yes. So our budget for this current year is just under \$800 million. I would guess that that is comparable to almost twice that amount in NIH dollars, because we pay people's salaries from different lines. In fact, I used to review grants at VA before I came to VA and I was always surprised by the budget numbers, because they didn't quite make sense to me, in part because I was used to looking at budgets that paid for every single minute of everyone's time.

So that would put us at one and a half to \$2 billion in equivalent buying power, I believe, which would put us in the scope of some of their larger institutes. I guess the Cancer Institute is in the ballpark of 5 to \$7 billion. The entire National Institutes of Health, which is immense, is somewhere in the \$30 billion.

Ms. BROWNLEY. But the research component is—

Dr. CLANCY. Oh, they are all research.

Ms. BROWNLEY. Yes.

Dr. CLANCY. Yes.

Ms. BROWNLEY. So, okay. Well, I think that is it for me, I think I don't have any further questions.

Mr. Dunn, do you have any closing remarks you would like to make before we—

Mr. DUNN. Yes, I thank the panel for your patience. I know we dinged you on your schedule today; we dinged ourselves, so we know we dinged you too, but it is our fault, and I appreciate your

patience and your willingness to come and educate us. And I would like you to think that this actually is not a waste of your time, because we need the information in order to make decisions.

And so thank you for your efforts on our behalf and the behalf of your patients.

Mr. KUNTZ. Thank you.

Dr. CLANCY. Well, thank you for your interest. This has really been phenomenal.

Ms. BROWNLEY. Well, and I appreciate all of you being here. Mr. Kuntz, we didn't ask you a question, but your testimony was invaluable. So thank you very, very much for being here.

And, Dr. Clancy, I am very serious about following up with how we can break these barriers down to be able to do what we need to do within the VA, but to open up this sort of treasure chest that we have to the private industry, so that we can really help and move towards some of these successes. Clearly, suicide and post-traumatic stress and traumatic brain injury, we know that all of these things lead ultimately to suicide. Cancer, obviously for our veterans, these are areas that our veteran community needs very, very desperately. And if we could truly be the leaders in all of this, I think it would be quite extraordinary.

So I really commend all of you for the work that you are doing, and this is really a high point in what the VA does, and so I thank all of you and your expertise.

And, with that, all Members will have 5 legislative days to revise and extend their remarks, and include extraneous material. And, without objection, the Subcommittee stands adjourned.

Thank you.

[Whereupon, at 4:27 p.m., the Subcommittee was adjourned.]

A P P E N D I X

Prepared Statement of Carolyn Clancy, M.D.

Good afternoon, Chairwoman Brownley, Ranking Member Dunn, and distinguished Members of the Subcommittee. Thank you for the opportunity to discuss VA's Million Veteran Program and Precision Medicine research efforts. I am accompanied today by Dr. Rachel Ramoni, Chief Research and Development Officer, and Dr. Sumitra Muralidhar, Director of the Million Veteran Program.

Introduction

Precision medicine is the prevention, diagnosis, prognosis, and treatment of health conditions that considers individual variability in biology, environment, and lifestyle. Advances in biomedical research, informatics, computational science, and medical care are converging in the 21st century to reveal the complexity of human physiology and enable us to decode that information to improve health and well-being.

VA is the largest and most diverse health care system in the United States and has some of the richest data in the world. In combination, those two factors give VA the ability and the responsibility to lead the world in the practice of precision medicine. VA Research, in close partnership with clinical operations and education, is the discovery engine that drives the evolution towards ever more precise care of our Veterans.

As Deputy Under Secretary for Health for Discovery, Education, and Affiliate Networks, which includes the Office of Research and Development (ORD), I am pleased to be here to share our vision, investments, and deliverables in the field of precision medicine.

Strategic Priorities that Reflect VA Research Values

For more than 90 years, VA has conducted research within its health care system. In establishing VA Research, Congress recognized both the need to study Veterans' unique concerns and how essential research is to excellent clinical care. This was prescient: VA Research has resulted in three Nobel prizes, seven Lasker Awards, and numerous other national and international honors.

Today, ORD continues to honor its statutory commitment through the execution of three strategic priorities, which Dr. Rachel Ramoni, VA's Chief Research and Development Officer, articulated in early 2018 and includes the following:

1. To increase Veterans' access to high quality clinical trials;
2. To increase the substantial real-world impact of VA research; and
3. To put VA data to work for Veterans.

VA's Commitment to Real-World Innovation

Since its inception, VA Research's discoveries have contributed to real-world impact. The pacemaker and liver transplantation are well-known examples of early VA research advances that transformed health care. Fewer people know that the Gleason grading system, which is used worldwide predicting the prognosis of a man with prostate cancer, is named for its creator, Donald Gleason, who was a pathologist at the Minneapolis VA Health Care System. More recently, VA conducted the foundational trial that established active surveillance as a safe alternative to prostatectomy in low-risk prostate cancer. Importantly, this work not only led to several publications in the prestigious New England Journal of Medicine, but it also reshaped the care we provide. VA is ahead of the curve in adhering to this best practice, which improves the quality of life of men with prostate cancer.

The promise of ever more precise medicine is that we can go beyond general predictions like low-, medium-, and high-risk prostate cancer to specific predictions that will guide an individual Veteran's care. One of the ways that ORD is making this vision a reality for Veterans who are cared for by the Veterans Health Administration (VHA) is through our partnership with the VA National Clinical Oncology Pro-

gram Office and the Prostate Cancer Foundation. The beachhead of this effort is six VA medical centers that will act as hubs of best-in-class care. The next phase will include adding hubs and extending from hubs to spokes. The first precision oncology milestone is to ensure that men with metastatic prostate cancer receive Deoxyribonucleic acid (DNA) sequencing. Already, this effort has identified men who, based on their genetic variations, will benefit from precision therapies that are known to be effective against the specific type of cancer they have.

The Million Veteran Program: A Partnership with Veterans

One of ORD's major investments in precision medicine is the Million Veteran Program (MVP). The program was launched in 2011 with a goal to enroll at least one million Veteran partners by 2021 to build the world's largest research database of genetic, health, lifestyle, and military exposure information.

Enrollment

MVP has achieved its goal of being the largest program of its kind in the world, with over 750,000 Veterans enrolled. MVP includes Veterans from all 50 states, Guam, and Puerto Rico. MVP makes it easy for Veterans to become a part of the program by having enrollment sites at 58 VA medical centers; 83 community-based outpatient clinics; and Veterans Service Organization conventions.

To ensure that all can benefit from precision medicine, we must understand the genetic basis of diseases in diverse racial and ethnic populations. Most genetic research to date has been conducted in Caucasian populations. Findings in this group sometimes do not translate well to other groups. MVP demographics track well with that of Veterans enrolled in VA health care. Approximately 18 percent are African American, and 7 percent are Hispanic. To enhance our ability to serve all Veterans, MVP is repeating the genetic analysis of samples from African American participants using a genetic test (genotyping chip) enriched for genetic variants found in the African American population.

Science

To put these data to work for Veterans, we must make use of the best technologies and engage the best researchers. MVP is at an important transition point, moving from a program focused exclusively on enrolling a diverse set of Veteran partners to a program that is both enrolling participants and making discoveries that will benefit those Veterans. At present, MVP is undertaking three primary scientific lines of effort:

1. Thirty-one alpha, beta, and gamma research projects have been funded by ORD to both make discoveries and to establish the resources, processes, and infrastructure necessary to responsibly support large-scale science. The research topics span diseases of high relevance to Veterans such as suicidality, posttraumatic stress disorder (PTSD), multi-substance abuse, schizophrenia and bipolar disease, Gulf War Illness, traumatic brain injury (TBI), Alzheimer's Disease, tinnitus, and Parkinson's Disease. They also include chronic diseases highly prevalent in Veterans such as cardiovascular and cardiometabolic diseases, chronic kidney disease, cancer (prostate, breast, lung, and multiple myeloma), osteoarthritis, and age-related macular degeneration.

2. Three exemplar projects are being conducted in collaboration with the Department of Energy (DOE). These data science-intensive projects focus on suicide, prostate cancer progression, and cardiovascular disease risk prediction. Over 75 researchers from VA and DOE national laboratories are engaged in these projects. Each project includes a requirement to work collaboratively with VHA clinical operations to ensure real-world impact. For example, more accurate prostate cancer progression risk predictions will improve our ability to identify those Veterans with low-risk prostate cancer who should undergo surgery versus active surveillance. The suicide risk prediction project will use the power of artificial intelligence (AI) to improve the precision of VA's Recovery Engagement and Coordination for Health - Veterans Enhanced Treatment (REACH VET) algorithm, which is used to identify Veterans at highest risk of suicide.

3. ORD is funding two projects to determine the feasibility and value of offering to return important individual genetic results to MVP participants, following re-consenting of the MVP participant and validating the MVP finding in certified clinical laboratories. The first is the return of genetic variants for familial hypercholesterolemia (FH), which is genetic high cholesterol. Veterans found to have FH will be offered treatment, which reduces the risk of serious health problems like heart attacks and stroke. The second project will reach out to Veterans with a diagnosis of metastatic prostate cancer and harmful variants in three DNA repair genes.

This information will guide treatment options and participation in clinical trials. These projects are in the regulatory review phase and are expected to launch by the end of Fiscal Year (FY) 2019.

Since the initiation of the MVP science effort in 2017, VA researchers have presented over 100 abstracts at national and international scientific and medical meetings, and over 15 peer-reviewed original scientific papers have been published. Six recent publications are in high-impact journals such as *Nature Medicine*, *Nature Genetics*, and *Nature Communications*. These communicate novel discoveries in the genetics of high blood pressure, high cholesterol, alcohol use disorder, and PTSD.

