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ARPA-H: THE NEXT FRONTIER OF BIOMEDICAL RESEARCH

TUESDAY, FEBRUARY 8, 2022

House of Representatives,

Subcommittee on Health,

Committee on Energy and Commerce,

Washington, D.C.

The subcommittee met, pursuant to call, at 10:34 a.m. in the John D. Dingell Room, 2123 of the Rayburn House Office Building, Hon. Anna Eshoo [chairwoman of the subcommittee], presiding.

Present: Representatives Eshoo, Butterfield, Matsui, Castor, Sarbanes, Welch, Schrader, Cardenas, Ruiz, Dingell, Kuster, Kelly, Barragan, Blunt Rochester, Craig, Schrier, Trahan, Fletcher, Pallone (ex officio); Guthrie, Upton, Burgess, Griffith, Bilirakis, Long, Bucshon, Carter, Curtis, Crenshaw, Joyce, and Rodgers (ex officio).

Also present: Representatives Rush and DeGette.

Staff Present: Elizabeth Ertel, Office Manager; Waverly Gordon, Deputy Staff Director and General Counsel; Tiffany

Guarascio, Staff Director; Mackenzie Kuhl, Press Assistant; Una Lee, Chief Health Counsel; Meghan Mullon, Policy Analyst; Juan Negrete, Junior Professional Staff Member; Kaitlyn Peel, Digital Director; Caroline Rinker, Press Assistant; Chloe Rodriguez, Clerk; Andrew Souvall, Director of Communications, Outreach, and Member Services; Asad Ramzanali, Legislative Director; Kate Arey, Minority Content Manager and Digital Assistant; Sarah Burke, Minority Deputy Staff Director; Grace Graham, Minority Chief Counsel, Health; Nate Hodson, Minority Staff Director; Peter Kielty, Minority General Counsel; Emily King, Minority Member Services Director; Bijan Koohmaraie, Minority Chief Counsel, O&I Chief Counsel; Clare Paoletta, Minority Policy Analyst, Health; Kristen Shatynski, Minority Professional Staff Member, Health; Olivia Shields, Minority Communications Director; Michael Taggart, Minority Policy Director; and Everett Winnick, Minority Director of Information Technology.

*Ms. Eshoo. Good morning, colleagues. The Subcommittee on Health will now come to order. And due to COVID-19, today's hearing is being held remotely, as well as in person.

I would just like to make a brief statement, and then move on with our hearing.

On the first day of President Biden's presidency, he announced a very high standard in terms of conduct in his Administration. Dr. Eric Lander mistreated subordinates. It is a long record, and I believe that, because he didn't live up to that standard that the President set, that his resigning was the right thing to do. And so he, obviously, is not here this morning. He resigned last evening, one of our nation's most brilliant scientists. And so he has stepped down from being the director of the Office of Science and Technology Policy. Again, I think that was the right thing to do. Women are not lesser beings.

For members and witnesses taking part in person, we are following the guidance of the CDC and the Office of the Attending Physician. So we are asking everyone to please wear your mask when you are not speaking.

For members and witnesses taking part remotely, microphones will be set on mute to eliminate background noise. Members and witnesses, you will obviously need to unmute your microphone when you wish to speak.

Since we have some witnesses appearing virtually today,

I need to ask my colleagues in the hearing room to mute themselves whenever they are not speaking, so we can clearly hear the witnesses' responses. If there is background noise, it really diminishes the voices of those that are testifying.

Since members are participating from different locations at today's hearing, recognition of members for questions will be in the order of subcommittee seniority.

Documents for the record should be sent to Meghan Mullon at the email address we have provided to the staff. All documents will be entered into the record at the conclusion of the hearing.

The chair now recognizes herself for five minutes for an opening statement. And before I begin that, I want to thank our witnesses this morning for being so cooperative to move your presence up in the hearing, given the absence of and the resignation of Dr. Lander.

ARPA-H, the Advanced Research Projects Agency for Health, presents a unique opportunity to take a major leap forward in biomedical sciences by funding high-risk, high-reward innovation that will improve the quality of life for all.

Let me start by describing where ARPA-H fits by painting a picture of the current landscape of biomedical innovation, which I think of as a tale of two mountains, with a valley in between.

On one end of the landscape, we have a mountain called basic research, which is supported by the National Institutes of Health, a research lab that traces its roots to a 1887 lab in the Marine Hospital Service. Basic research is curiosity-driven, motivated by a desire to expand humanity's knowledge. Discoveries in basic research are the critical building blocks for modern medicine. Everyone on this subcommittee supports NIH. We have worked to strengthen it and fund it, and we take great pride in it.

On the other end of the biomedical innovation landscape is a mountain called applied research. Companies have a profit motive to commercialize scientific discoveries with market potential. Investors take risks in applied research, but only within a narrow band of what is foreseeable from the industry's perspective. The public depends on private investments to bring biomedical discoveries to market.