MVP Data Access

MVP exists because our Veteran partners are willing to continue to serve our Nation through participation in research. Respecting the concerns voiced by Veterans in focus groups and surveys, MVP committed to not distribute its datasets. Instead, researchers come to the data to conduct their work in a secure environment. Thus, an essential first step to realize our promise to MVP participants to advance precision medicine among Veterans is to establish a modern computational infrastructure that can scale to many studies occurring in parallel. To this end, ORD is establishing a pilot with the University of Chicago and the Open Commons Consortium to make de-identified MVP and electronic health record data broadly available to approved VA and non-VA researchers in a VA Data Commons. Continued investment in information and technology modernization will support projects in the VA Data Commons within the next two years.

To complement this effort, ORD is in the process of large-scale curation of the data contained within the electronic health record using natural language processing and other advanced computational techniques. What we mean by curation is transforming the wealth of disparate and identifiable information contained within electronic health records into valid descriptors of an individual's health conditions, such as metastatic prostate cancer, Gulf War Illness, and PTSD. Having these curated data means that research projects can begin more quickly and that we can share more meaningful de-identified data with non-VA collaborators while protecting Veterans' privacy. By the end of FY 2021, we pledge to create a library of at least 1,000 curated health conditions.

Beyond MVP: Big Data, Biomarkers, and the Invisible Wounds of War

While MVP is a substantial VA Research investment in precision medicine for Veterans, it is by no means the only such effort. The individual projects are too numerous to enumerate in this statement, so I highlight some exemplars focused on healing the invisible wounds of war.

In 2017, ORD funded the Precision Medicine for Mental Health (PRIME) Care clinical trial which is conducting genetic testing to guide the selection of antidepressant medication among 2,000 Veterans with major depressive disorder. The trial will determine both how Veterans and clinicians use this information and whether it improves outcomes. As of May 2019, the study was past the halfway point in recruitment.

The Chronic Effects of Neurotrauma Consortium (CENC), pronounced "sen-see," is a nationwide effort to understand the mechanisms of combat-associated mild traumatic brain injury (mTBI), to evaluate how co-morbidities like mental health conditions may be affected by combat-associated mTBI, and to study treatment and rehabilitation strategies for the short- and long-term effects of combat-associated mTBI. It includes a longitudinal study with intensive biosampling and imaging for biomarker development. CENC is funded by VA and the Department of Defense (DoD). Data from CENC are available through the Federal Interagency Traumatic Brain Injury Research (FITBIR) Informatics System, which shares TBI research data, methodologies, and associated tools. As of March 1, 2019, the consortium has submitted approximately 171,000 records on over 2,000 subjects who are enrolled in CENC studies. In addition, CENC is in the process of uploading over 1,500 Magnetic Resonance Images to FITBIR. Notably, the epidemiologic components of CENC already are yielding important findings, such as that women Veterans with diagnoses of TBI, PTSD, or depression had a significantly increased risk of dementia compared to women Veterans without these diagnoses.

The Translational Research Center for TBI and Stress Disorders (TRACTS) study is another longitudinal study with biomarker collection to understand the complex changes in the brain, thinking, and psychological well-being that result from TBI and PTSD. TRACTS focuses on Veterans who served in Operation Enduring Freedom/Operation Iraqi Freedom.

Expanding Veterans' Access to Clinical Trials

Clinical trials are essential to both generating the evidence necessary to bring precision medicine research discoveries into the clinic and to provide hope when Veterans reach the limits of what standard medical care can provide. To achieve their goal to increase Veterans' access to high quality clinical trials, ORD launched the Access to Clinical Trials (ACT) for Veterans initiative in 2018 with the support of several non-profits including the National Association of Veterans' Research and Education Foundations (NAVREF), Us Against Alzheimers, Longevity, and Cohen Veterans Bioscience. ACT's goal is to get VA clinical trial startup times to within 25 percent of industry standards by the end of FY 2021.

Policy, infrastructure, and education must also evolve to support the changing landscape of clinical trials, especially in light of the single Institutional Review Board (IRB) review mandate that will take effect on January 20, 2020. To lead this change, in late October 2018, ORD welcomed Dr. Molly Klote, a retired Army colonel, as Director of the Office of Research Protections, Policy, and Education. In December 2018, she and her team began a "moonshoot" initiative that identified 13 regulatory steps needed to be ready to meet the new national mandate. They have thus far completed 7 of those required elements and are on track to complete all by Jan 2020

Policy changes

The use of commercial IRBs was prohibited in VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research. This will be revised to allow their use in circumstances where a third party pays the IRB fees. This update will dramatically increase VA's ability to participate in multi-site clinical trials and to offer Veterans the benefit of these trials. Master service agreements with the country's two largest commercial IRB companies are being finalized. The item remaining to realize these groundbreaking agreements is the Federal Information Security Modernization Act (FISMA) data rating for data that will need to be transferred to the commercial IRB to complete their reviews.

Additionally, to facilitate our ability to partner with DoD to help Servicemembers and Veterans, ORD is hosting a meeting on August 23, 2019, to document differences in regulatory, legal, privacy, contracting, human resources and information security as it relates to data sharing and clinical trial operations. At that point, we will begin needed updates to the VA/DoD research handbook. DoD and VA already allow for reliance on each other's IRBs.

Infrastructure

ORD is in the process of contracting to purchase a commercial off-the-shelf, VHA-wide research management platform to support multisite trials, increase efficiency, standardize process, and allow more complete tracking and oversight of research and the research review process. We anticipate a contracting decision by mid-July 2019. In addition, ORD is standing up a process to review and approve applications from VHA facilities to rely on non-affiliated IRBs for research studies to support the single IRB review mandate. Finally, VA Central IRB is doubling its capacity by adding a second national expansion panel to decrease the wait time to receive IRB review. We anticipate stand up by the end of this fiscal year. Future panel will be added as the review demand is assessed.

Education

In addition to numerous regular education Webinars, ORD will be hosting a workshop on August 20–21, 2019, to prepare local VA medical center IRB personnel for research and regulatory requirements for the shift to single IRB review.

Conclusion

On behalf of ORD and the many VA researchers across the country, I thank you for your attention. As the Deputy Under Secretary for Health for Discovery, Innovation, and Affiliate Networks, I am fortunate to represent these superlative individuals in sharing the progress we have made towards fulfilling our commitment to discover and bring the advances of precision medicine to our Nation's Veterans. My colleagues and I look forward to responding to your questions.

Prepared Statement of Dr. Magali Haas

Introduction

Dr. Magali Haas, PhD. CEO and President of Cohen Veterans Bioscience and co-founder of the Coalition to Heal Invisible Wounds.

Good afternoon, Chairwoman Brownley, Ranking Member Dunn, and distinguished Members of the Subcommittee. Thank you for the honor to testify before the Subcommittee and for the opportunity to discuss the barriers to precision medicine. It is also a pleasure to testify alongside Dr. Carolyn Clancy, Deputy Under Secretary for Health for Discovery, Education and Affiliated Networks with the Veterans Health Administration Department of Veterans Affairs (VA), and with fellow Coalition Member, Matt Kuntz.

Cohen Veterans Bioscience

Cohen Veterans Bioscience (CVB) was founded in 2014 under its original name of Orion Bionetworks to address brain disease research and in 2015 expanded its focus in response to the clear need to provide optimized care for our nation's Veterans suffering from post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI). We are a national, nonpartisan research 501(c)(3) public charity organization dedicated to fast-tracking the development of diagnostic tests and personalized therapeutics for the millions of Veterans and civilians who suffer the devastating effects of trauma-related and other brain disorders. CVB is leading the way in responding to this critical challenge by organizing a multi-stakeholder complementary network of international subject-matter experts and employing the most innovative scientific tools to support a common roadmap for identifying diagnostic biomarkers, building predictive disease models and developing treatments for PTSD and TBI. We are rethinking how we study brain disease, how we define it, how we identify new targets and how we advance precision medicine approaches, and our portfolio of projects exemplifies our commitment to accelerating the field of brain health.

Our portfolio includes several large-scale programs, specifically in the area of PTSD and TBI, which allow us to rapidly and empirically develop and test new diagnostics and treatments that will speed personalized medicine approaches to clinicians and will directly benefit the Veteran and civilian communities. Examples of our research programs are listed below:

- **Adaptive Platform Trial in Post-traumatic Stress Disorder:** The only approved medications for the treatment of PTSD are the selective serotonin reuptake inhibitors (SSRIs) sertraline (Zoloft) and paroxetine (Paxil), which were approved over 17 years ago¹. However, their efficacy for treating PTSD is limited, with response rates rarely exceeding 60% and only 20–30% of patients achieving complete remission². The VA 2017 Consensus Statement of the PTSD Psychopharmacology Working Group concluded that there is a deficient pipeline of new PTSD medications and an assessment of recent trial failures has generated concerns about how to best identify new targets for medication development and optimally design clinical studies³. The high failure rate of previous clinical trials can be attributed not only to the lack of validated biomarkers for PTSD, which prevents clinicians from predicting whether a patient will respond to a given therapeutic in a clinical trial, but also, and most critically, to the field's historical use of traditional clinical trial designs, which lack the ability to implement prospectively planned modifications to one or more aspects of the trial based on the heterogeneity of the patient population.

In September 2018, Cohen Veterans Bioscience was granted a research award by Advanced Technology International (MTEC Consortium Manager) on behalf of the U.S. Army Medical Research and Materiel Command (MRMC)⁴. The award is for a three and a half year study to comparatively test the efficacy and safety of pharmacotherapeutics for PTSD via a well-powered adaptive platform trial (APT). Cohen Veterans Bioscience will lead this program and serve as a Clinical Coordinating Center, establishing a clinical trial infrastructure for the trial's governance structure that includes a Joint Steering Committee with representatives from the VA, the National Institute of Mental Health, the FDA, and the Defense Health

¹Jeffereys M. Clinician's guide to medications for PTSD. Sep 12, 2011. Available at: <http://www.ptsd.va.gov/professional/pages/clinicians-guide-to-medications-for-ptsd.asp>. Accessed October 20, 2011.

²Berger W et al. Pharmacologic alternatives to antidepressants in posttraumatic stress disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2009; 33:169–180.

³Krystal J. et al., It Is Time to Address the Crisis in the Pharmacotherapy of Posttraumatic Stress Disorder: A Consensus Statement of the PTSD Psychopharmacology Working Group, *J. Biological Psychiatry* (2017). [http://www.biologicalpsychiatryjournal.com/article/S0006-3223\(17\)31362-8/abstract](http://www.biologicalpsychiatryjournal.com/article/S0006-3223(17)31362-8/abstract).

⁴Cohen Veterans Bioscience Adaptive Clinical Trial press release. October, 2018. Available at: <https://www.cohenveteransbioscience.org/2018/10/04/cvb-receives-research-award-dod-ptsd-clinical-trial/>. Accessed on June 24, 2019.

Agency’s Psychological Health Center of Excellence. This clinical trial is scheduled to start in the spring of 2020 and will incorporate biological measurements to support a precision medicine approach to PTSD treatment. During the period of performance, at least two active drugs (pending selection) will be tested simultaneously incorporating biological measurements to support a precision medicine approach to PTSD treatment. The APT will also incorporate extensive biomarker testing to identify and enable the validation of more precise diagnostics, biomarkers that can predict the response to specific treatments, or biomarkers that could be used for stratifying patients in clinical trials. The results of this trial aim to identify a drug to move forward for Phase 3 testing starting in 2023 and ultimately lead to an alternative FDA- approved drug or changes to clinical practice guidelines for the treatment of military- related PTSD.

- Research Alliance for PTSD/TBI Innovation and Discovery Diagnostics (RAPID-Dx):

RAPID-Dx is CVB’s flagship biomarker discovery collaborative, with the aim to fast-track the development of objective diagnostics for PTSD, TBI and other trauma-related brain disorders. Developing biomarker-based diagnostics is essential to shifting diagnosis & treatment of PTSD and TBI from a syndromic, symptom-based approach to a biological, mechanistically-based one that targets the effects of trauma at their molecular roots. To date, no biomarkers have been sufficiently validated and independently replicated to allow for use in stratifying these highly heterogeneous patient populations, predicting disease course, or supporting diagnostic development. To advance discovery and validation, CVB is coordinating a multi-disciplinary, multi-institution, public private partnership program that will bring together large, well-characterized cohort studies of PTSD and TBI, encourage collaboration amongst investigators to share large biomarker and imaging legacy datasets in a centralized, cloud-based platform, and support large-scale analyses of stored bio-samples on high performance bioassay platforms. This will ultimately inform precision medicine approaches for more effectively treating veterans and others suffering from trauma-related brain disorders.

- Digital Health: In July 2018, we announced the formation of Early Signal, LLC, a wholly owned, non-profit subsidiary of Cohen Veterans Bioscience.⁵ The new subsidiary allows CVB to continue its innovative approach to translational research by advancing needed diagnostics and precision medicine for brain disorders including PTSD, TBI and MDD, and expands our capabilities in digital health and data-driven research. Early Signal has developed a leading digital health platform for recording and analyzing a range of information, reported from wearables and other sensors, directly related to the well-being of patients living with brain disorders. By tracking variables such as sleep, physical activity, stress and cognition, we aim to better understand what changes in patients with brain disorders over time and to use this multifactorial data to improve the ability of clinicians to diagnosis a wide range of brain disorders and to treat them using precision medicine approaches.

The Coalition to Heal Invisible Wounds

CVB is a founding co-chair of the Coalition to Heal Invisible Wounds, which launched in February 2017.⁶ The Coalition advocates for policy reforms to widen and expedite the pipeline for new therapies and diagnostics for PTSD and TBI. By deepening public-private cooperation and adopting targeted reforms, the VA and Department of Defense (DoD) can become leading partners in delivering new therapies and diagnostics to doctors.

Doctors need better tools to diagnose and treat Servicemembers and Veterans suffering from PTSD and TBI. Only 16 percent of IAVA members, as surveyed in 2017, believe troops and Veterans are getting the care they need for mental health injuries, and stigma remains the top reason Service members and Veterans are not seeking care.⁷ The Coalition’s mission is guided by four overlapping concerns:

⁵ Cohen Veterans Bioscience press release, September, 2018. Available at: <https://www.cohenveteransbioscience.org/2018/09/06/cohen-veterans-bioscience-expands-digital-health-platform-with-early-signal-expertise/>. Accessed June 24, 2019.

⁶ The Coalition’s members are Cohen Veterans Bioscience (co-chair), the Military Veterans Project, NAMI Montana, Otsuka America Pharmaceutical Inc. (co-chair), and Tonix Pharmaceuticals. More on the Coalition to Heal Invisible Wounds is available at invisiblewounds.org.

⁷ “IAVA 2017 Annual Member Survey: A Look into the Lives of Post-9/11 Veterans” Published October 2017. Available at: <https://iava.org/wp-content/uploads/2016/05/IAVA-Survey-2017-v11update.pdf>.

1.A staggering 6,000 Veterans have committed suicide each year from 2008 to 2016. In 2016, the suicide rate was 1.5 times greater for Veterans than for non-Veteran adults.⁸

2.Treating the underlying condition can help reduce the risk of suicide, but a 2015 Journal of the American Medical Association (JAMA) study found that about two-thirds of Veterans receiving prolonged exposure therapy, considered by Stanford researchers to be “the gold standard of behavioral therapy for PTSD,”⁹ “retained their PTSD diagnosis after treatment.”¹⁰

3.Treatment-resistant PTSD is a common clinical problem in Veterans, since currently “available medications are often ineffective in usual clinical practice.”³

4.The VA found in 2016 that “most [PTSD] patients are treated with medications or combinations for which there is little empirical guidance regarding benefits and risks,” and there is “no visible horizon for advancements in medications that treat PTSD.”

The lack of clinical research in PTSD and TBI has led to treatment regimens that resemble trial and error. In 2013, while still serving as Director of the National Institute of Mental Health, Dr. Tom Insel stated that “the diagnostic system [for mental disorders] has to be based on the emerging research data, not on the current symptom-based categories.”¹¹ In Veterans mental health, precision medicine has a simple meaning: we want diagnostics and therapies that work.

The lack of precision medicine in PTSD care contributes to the high rate of treatment-resistant PTSD in Veterans. Clinicians need new tools to diagnose precisely those suffering from PTSD and TBI, which can only be achieved by systematic reviews of existing evidence, and a greater investment in both basic and translational research and in large-scale and well controlled clinical trials. It also requires improved clinical trial processes and clinical trials that include Veterans. We owe Veterans our commitment to prioritize clinical research.

The 100 Days Faster Initiative

We ask today that the Subcommittee help the VA overhaul its clinical trial start-up practices. According to data from two major contract research organizations, in the last four years VA sites have taken an average of 265 days to activate a site (from receipt of registration and contract to active).¹² Non-VA sites have averaged 141 days. Because of these lengthy delays, many clinical research sponsors do not attempt to bring clinical research to the VA, and have not done so for decades.

The lack of clinical trials at VA sites means that Veterans lack access to the frontier of medicine for many disease conditions. For Veterans suffering from PTSD, TBI, hearing loss, alcohol and other substance use disorders (SUDs), cancer, and other conditions, a clinical trial may be the next or only available treatment option. This is most acute in oncology, where only a small fraction of the hundreds of clinical trials annually in the United States use VA sites. Of 34,000 oncology clinical trials in the United States listed on clinicaltrials.gov, fewer than 800 have taken place at a VA facility.¹³ What happens when a cancer study does not open in a VA facility? A Veterans suffering from that form of cancer is more likely to die sooner. Countless birthday, anniversaries, graduations, births, and other milestones missed in part because of inadequate clinical trial procedures at VA sites.

We believe that timely and high impact reform is within reach. The VA Office of Research and Development (ORD) and the National Association of Veterans Research and Education Foundations (NAVREF), have led a multi-stakeholder review

⁸“VA National Suicide Data Report 2005–2016.” Published September 2018. Available at: <https://www.mentalhealth.va.gov/docs/data-sheets/OMHSP-National-Suicide-Data-Report-2005-2016-508.pdf>.

⁹Stanford Medicine News Center. “Biology may make certain PTSD patients unresponsive to behavioral therapy.” April 3, 2019. Available at: <http://med.stanford.edu/news/all-news/2019/04/biology-may-affect-ptsd-patients-response-to-therapy.html>.

¹⁰Steenkamp, MM, et. al. “Psychotherapy for Military-Related PTSD: A Review of Randomized Clinical Trials.” Journal of the American Medical Association. 2015 Aug 4. pp. 489–500.

¹¹Krystal J. et al., It Is Time to Address the Crisis in the Pharmacotherapy of Posttraumatic Stress Disorder: A Consensus Statement of the PTSD Psychopharmacology Working Group, J. Biological Psychiatry (2017). [http://www.biologicalpsychiatryjournal.com/article/S0006-3223\(17\)31362-8/abstract](http://www.biologicalpsychiatryjournal.com/article/S0006-3223(17)31362-8/abstract).