In between these mountains of basic and applied research, it is what is called the valley of death. There are countless ideas that have the potential to be breakthrough cures, but the needed investment can't be raised because the risk is too great for private actors and is outside the realm of basic research. ARPA-H aims to turn this sunken valley into a lofty mountain, where breakthrough discoveries can be realized on the deadliest diseases we face.

How will this work in practice? For that answer, we turn to DARPA, which is the inspiration for ARPA-H. In many ways, DARPA mirrors the culture of Silicon Valley, which I am very proud to represent. In the Valley, every successful entrepreneur stands on the shoulders of failed bets that came before them. Investors take many bets within a given area, and then they quickly double down on what works.

This similarity in cultures between Silicon Valley and DARPA is not a coincidence. Many of DARPA's successes happened in the Valley. ARPANET, the precursor of the modern internet funded by DARPA, had one of its four original network nodes at Stanford Research Institute. DARPA also funded major developments in semiconductors made of silicon, the namesake of my region. And DARPA is the source of GPS, which has countless academic and commercial linkages to Silicon Valley.

ARPA-H, as proposed in H.R. 5585, the ARPA-H Act, would be an independent agency within HHS designed to make high-risk, high-reward investments. I have worked on the legislation for several months after the President convened a small group of bipartisan representatives -- and bicameral -- in the West Wing last March to describe his vision for the agency.

Like DARPA, my legislation proposes ARPA-H to be made up of highly empowered program managers who are not career

government employees, but are instead experts in their field who dedicate their time to short-term projects for long-term results. Some of these program managers could be NIH-funded career academic scientists ready to break the mold. Others could be leading computer scientists that build new methods of deploying AI to find discoveries for rare diseases.

I have talked to many members of this subcommittee personally about the legislation to create ARPA-H, and it is my top legislative priority in this Congress, and I welcome your ideas on the topic. So if you haven't expressed them, make sure you do to me.

Let me thank my colleagues, Congresswoman Diana DeGette and Congressman Fred Upton. They have also put a great deal of time and thought into this issue, and I am pleased with their support of the legislation. Their work on Cures 1.0 -- we hear a continuing refrain about the effectiveness of that -- with that legislation that became law, and now their work on Cures 2.0 -- many scientists have told me that the two bills are complementary, and I look forward to advancing both.

Finally, this hearing was noticed, as we said -- as I said at the beginning, as a two-panel, and I want to welcome the panelists that changed their schedules to be the starting brilliant panel that I know that you are.

[The prepared statement of Ms. Eshoo follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. So the chair is now pleased to recognize Mr. Guthrie, the ranking member of our subcommittee, for his five minutes for an opening statement.

*Mr. Guthrie. Thank you, Chair Eshoo, and thank you. I want to associate with your words on Director Lander. Everybody deserves to be respected. Everybody deserves to be respected. And the ones who always think they are the smartest people in the room, sometimes other people are a lot smarter than you think they are, and we need to be mindful of that, and I am just disappointed that -- I am glad he is not here today, but, you know, he has answers that we need to -- hopefully, the White House will have somebody that can answer the questions as well.

Today we are discussing the proposal creating the Advanced Research Projects for Health, ARPA-H, that would establish a DARPA-like agency housed in the National Institutes of Health. Others and I on this committee have been strong supporters of health care innovation, specifically biopharmaceutical and biomedical research, and the great success stories -- Operation Warp Speed, which was established by President Trump at the beginning of the COVID-19 pandemic.

I think very early in President Biden's term a group of us went to the Oval Office. I remember being in the Oval Office very early in the term, and we were talking about

this, and I made the comment when we left -- I don't know if any of you remember -- I think I said that people are getting tired of votes going 220 to 215 in the House. People are ready to have agencies and things that we can work on and work on together, and health care is something we have always been able to work on together.

And you know, we just -- we have seen -- we didn't see that, we didn't see bills that were -- could generate bipartisan support moving forward, and we want to work together. But there are a couple of questions that we really need to ask, and I had told Dr. Lander before that these would come up, and -- because we had a phone call before all of his situation.

And the questions is NIH itself, and one is just the role of a new agency. And there is one point at NIH. Last Congress, as ranking member of the Oversight and Investigation Subcommittee, I co-led a letter to Director Collins of NIH and the Director Wray of the FBI to request information on how their agencies are working to remove foreign influence from biomedical research.

NIH is the largest funder of biomedical research in the world. And Director Wray described how researchers from China can mask their identity to accept millions of U.S. grant dollars to steal U.S.-backed biomedical research to give China a competitive edge. And I know that some of my

Republican colleagues have actively led on trying to get other information on grants from the NIH, and we have not been able to move forward. So it makes this more difficult to try to create a new agency that would be part of NIH.

To be clear, I believe these hearings are important, and we need to understand the gaps in care across our health care system, and how an agency like ARPA-H could close these gaps. So we need to -- but we do have questions about how this new agency would impact research efforts being led by similar Federal agencies in addition to our private sector partners.