¹²“Post by Former NIMH Director Thomas Insel: Transforming Diagnosis.” NIMH Director’s blog. Posted April 29, 2013. Accessed May 9, 2018. <https://www.nimh.nih.gov/about/directors/thomas-insel/blog/2013/transforming-diagnosis.shtml>.

¹³Personal communications with contract research organizations in July 2018 and January 2019.

¹⁴Source: [Clinicaltrials.gov](http://clinicaltrials.gov) search of clinical trials conducted in oncology at VA sites. Accessed June 24, 2019.

of the causes of clinical trial startup delays. Both CVB and the Coalition have engaged in this review, called Access to Clinical Trials (ACT) for Veterans, which has identified numerous areas ripe for immediate reform.

We believe that with targeted reforms, the VA can become 100 days faster, on average, at clinical trial startup by 2021. We call this the 100 Days Faster Initiative, and last month organized a multi-stakeholder letter to the House and Senate Committee leadership calling for congressional support of the goal. Achieving this goal would build the institution of the VA, bringing it to near-parity with leading clinical research institutions in the United States.

As the causes of clinical trial startup delays extend throughout numerous functions within the VA, it is imperative Congress provide the VA statutory guidance to achieve the 100 days faster objective.

Informed by the ACT for Veterans process and other engagement with leading stakeholders in the clinical research community, we recommend that the Subcommittee develop legislation that provides for the following reforms:

1.Allow the use of commercial Institutional Review Boards (IRBs) in sponsored clinical research.

Slow and inconsistent reviews by IRBs constitute a major factor in start-up delays. IRB reviews ensure that clinical trials abide by clear ethical guidelines and protect the well-being of research participants. VHA Handbook 1200.05, revised January 2019, states: "A VA facility may not use a commercial IRB as an IRB of Record." Yet, commercial IRBs accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) are widely employed outside of the VA and are highly regarded in the research community for thorough and timely procedures. Over the past two years, the VA ORD has been exploring policy changes to allow the use of commercial IRBs as another option to local IRBs or the VA Central IRB. The VA should immediately remove all barriers to allowing the use of commercial IRBs in sponsored clinical research.

2.Authorize and provide performance benchmarks for Office of Research Reviews within the Office of Information Technology (IT)

A centralized information security analysis would allow for a more thorough and appropriate review, while reducing delays that often occur at the local level. Local information security officers (ISOs) have variable levels of knowledge related to clinical research data storage and transfer requirements, and limited time to understand the research requirements which leads to security requirements for the same study that differ by VA clinic.

Since 2018, the VA Central Office, Office of IT, has hired ten ISOs to assist local ISOs with clinical research approvals, covering the entire national research program for activities across all of the more than 100 VA sites. Codifying this function within the Office of IT and requiring that it fulfill specific objectives, such as developing an approved vendor list, would allow for a more thorough and appropriate review, while reducing delays that often occur at the local level.

3.Authorize and provide performance benchmarks for Office of Research Reviews within the Office of Privacy (IT)

Similar to information security reviews, a centralized privacy review would allow for a more thorough and appropriate review, and standardize outcomes. Medical Center privacy officers have variable levels of knowledge related to clinical research privacy requirements, and thus privacy protocols can vary significantly between clinical trial sites. Similar to the Central Office IT Team, the VA should hire dedicated privacy officers dedicated to multi-site clinical research. Codifying this function within the Office of Privacy and requiring that it fulfill specific objectives would allow for a more thorough and appropriate review, while reducing inconsistencies that often occur at the local level.

4. Refocus the Role of the Research and Development Committee

Stakeholders both within and outside of the VA have identified the R&D Committee as worthy of refocusing toward other aspects of the research and development process, including identifying emerging research needs at local VA facilities, and removing the R&D Committee's role as the final approval for a clinical trial site. Unique to VA facilities, after a trial sponsor has secured all of the required substantive approvals for a trial site, the local Research and Development (R&D) Committee provides the final approval before a site can begin its trial (VHA Directive 1200.01). This is a unique requirement, not found at academic and other institutions that host clinical trials, and can delay start-up by several weeks.

Taken together, these four reforms would help the VA make substantial progress toward improving its average clinical trial start-up period by 100 days. We look for-

ward to working with the Subcommittee to identify other steps Congress can support toward this goal.

Conclusion

The Coalition to Heal Invisible Wounds thanks the Subcommittees for its work to strengthen the VA's capacity to support the development of precision medicine. Veterans have earned the right to world-class health care, and an implicit promise of world-class health care is a strong research function. We strongly believe that the VA has the potential to be a world-class research partner, enabling better healthcare for Servicemembers and Veterans. Achieving the 100 Days Faster Initiative would provide significant initial progress toward that goal. On behalf of CVB and the Coalition to Heal Invisible Wounds, I thank you for your attention to these matters.

Prepared Statement of Matt Kuntz, J.D.

I. Introduction

Chairwoman Brownley, Ranking Member Dunn and distinguished members of the Subcommittee, on behalf of NAMI, the National Alliance on Mental Illness, and NAMI Montana, I would like to extend our gratitude for the opportunity to share with you our views and recommendations regarding "Beyond the Million Veterans Program: Barriers to Precision Medicine." NAMI Montana and the entire NAMI community applauds the Committee's dedication in addressing the critical issues around the veterans' brain healthcare system. NAMI is the nation's largest grassroots mental health organization dedicated to building better lives for the millions of Americans affected by mental illness. NAMI advocates for access to services, treatment, support and research, and is steadfast in its commitment to raising awareness and building a community of hope for all of those in need.

NAMI works closely with many partners to accelerate research and advance treatment for mental health conditions. For example, NAMI Montana is a member of the Coalition to Heal Invisible Wounds (Coalition). The Coalition was founded in February 2017 to connect leading public and private scientific investigators of new post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI) treatments with policymakers working to improve care for veterans. Coalition members support innovators at all stages of the therapy development lifecycle, from initial research to late-stage clinical trials.

In addition to serving as the Executive Director of NAMI Montana, I am also the Director of the Center for Mental Health Research and Recovery (CMHRR) at Montana State University. While the CMHRR does have statewide suicide prevention research, none of that research funding presents a conflict with this testimony. I have also been appointed to the Creating Options for Veterans' Expedited Recovery (COVER) Commission. This testimony does not reflect the views of Montana State University, the Montana University System, or the COVER Commission.

I. Overview

With our commitment to promote innovation to accelerate research and advance treatment for mental health conditions, NAMI remains very supportive of the research and development of psychiatric biomarkers for brain health conditions, and we encourage Congress to make the necessary investments in research to begin to accomplish this goal.

NAMI continues to advocate for VA to work in coordination with the Department of Defense (DoD) to develop and carry out a longitudinal research study which will identify biomarkers or non-survey diagnostic tools, which will enable clinicians to make a more precise diagnosis.

NAMI advocates for improving mental health and brain condition diagnostics because an accurate, quick, and early diagnosis has the potential to save countless lives and is a critical step to effective care. Currently, the only tools available to diagnose a mental health condition are survey-based. This results in a large amount of misdiagnosis of conditions, and therefore lack of timely and appropriate treatment. We are dedicated to working with the VA, legislators, and researchers to improve the process and get veterans the treatment and care they need for their recovery. Earlier identification of conditions will lead to better treatment for these conditions, which is a necessary component to reducing suicides among Veterans.

II. Background

A. Scientific Justification

Suicide is the 10th-leading cause of death in the United States, and Veteran suicide is a national concern. According to the VA National Suicide Data Report, in 2016, the suicide rate was 1.5 times greater for Veterans than for non-Veteran adults. According to the authors of *Suicide Among Soldiers: A Review of Psychosocial Risk and Protective Factors*, “The fact that the vast majority of suicides occur among people with a current mental disorder makes this risk factor a prime target for screening and prevention efforts.”¹

However, the state of the science in the screening, diagnosis and treatment of mental health conditions is in flux. A strong analysis of this issue is given by Dr. Thomas Insel, MD, et al. in the paper introducing the National Institute of Mental Health’s Research Domain Criteria effort. At the time this article was published, Dr. Insel was the Director of the National Institute of Mental Health (NIMH):

Current versions of the DSM and ICD have facilitated reliable clinical diagnosis and research. However, problems have increasingly been documented over the past several years, both in clinical and research arenas. Diagnostic categories based on clinical consensus fail to align with findings emerging from clinical neuroscience and genetics. The boundaries of these categories have not been predictive of treatment response. And, perhaps most important, these categories, based upon presenting signs and symptoms, may not capture fundamental underlying mechanisms of dysfunction. One consequence has been to slow the development of new treatments targeted to underlying pathophysiological mechanisms.

History shows that predictable problems arise with early, descriptive diagnostic systems designed without an accurate understanding of pathophysiology. Throughout medicine, disorders once considered unitary based on clinical presentation have been shown to be heterogeneous by laboratory tests—e.g., destruction of islet cells versus insulin resistance in distinct forms of diabetes mellitus. From infectious diseases to subtypes of cancer, we routinely use biomarkers to direct distinct treatments. Conversely, history also shows that syndromes appearing clinically distinct may result from the same etiology, as in the diverse clinical presentations following syphilis or a range of streptococcus-related disorders.²

The critical nature of this issue to the VA’s services is one of both severity (veteran suicide) and scope. According to the VA’s Office of Research and Development, “More than 1.8 million Veterans received specialized mental health care from VA in fiscal year 2015.”³

Therefore, the VA serves almost 2 million veterans a year in a treatment system based upon mental health diagnosis categorizations that the former Director of the National Institute of Mental Health has deemed not to be “predictive of treatment response”⁴ (emphasis added). The ramifications of that dramatic flaw in the VA’s mental health treatment system presents a glaring fissure in our ability to prevent veteran suicides.

B. Personal Justification

My family lost my stepbrother Specialist Christopher Dana to a post-traumatic stress injury in March of 2007. His post-traumatic stress injury stemmed from a brutal tour in Iraq as a HUMVEE machine gunner with the Montana National Guard. The Montana National Guard medical professionals had no idea that Chris was struggling with a brain health condition until he took his life. I will not go into depth about Chris’s story now. However, I can’t help but wonder what a more effective system for screening, diagnosing, and treating brain health conditions would have done for Chris.

Instead I will focus the personal side of this testimony on two of my dear friends, John Scott Hannon and Mike Franklin, who tragically died by suicide, and how their stories relate to precision mental health.

1. Commander John Scott Hannon

(a) Obituary

Commander John Scott Hannon USN (Ret.), affectionately known to his family as “Scott,” was born April 11, 1971, in Nairobi, Kenya. Born to a U.S. Diplomatic Corps

¹ Nock, Matthew K., et al. “Suicide among soldiers: a review of psychosocial risk and protective factors.” *Psychiatry: Interpersonal & Biological Processes* 76.2 (2013): 97–125.

² Insel, Thomas, et al. “Research domain criteria (RDoC): toward a new classification framework for research on mental disorders.” (2010): 748–751.

³ Office of Research & Development website. Department of Veterans Affairs. Accessed on June 19, 2019. <https://www.research.va.gov/topics/mental-health.cfm>

⁴ Insel, Thomas, et al. “Research domain criteria (RDoC): toward a new classification framework for research on mental disorders.” (2010): 748–751.

family, he grew up living in Tanzania, the Soviet Union, England, Belgium, as well as McLean, VA, and Helena, MT. In 1989, Scott enlisted in the U.S. Navy and qualified as a Gunner's Mate in 1990. He graduated with BUD/S Class 173 in March 1991 and, upon completion of SEAL Qualification Training, was assigned to SEAL Team Two. From 1995 to 1998, Scott completed multiple deployments in Europe, Middle East and Asia with SEAL Team Five, where he was top ranked SEAL Assistant Platoon Leader. He served with SEAL Team Three in the Pacific and Southwest Asia and was named top ranked SEAL Platoon Commander. From 2000 to 2003, Scott was assigned to SEAL Delivery Vehicle Team Two operating mini submarines and became Task Unit Commander. Scott was the top-rated officer during a six-month advanced maritime special operations course, the most demanding joint training available in the military, and was hand-selected to lead a covered unit in a sensitive "Preparation of Battlespace" mission. In 2003, he joined the Naval Special Warfare Development Group, commonly known as SEAL Team Six, and was eventually responsible for all aspects of curriculum development and individual certification. John Scott graduated in 1995 from the University of Colorado with a B.A. in Political Science. He attended school on a Naval Reserve Officers Training Corps (NROTC) scholarship. From 2006 to 2008, he received a scholarship to attend the Tuck Business School at Dartmouth College, then worked as a Special Operations and Policy Staff Officer at the U.S. Special Operations Command (USSOCOM) until he retired in 2012.⁵

John Scott's supervisory, technical and safety qualifications include Military Freefall Specialist, Static Line Parachutist, NSW Sniper (Honor Graduate), Naval Gunfire Forward Controller, Lead Climber, High Performance Small Boat Coxswain, Diving Supervisor, Cast Master, Rope Master, Live Fire Range Supervisor, Joint Special Operations Planner, Amphibious Operations Planner, Advanced High Risk Survival & Hostage Survival, Advanced Combat Trauma Care Provider, Long Range MAROPS, Expeditionary Warfare Staff Planning, Customized Military Mobile Force Protection and others. Scott was also awarded the Joint Service Commendation medal, Defense Meritorious Service medal, Navy and Marine Corps Commendation medal (3), Joint Service Achievement medal, and the Navy, Marine Corps Achievement medal (2) and Joint Meritorious Service Award, and Bronze Star Medal (Gold Star in lieu of the Second Award). After 23 years of military service, Scott retired to his family home near Helena, Montana. In addition to VA Montana treatment for Post-Traumatic Stress Disorder, Traumatic Brain Injury, severe depression and bipolar disorder, he was a committed volunteer with a number of local organizations. He was involved with the Montana chapter of NAMI, speaking candidly at events about his wartime injuries. Scott also rescued and rehabilitated injured wild animals at Montana Wild, provided training support for the Lewis and Clark Search and Rescue, worked with at-risk youth with Habitat for Humanity and collaborated with the Prickly Pear Land Trust to help veterans access nature trails.⁶

John Scott was open about his invisible wounds of war and found solace and recovery in many of the causes that also allowed him to give back to his fellow veterans and his community. He was passionate about improving veterans' access to mental health care and integrating service animals into mental health care. Scott worked closely with Montana Wild and VA Montana to develop a group therapy program for veterans that involved birds of prey. Scott was embraced on his journey to recovery by his family, friends, and community. He died from his invisible wounds of war on February 25, 2018.⁷

(b) Relationship to Precision Medicine

I became friends with John Scott and his family after they asked me to help him connect to resources and build social support. I was there for many of the good times and hard times throughout his battle with brain health conditions.

A few months after John Scott's death, I met with his family at their ranch near Helena. We laughed and cried. We especially talked about how frustrating it was that he had worked so hard for recovery only to lose his life at the end. John Scott had come to a good place with his post-traumatic stress injury. He had overcome addiction. He was learning to live with his mild traumatic brain injury, but it was the dramatic highs and lows of bipolar disorder which could not be overcome.

I will never forget the words that John Scott's sister Kim Parrott said that day. "I just wish we had known about the bipolar disorder earlier." I couldn't agree more that the missed diagnosis, the missed factor in brain health treatment, could have

⁵ <https://www.veterans.senate.gov/imo/media/doc/hannon.bio.pdf>

⁶ Id.

⁷ <https://www.veterans.senate.gov/imo/media/doc/hannon.bio.pdf>

made a significant difference if it had been factored into his treatment from the start.

2. Mike Franklin

(a) Obituary

Mike Franklin, age 59, died September 20, 2014 of depression after a long and courageous battle. Born and raised in Anderson, South Carolina, he was a true Southern gentleman who fell in love with Montana's Rocky Mountains.

Where he worked last was what he loved most: his job at Carroll College for the last 11 years as the Director of Counseling Services. He loved the students and his colleagues. In the 15 years before coming to Carroll College he served as a U.S. Naval chaplain and earned a master's degree at Yale University. He spent three years as a Methodist minister after earning his Master of Divinity from Duke University and, true to his nature, he was still in contact with the parishioners of the small parish he ministered to 29 years ago. Prior to finding his calling as a spiritual minister, he served as a U.S. Army officer for five years after graduating from West Point. He graduated from T.L. Hanna High School in Anderson, SC in 1973 where he played football, the start of a passion for intense sports. He found joy in parachute jumping, rugby, skiing, kayaking and river boarding in rivers above his skill level and hiking off the beaten path.

Who he loved last and loved best was his wife Georgia Lovelady, whom he married on July 9, 2011 on the campus of Carroll College. A close second was his dog and constant companion, Gracie, who died in May, four months before his own death. Mike was generous in all ways including with his time, his knowledge, and mentoring others. He was unfailingly kind, gregarious, spiritual, and funny (including two stints of stand-up comedy at the local brewery). He reached out to others even when he himself was struggling.

Mike is survived by so many who loved him dearly. If love alone could have kept him from the depths of depression, he would have sailed above his mental illness.

(b) Relationship to Precision Medicine

My friend Mike Franklin had treatment-resistant depression. This condition is described by the Depression Task Force that authored "Treatment Resistant Depression: A Multi-Scale, Systems Biology Approach."

An estimated 50% of depressed patients are inadequately treated by available interventions. Even with an eventual recovery, many patients require a trial and error approach, as there are no reliable guidelines to match patients to optimal treatments and many patients develop treatment resistance over time. This situation derives from the heterogeneity of depression and the lack of biomarkers for stratification by distinct depression subtypes. There is thus a dire need for novel therapies.⁸

One of the Depression Task Force's members is Dr. Joshua Gordon MD, PhD. Dr. Gordon is now the Director of the National Institute of Mental Health. From that position, Dr. Gordon is able to advance the Depression Task Force's vision of developing more effective depression treatments based upon more specific measurements and categorization-precision medicine.

Recent advances in methodologies to study genetic and epigenetic mechanisms, as well as the functioning of precise brain microcircuits, prompt new optimism for our ability to parse the broad, heterogeneous syndrome of human depression into biologically-defined subtypes and to generate more effective and rapidly-acting treatments based on a knowledge of disease etiology and pathophysiology and circuit dynamics.⁹

This is exactly the kind of breakthroughs that will save the lives of veterans with treatment-resistant depression like my friend Mike Franklin.

III. Scientific Progress

A. The emergence of transdiagnostic biological indications of brain conditions and susceptibility for brain conditions expand the paradigm of thinking about how these biosignatures can be used beyond the traditional psychiatric diagnostic categories.

⁸ Akil, Huda, et al. "Treatment resistant depression: a multi-scale, systems biology approach." *Neuroscience & Biobehavioral Reviews* 84 (2018): 272–288.

⁹ Akil, Huda, et al. "Treatment resistant depression: a multi-scale, systems biology approach." *Neuroscience & Biobehavioral Reviews* 84 (2018): 272–288.

The scientific search for biological signatures to guide the screening, diagnosis, and treatment of psychiatric conditions has evolved beyond the traditional diagnostic categories into more of a transdiagnostic viewpoint. As described by Beauchaine and Constantino:

An emerging consensus in the psychopathology research community is that complex functional interactions among a limited number of neural and hormonal systems - far fewer in quantity than syndromes defined in the psychiatric nomenclature - give rise to many if not most mental health conditions.¹⁰ From this perspective, endophenotypes might be more effectively reconstrued as markers of genetic liability to transdiagnostic vulnerability traits (e.g., impulsivity, irritability, anhedonia). As Skuse noted over 15 years ago, ‘a focus on traits, rather than syndromes, is appropriate and could in due course contribute to the redefinition of traditional psychiatric syndromes.’ When reframed in this way, common neural correlates of psychopathology among what have traditionally been considered as distinct disorders are no longer a nuisance in our quest for greater specificity, but are instead opportunities to better understand common etiologies.¹¹

This is a critical move forward for the scientific research of biosignatures that can affect the care of brain health conditions. I have included a couple of block quotes below from this line of research in Functional Magnetic Resonance Imaging, Genetics, and Blood Plasma. Interestingly, the transdiagnostic nature of these measurements also make it clear that these units of analysis will not replace, but will only add to additional insights and to a variety of treatment occupations: psychiatrics, psychologists, primary care providers, therapists, peer support specialists, etc.

1. Functional Magnetic Resonance Imaging

Neuropsychological performance, gray matter volume, and now functional brain activation evidence converge to implicate transdiagnostic disruptions in the neurocircuits underlying general cognitive control capacity. Functional disruptions parallel the multiple demand network and its interface with the salience network. Essentially, networks intrinsic to adaptive, flexible cognition are vulnerable to a broad spectrum of psychopathology. These findings highlight a common intermediate phenotype, which could be leveraged to advance therapeutics. Multimodal interventions that target the foundation of intact, dynamic cognition seated in these frontal-parietal-cingular-insular networks could be powerful for ameliorating not only symptomatic distress but also the often-pervasive functional impairments and diminished quality of life prevalent across psychiatric disorders.¹²

2. Genetics

In recent years, there has been considerable progress in our understanding of the genetics of common neuropsychiatric disorders, for which neurobiological leads have been elusive. It is now clear that these disorders are highly polygenic, involving thousands of common as well as rarer genetic variants that, together with environmental risk factors, collectively increase an individual’s chances of developing such a condition. It is also apparent that many of these risk variants are shared between neuropsychiatric diagnoses. As sample sizes have grown, both common and rare genetic risk loci for neuropsychiatric disorders have been identified with high confidence. Associations between neuropsychiatric disorders and common variants identified by GWAS appear to largely reflect regulatory genetic variation, which might operate on specific gene transcripts, in circumscribed cell populations and at particular developmental stages. For some neuropsychiatric phenotypes, particularly those with clear neurodevelopmental features, stronger effects on risk may be conferred by rare and de novo CNVs and exonic mutations that can result in hemizygous loss of gene function. With even greater sample sizes, and comprehensive genotyping through whole genome sequencing, many more genetic risk loci for neuropsychiatric disorders will be identified in coming years. Translating these discoveries into an understanding of molecular, cellular and neurophysiological mecha-

¹⁰ Beauchaine, Theodore P., and John N. Constantino. “Redefining the endophenotype concept to accommodate transdiagnostic vulnerabilities and etiological complexity.” *Biomarkers in medicine* 11.9 (2017): 769–780.

¹¹ Beauchaine, Theodore P., and John N. Constantino. “Redefining the endophenotype concept to accommodate transdiagnostic vulnerabilities and etiological complexity.” *Biomarkers in medicine* 11.9 (2017): 769–780

¹² McTeague LM, Huemer J, Carreon DM, Jiang Y, Eickhoff SB, Etkin A. Identification of Common Neural Circuit Disruptions in Cognitive Control Across Psychiatric Disorders. *Am J Psychiatry*. 2017;174(7):676–685. doi:10.1176/appi.app.2017.16040400

nisms underlying neuropsychiatric conditions will require the expertise of researchers in many areas of neuroscience.¹³

3. Blood Plasma

Of the six molecules most commonly studied as plasmatic markers of schizophrenia, major depressive disorder or bipolar disorder, five (BDNF, TNF-alpha, IL-6, C-reactive protein and cortisol) were the same across diagnoses. Meta-analyses showed variation in the levels of these molecules to be robust across studies, but similar among disorders, suggesting them to reflect transdiagnostic systemic consequences of psychiatric illness.¹⁴

B.Examples - Precision Mental Health to Advance Care for Post-Traumatic Stress Injuries and Depression

Dr. Amit Etkin MD, PhD, and his team at the Palo Alto VA and Stanford University are tackling some of the most critical questions about how to improve the diagnosis and treatment of psychiatric conditions. The group recently published the results of its groundbreaking study, "Using fMRI Connectivity to Define a Treatment-Resistant Form of Post-Traumatic Stress Disorder."¹⁵ As stated in that research:

"We found that a subgroup of patients with PTSD from two independent cohorts displayed both aberrant functional connectivity within the ventral attention network (VAN) as revealed by functional magnetic resonance imaging (fMRI) neuroimaging and impaired verbal memory on a word list learning task. This combined phenotype was not associated with differences in symptoms or comorbidities, but nonetheless could be used to predict a poor response to psychotherapy, the best-validated treatment for PTSD."¹⁶

The "Establishing Moderators and Biosignatures of Antidepressant Response for Clinical Care for Depression (EMBARC)" has made significant strides in their analysis of depression.¹⁷ That effort and related efforts by Dr. Madhukar Trivedi's team at the University of Texas Southwestern have identified potential biosignatures involving inflammation,¹⁸ blood,²⁰ and advanced imaging.²¹

IV. Recommendations

NAMI offers the following recommendations to help reduce barriers to precision medicine.

A.Enact the Precision Mental Health initiative in the bipartisan Commander John Scott Hannon Veterans Mental Health Care Improvement Act of 2019 (S. 785).

On March 13, 2019, Senators Jon Tester (D–Mont.) and Jerry Moran (R–Kan.) introduced the Commander John Scott Hannon Veterans Mental Health Care Improvement Act of 2019. The bill was named after my friend, Navy SEAL Commander John Scott Hannon, who served for 23 years and fought a courageous battle with post-traumatic stress, traumatic brain injury and bipolar disorder. NAMI believes that this legislation has the potential to increase access to mental health care, expand diagnostic research and authorize new programs to combat veteran suicides.

Significantly, the legislation also includes a requirement for the VA to implement an initiative to identify and validate brain and mental health biomarkers among veterans (Section 305). The initiative would be modeled after the National Institutes of Health's All of Us program, with a focus on post-traumatic stress disorder, traumatic brain injury, depression, and severe anxiety disorders. NAMI believes that if

¹³Bray NJ, O'Donovan MC. The genetics of neuropsychiatric disorders. *Brain Neurosci Adv*. 2019;2:10.1177/2398212818799271. doi:10.1177/2398212818799271

¹⁴Pinto, Jairo Vinicius, Thiago C. Moulin, and Olavo B. Amaral. "On the transdiagnostic nature of peripheral biomarkers in major psychiatric disorders: a systematic review." *Neuroscience & Biobehavioral Reviews* 83 (2017): 97–108.

¹⁵Etkin, Amit, et al. "Using fMRI connectivity to define a treatment-resistant form of post-traumatic stress disorder." *Science translational medicine* 11.486 (2019): eal3236.

¹⁶Id.

¹⁷National Institute of Health, National Library of Medicine, Clinical Trials.gov website. Accessed on June 19, 2018. <https://clinicaltrials.gov/ct2/show/NCT01407094>

¹⁸Jha, Manish, and Madhukar Trivedi. "Personalized antidepressant selection and pathway to novel treatments: clinical utility of targeting inflammation." *International journal of molecular sciences* 19.1 (2018): 233.

¹⁹Czys, Andrew H., et al. "Can targeted metabolomics predict depression recovery? Results from the CO-MED trial." *Translational psychiatry* 9.1 (2019): 11.

²⁰Furman, Jennifer L., et al. "Adiponectin moderates antidepressant treatment outcome in the combining medications to enhance depression outcomes randomized clinical trial." *Personalized medicine in psychiatry* 9 (2018): 1–7.

²¹Cooper, Crystal M., et al. "Cerebral blood perfusion predicts response to sertraline versus placebo for major depressive disorder in the EMBARC trial." *EClinicalMedicine* (2019).

enacted, this initiative has the potential to have a lasting effect on the future of the diagnosis and treatment for mental health conditions.

B.Ensure that the Veterans Equitable Resource Allocation (VERA) model supports precision healthcare initiatives.

The next stage of developing Precision Medicine in the VA requires both research and translation into clinical practice. This will require the participation of VA facilities outside of the flagship institutions. This will be essential not only for assuring the right number of participating veterans, but also to ensure that a diversity in the types of veterans are included. Precision medicine will be specific enough that groups that are not included in the research will not benefit from all of the findings.

NAMI recognizes that VERA is critical to how facility administrators are measured. The VERA model must be aligned to support a broadscale research and translational initiative. If precision medicine efforts are not properly incentivized in VERA, NAMI fears that the lack of local incentivization will stunt precision medicine efforts in the VA.

C.Structure VA research data in a manner where a machine learning natural language processing program can generate the beginnings of the first draft of a research article based on the data in the system.

The success of the VA's Precision Medicine efforts will depend on a variety of factors. There are issues of safety, regulation, investigator recruitment, technology, etc. One of the issues that is easily overlooked is that there will have to be a lot of papers written about the VA's Precision Medicine results. Published articles are critical to how the VA makes its own internal treatment decisions through Clinical Practice Guidelines.²² Published articles are also essential to have the lessons learned in the VA's Precision Medicine efforts translate over to clinicians in the community.

In my time at the COVER Commission, I have met VA researchers who have data that they do not have the time to write manuscripts to publish. This presents a serious wasted opportunity to advance veterans' mental health care. NAMI recognizes that the VA does not have as many clinician researchers as would be ideal to tackle the enormous challenge of addressing mental health challenges amongst veterans. Therefore, the VA must take as much of the "busy work" as possible out of the process of writing papers to enable the researchers to focus on their clinical work.

While there may not have been a lot of options to do this in the past, the current machine learning natural language processing technology has made an additional option available. NAMI recommends that VA consider this technology.

The extent of this "not having time to write up the data" problem is only going to get worse as the amount of actionable medical data increases as the world moves toward precision medicine. It's a problem that can and should be partially resolved through technology. We can't afford to have critical veteran medical research data left outside of the research community. There is just too much at stake.

V. Conclusion

Thank you again for the opportunity to testify in front of this honorable Committee. Your attention to this issue means a lot to me, our entire NAMI organization, veterans and their families. We look forward to working with you to save the lives of America's heroes.

STATEMENTS FOR THE RECORD

National Association of Veterans' Research and Education Foundations

The National Association of Veterans' Research and Education Foundations is the 501(c)(3) nonprofit membership organization of research and education foundations affiliated with Department of Veterans Affairs (VA) medical centers. These nonprofits, also known as the VA-affiliated nonprofit research and education corporations (NPCs), were authorized by Congress under 38 USC §§7361–7366 to provide flexible funding mechanisms for the conduct of research and education at VA facilities nationwide. Currently, there exist 81 NPCs supporting research and education activities at almost 100 VA medical centers.

²² See e.g. VA/DoD Major Depressive Disorder Clinical Practice Guidelines, Version 3.0–2016. Available at <https://www.healthquality.va.gov/guidelines/MH/mdd/VADoDMDDCPGFINAL82916.pdf>

NAVREF's mission is simple—we exist to advance the success of the NPCs. Together, NAVREF and the NPCs serve not only the Veteran, but the team of VA research and educational experts committed to improving the lives of Veterans. Ultimately, NAVREF envisions a nation in which Veterans receive the finest care based on innovative research and education. We believe that by working closely with Congress, VA leadership, NPC boards and leaders, and the great researchers and scientists working across the country in VA medical centers that our lofty vision can be achieved.

NAVREF has been encouraged by the leadership of Dr. Carolyn Clancy throughout her various roles across the Veterans Health Administration, but we are especially pleased to have her leading the recently established office of Discovery, Education, and Affiliate Networks, which oversees research and development. We strongly support the transformation efforts of VA's Chief Research & Development Officer, Dr. Rachel Ramoni, and the three high-level priorities she established last year—enhancing access to high quality clinical trials, driving substantial real-world impact, and putting VA data to work for Veterans. We look forward to continued collaboration with Dr. Clancy, Dr. Ramoni, and the first-rate team they've assembled at the Office of Research and Development (ORD) to address these priorities.

NAVREF's top priority initiative is to bring more clinical trials to Veterans in VA medical centers. It is critical that Veterans have the same level of access to these cutting-edge therapies as their counterparts outside the VA. In some therapeutic areas—most prominently in oncology—clinical trials are the standard of care, yet many Veterans do not have access to this life-altering research.

In December 2017, ORD and NAVREF embarked on a new effort to increase Veterans' access to clinical trials. The initiative, titled Access to Clinical Trials for Veterans (ACT for Veterans), kicked off with a Stakeholder Summit in April 2018 which brought together representatives from industry, VA Central Office, VA medical centers, patient advocacy groups, and the NPCs to participate in facilitated discussions centered around study start-up. It was important for all of us to hear industry's perspective on doing business with VA, so that we could understand where we needed to direct our energy to effect meaningful change. Since that initial meeting, five top priorities were identified, and workgroups were commissioned to address these priorities. NAVREF continues to solicit external stakeholder feedback at every step of the process. In February 2019, a Workgroup Summit was held in Washington DC which allowed the five workgroups to come together, present their respective products, and receive feedback on those deliverables.

Throughout this effort, ORD has been a steady partner, devoting time and manpower to every workgroup and completing additional tasks in support of ACT's objectives. But ORD cannot do this alone. Properly supporting clinical research requires a much broader effort across VA and VHA. One of the most important steps taken over the last ten years to support industry-sponsored clinical trials at VA medical centers was the establishment of the Specialty Team Advising Research (STAR) within the Office of General Counsel. Prior to the establishment of STAR, all legal reviews of research agreements (such as Non-Disclosure Agreements and Cooperative Research and Development Agreements) were handled by regional attorneys who had broad portfolios of higher priority matters and limited experience handling research issues. Timelines for review were understandably lengthy and unpredictable, such that some pharmaceutical companies were unwilling to work with VA sites. The establishment of STAR—a dedicated team of attorneys specializing in medical research matters—quickly reduced the backlog of agreements and led to predictable and reasonable timelines.

Similar to the legal delays that occurred ten years ago, clinical trials are now challenged by the unpredictability of reviews from the local offices of information security and privacy. Most VA hospital-based information security officers and privacy officers have limited expertise in research, which has many unique aspects that differ from the typical health care delivery setting. Therefore, they require additional time to review research proposals and frequently give inconsistent answers to the same question from site-to-site. This unpredictability causes delays and creates uncertainty among pharmaceutical companies seeking efficient, consistent trial sites. The solution for information security and privacy reviews should be the same as for legal reviews—centralization and standardization.

In 2018, the Office of Information Technology established a team of three Information Security Officers (ISOs) at the VA Central Office to assist local ISOs with clinical research approvals. This is a good first-step to clearing the obstacle currently faced at local sites with ISO reviews. NAVREF urges VA to make permanent the Office of Research Reviews within OIT and to create a similar permanent office for privacy reviews. These offices need to be given the people, resources, and authority necessary to accomplish their intended mission of supporting research activity

and reducing review timelines so that industry sponsors are compelled to bring clinical trial opportunities to Veterans at VA medical centers.

Another primary component of extended start-up timelines at VA facilities is the use of VA institutional review boards (IRB). IRBs play a critical role ensuring human research is conducted ethically and appropriately without causing harm to research participants. VA IRBs have a proud history of high-quality reviews that put the veteran's well-being first. However, the extended timeframe for these reviews exceeds typical industry expectations and can lead pharmaceutical firms to avoid VA sites. The Department of Defense faced a similar dilemma several years ago and successfully addressed the situation by allowing the use of commercial IRBs. VA should do the same and allow the use of commercial IRBs. The commercial IRB industry has demonstrated the highest standards of protections for patients-research-based risk protections, health information privacy protections, and information security protections. They undergo rigorous accreditation processes in order to safely and effectively conduct timely research reviews across the United States and the world.

As part of the ACT for Veterans initiative and to comply with the single Institutional Review Board (IRB) review mandate that will take effect on January 20, 2020, ORD is seeking policy change to allow for the use of commercial IRBs. Within VA, a risk assessment will need to be completed to determine whether Veterans' health information should be shared with commercial firms outside of the VA information network. As stated previously, commercial IRBs have a strong history of protecting patient data and privacy-they could not survive without privacy and security as foundational elements of their business. The DoD has acknowledged that commercial IRBs are sufficiently trustworthy to be considered minimal risk when it comes to handling the health information of military personnel. VA should make the same determination. The importance of giving Veterans access to potentially life-changing medical therapies should be heavily weighted when conducting these risk-reward assessments.

SUMMARY

- NAVREF supports the ACT for Veterans initiative and ORD's priority efforts to enhance access to clinical trials for Veterans;
- NAVREF supports centralization of VA privacy and information security reviews of research protocols to enhance efficiency, increase predictability, and reduce timelines;
- NAVREF supports VA's ability to allow use of commercial IRBs, especially for multi-site industry-sponsored trials already using an accredited commercial IRB.

Thank you again for your attention to these matters. We greatly appreciate your continuing support of the VA research program and your support of the VA-affiliated nonprofit corporations. We look forward to working with you to achieve our vision of a nation in which Veterans receive the finest care based on innovative research and education.

Sanford Health

We applaud the Chairman for holding this oversight hearing on a critical topic to our Veterans. Serving those who served our nation is an important mission for Sanford Health. We want to ensure that our nation's heroes have access to the most cutting-edge personalized medicine. In March, we announced a bold impactful partnership with the U.S. Department of Veterans Affairs that will help the VA meet new and emerging needs for Veterans, their families and caregivers.

About Sanford Health

Sanford Health, one of the largest health systems in the United States, is dedicated to the integrated delivery of health care, genomic medicine, senior care and services, global clinics, research and affordable insurance. Headquartered in Sioux Falls, South Dakota, the organization includes 44 hospitals, 1,400 physicians and more than 200 Good Samaritan Society senior care locations in 26 states and nine countries. Nearly \$1 billion in gifts from philanthropist Denny Sanford have transformed how Sanford Health improves the human condition.

The Sanford Health Department of Veterans and Military Services helps Veterans and military personnel obtain health care services, navigate care and insurance coverage, identify wellness services and search for employment opportunities. The Department also offers family support services and veteran community outreach.

The PHarmacogenomics Action for cancer SuRvivorship (PHASeR) Initiative

On March 12, 2019, the U.S. Department of Veterans Affairs and Sanford Health announced a new initiative aimed at improving patient care and lowering costs related to adverse reactions to medications, which research shows costs up to \$30 billion per year. Veterans across the United States will receive free pharmacogenetic testing through a partnership between the VA and Sanford Health called PHarmacogenomics Action for cancer SuRvivorship (PHASeR).

Pharmacogenetic testing can be a critically important tool for physicians in prescribing the proper medications at an optimized dosage. People respond to medications in different ways and frequently, their bodies will not respond to the prescribed medication properly. This difference in the ability of our bodies' to break down medications is partly determined by our genes. Leveraging this test means VA physicians are better-equipped to determine optimal therapy and dosing thereby avoiding intolerance to certain medications.

The tests are free to veterans and require no taxpayer resources. The program is made possible by a \$25 million gift from Denny Sanford and a matching fund-raising effort from Sanford Health.

The VA-Sanford Health partnership allows veterans to gain access to the testing at their local VA facility while Sanford Health will process the tests and supply confidential results to VA physicians. The program has started with patients who have survived cancer. A pilot is being conducted at the Durham VA Medical Center, Durham, North Carolina. To date, 25 Veterans have participated in the program. By 2020, the program will reach 250,000 U.S. veterans at 125 sites.

The two organizations are working together to embed the results into the patients' electronic health record, so that physicians get notified of potentially conflicting medications in the future. The program also supports genetic counseling for both patients and physicians.

Real-World Implications: Patrick McGuire, Navy Veteran

Patrick McGuire, 45, a Navy Veteran and stage 4 lung cancer survivor, is one of the first participants at the Durham VA Health Care System launch site. He was diagnosed with cancer in 2015. He underwent multiple surgeries for tumors in his brain and lungs in addition to a host of other ailments. He was initially treated outside of the VA and was prescribed medications that did not interact well with him. After seeing VA doctors, his condition improved, and he had fewer adverse reactions to treatment.

Following his final chemotherapy treatment, McGuire used a wheelchair for several months due to the loss of muscle and strength. He was unable to swallow from the radiation damage to his esophagus. He worked hard in physical therapy and progressed to a walker and cane. Against all odds, he recovered. Today, he rarely uses his cane at all.

Benefits of Pharmacogenetics

Pharmacogenetics saves lives, improves quality and efficiency and saves money.

- It is estimated that nearly 50 percent of antidepressants are ineffective for a particular patient and approximately 25 percent of people cannot appropriately use clopidogrel for antiplatelet treatment after cardiovascular intervention.
- Some chemotherapy and immunosuppressant drugs used to treat cancer and autoimmune disorders can build up in the bodies of people who have reduced functions of the TPMT and DPYD enzymes. A genetic test to identify the level of enzyme function in patients can help oncologists adjust dosages to prevent sometimes life-threatening toxicity levels due to accumulation of the medicines in the body.
- As cancer treatment becomes more effective, patients are more likely to survive and go on to have other health conditions requiring various medications with strong pharmacogenetic implications:
- Plavix (clopidogrel) is an anti-platelet medication prescribed after cardiovascular intervention to inhibit the formation of clots which lead to costly and potential deadly adverse events such as heart attack or stroke. Plavix requires activation by an enzyme called CYP2C19 to provide benefit, but if a patient does not have the right pharmacogenetic profile to metabolize CYP2C19 correctly, a different drug may be needed to prevent these adverse events.
- Certain anti-depressants are prescribed for depression, anxiety, insomnia, and neuropathic pain that require CYP2C19 and CYP2D6 enzymes to properly regulate the medication. A genetic variant could lead to the lack of efficacy for these drugs or an increase in dangerous side effects.

- Some patients have genetic variants that lead them metabolizing certain opioids too quickly or too slowly. Pharmacogenetic testing can help identify the right dose of the right pain medication.

Long-Term Benefits for the Government and Medical Research

Data generated from this program is available to researchers within the VA to further expand upon the understanding of how a person's genetic makeup impacts their ability to metabolize medications - yielding better care for our veterans. It can also be expanded to other medical areas outside of cancer survivorship. VA is at the cutting edge of providing this care to patients.

Additionally, the initiative may be able to save money by avoiding medications that are ineffective or cause expensive and debilitating side effects - a win-win for both patients and taxpayers.

SHEPHERD Therapeutics and SHEPHERD Foundation

Testimony of David Hysong
Founder & CEO

I am honored to provide testimony before the House Veterans Affairs Committee with my family's deep connection to the military and my professional and personal experience developing therapeutics for rare cancers that require advancements in precision medicine.

My father attended Embry Riddle Aeronautical University and commissioned in the United States Air Force as a helicopter pilot. He flew Hueys, served as the Special Air Mission Aircraft Commander of the Presidential Airlift Wing, received the Air Force Meritorious Service Medal for hazardous rescue, and twice received the Air Force Commendation Medal.

I too have my own connection with the military. While completing graduate school at Harvard University, I was selected for the Navy's SEAL Officer Selection process four years ago. After successfully completing the process, my military experience was cut short by my diagnosis of adenoid cystic carcinoma, or ACC, at 27 years old. While my cancer was successfully resected, if it returns there will be no approved modern therapies with which to treat it. If it returns, it will likely metastasize to areas including my bones and brain. I'm not one to go down without a fight. I am determined to not just beat this but help millions of others do the same.

Unfortunately, over 60 cancers may disproportionately affect our nation's veterans and service members. Sixty-seven percent are rare and only 25 of these rare cancers have an FDA approved targeted therapy. Many of those cancers are potentially caused by service-related exposures such as asbestos, burn pits, radiation and Agent Orange. Even children of veterans who were exposed to Agent Orange have an increased risk of certain cancers, according to a 2018 National Academy of Sciences study. In addition, rare cancers occur more frequently among Hispanics, Asians and Pacific Islanders compared with non-Hispanic blacks and whites. These populations frequently suffer from worse outcomes and shorter survival times, and African American cancer patients have a lower 5-year survival rate than white patients. Regardless of ethnicity, age or exposures, the vast majority of new cancer patients - over 80% - who lack even one FDA-approved targeted therapy for their cancer are rare cancer patients.

SHEPHERD's research has shown that at least 380 forms of cancer meet the most conservative estimate of what constitutes a rare cancer, the American Cancer Society's metric of fewer than 6 new diagnoses per 100,000 people per year. Those 380 forms compose 95 percent of all forms of cancer, which collectively will afflict over 550,000 new patients this year. As more diagnostic testing is provided for all cancer patients, the molecular subtyping will enable precision diagnosis and hopefully, one day, precision treatment. This means the number of "rare" cancers will continue to rise as a greater proportion of all cancer types, which makes precision medicine and targeted therapeutics critical to saving lives.

Yet, current clinical trials - often a cancer patient's best option for treatment - lack rare cancer patients. Our analysis of all clinical trials between 2012 and 2016 showed that 74.89 percent of all trials did not include even one rare cancer. Only around 13 percent of all rare cancers were specifically named as a focus of a phase 3 clinical trial in those five years. More than four times as much money in that timeframe was spent on non-rare cancer trials than on trials which included a rare cancer. For minorities, those discrepancies are amplified, as minorities are less likely than Caucasians to be included in clinical trials, which can lead to underrepresentation of key biological variables that make drugs less effective among those

populations. As data presented at a recent MIT conference showed, only three percent of the U.S. population is represented in clinical trials. These trials fail to capture the genetic diversity present in the population as well as in many forms of cancer.

This is why I encourage the Department of Veterans Affairs to explore ways to improve how the VA engages with investigators. At SHEPHERD Therapeutics, I have built a team of researchers in rare disease and oncology who are developing therapies which can tackle multiple rare cancers by leveraging shared biology. This approach will enable targeted therapeutic development for many rare cancer patients who are currently neglected by a drug development market that favors common cancers because they produce the greatest financial rewards.

As of February 2019, 182 cancers lacked an FDA-approved targeted therapy and 181 of them were rare cancers. That means that in 2019 almost 200,000 new rare cancer patients will face their diagnosis without a modern treatment, and current reimbursement policies contribute to this failure. While CMS decided in March 2018 to ensure that Medicare and Medicaid patients whose cancer recurs after treatment can receive molecular diagnostics, patients ideally should receive molecular diagnostics when they are first diagnosed to best inform treatment decisions. Diagnostics are especially important for cancers without good treatment protocols, as the tests may identify genetic drivers that can be addressed with existing therapies. Many patients do not know to request molecular diagnostics, and cannot afford to pay for testing. Even at large NCI care centers, molecular diagnostics is frequently covered only by donations and internal hospital funding and policy. This increases the gap between the quality of care afforded to those who have access to large NCI care centers, and the care provided to the majority of cancer patients who are treated at community hospitals. In addition to supporting patient care, this data can be vital to NIH, DoD and the VA by advancing scientific understanding of what causes a disease, the types of therapies which may work on it, and the appropriate patient population for molecularly-targeted clinical trials.

With approximately 20 million veterans, plus the millions more in their families and those who are currently serving in the military today, the gap in rare cancer therapeutic options is disturbing. Millions of lives are touched by rare cancers for which there are no treatment options. This must end. As a patient and CEO of a therapeutic company working hard to change the current paradigm for drug development to advance targeted treatments, I urge you to make the necessary changes in a collaborative fashion with the VA, DoD and NIH to ensure patients are no longer neglected. The VA can take a critical role in collaborating with researchers to share data, cell lines and discoveries to advance the development of targeted therapeutics. Our veterans deserve this care. Thank you.