ARPA-H is anticipated to be housed within NIH, whose mission is to conduct fundamental basic research to ensure we have foundational understanding of how biological systems work. But remember the private sector, not NIH, is responsible for bringing the breakthrough therapies to market. Only 5 percent of NIH-funded research initiatives result in treatments that come to the market, and only yield 6 new patents for every 100 million spent on research. However, the research is built upon by the private sector to move forward.

And the CBO data further shows the pharmaceutical industry invested 83 billion in research and development in fiscal year 2019 alone, with over 60 percent more drugs first coming to the market in the U.S. between 2010 and 2019, which underscores how effective private markets are in quickly

adapting to patient needs. We ought to be finding out more about these opportunities and the innovation that they require, as well.

Further, the U.S. Food and Drug Administration, the Biomedical Advanced Research Development Authority, and Defense Advanced Research Projects Agency, DARPA, are all Federal entities working directly with our partnering -- with industry leaders, developing cutting-edge technologies, and we want to know how ARPA-H will fit within these ongoing efforts within the private sector, and these agencies, and especially since there are still some unanswered questions of how the agency will function, and I think still where it will actually be housed.

So we are looking forward to working with members of this committee. We want to get answers to these questions about ARPA-H, and we -- but we do want to work and find policies that will bring about innovations and cures that will help the lives of our fellow citizens. And we thank you so much.

[The prepared statement of Mr. Guthrie follows:]

**********COMMITTEE INSERT**********

*Mr. Guthrie. And Madam Chair, I will yield back.

*Ms. Eshoo. Thank you. The gentleman yields back.

The chair is now pleased to recognize the chairman of the full committee, Mr. Pallone, for your five minutes of --

*The Chairman. Thank you.

*Ms. Eshoo. -- or an opening statement.

*The Chairman. Thank you, Chairwoman Eshoo. Today the committee will examine the Biden Administration's proposal to establish the Advanced Research Projects Agency for Health, or ARPA-H, and how this proposal could enhance the landscape of biomedical research.

There is a lot of excitement for ARPA-H. Patient groups, academia, industry, and many others have voiced their support of this novel model to catalyze society-changing medical breakthroughs. Imagine a world with cancer-curing vaccines, no overdose deaths, a genetic test to detect and actually prevent illness, and a truly equitable health delivery system. It is hard to imagine at this point with COVID, but the possibilities with ARPA-H are endless.

Today America's existing biomedical research ecosystem is the best in the world. It is supported by the best universities, companies, and scientists. But there are still gaps and missed opportunities. Fundamental research conducted by universities, non-profits, and government agency requires a high degree of scrutiny in order to produce strong

and objective knowledge. Once fundamental knowledge is established, translational science within the commercial sector takes over to develop cures, treatments, and technologies that address patient needs.

And this process involves a degree of risk that often times stands in the way of making lifesaving discoveries. Some of the risk factors include cost and recruitment for clinical trials, scalability, regulatory pathways, and the question of profit. At the end of the day, the priorities of the academic and commercial sectors may result in ideas simply not being pursued that are considered too high-risk, having a significant cost, or where the potential commercial market would not support the cause.

So advanced research agencies like the Defense Advanced Research Projects Agency, or DARPA, have addressed these gaps. DARPA has done this by building on established fundamental research, and funding time-limited, milestone-based translational research. This high-risk, high-reward model allows the defense research ecosystem to understand what works and what does not, without spending decades of resources on trial and error. And as a result, DARPA has developed platform technologies that have changed the world, technologies that we use every day, including cell phones, the internet, flat screen displays, and global positioning systems.

DARPA is part of the Department of Defense and, importantly, it has not supplanted any function of the Department's vast structure because its mission is unique and specific. So the same is true for ARPA-H. Its mission is to make pivotal investments in breakthrough technologies that can't readily be accomplished through traditional research and commercial activity. And I look forward to hearing from our panel of expert witnesses who have decades of experience in academia, fundamental research, Federal public health agencies, and, of course, DARPA to discuss the mission structure, authority, timing, and funding of ARPA-H.

Now, although this is not a legislative hearing, appropriators have introduced legislation that will fund ARPA-H at $3 billion in the House and 2.4 billion in the Senate. And that funding is contingent on this subcommittee writing and passing authorizing legislation. There are two existing proposals that would do so, one introduced by Chairwoman Eshoo and the other introduced by Representative DeGette. And I want to thank both of them for their outstanding leadership on this important issue.

This subcommittee has a strong bipartisan history of supporting Federal biomedical research. The proposal for ARPA-H is another opportunity for us to work together and establish an agency that will have a direct impact on fundamental research, breakthrough technologies, and

healthier patient outcomes, and, of course, keep us at the forefront of biomedical research in the United States.

[The prepared statement of the Chairman follows:]

**********COMMITTEE INSERT**********

*The Chairman. So I thank you again, Chairwoman Eshoo, and I yield back the balance of my time.

*Ms. Eshoo. The gentleman yields back. The chair now recognizes the ranking member of the full committee, Representative Cathy McMorris Rodgers.

*Mrs. Rodgers. Thank you, Madam Chair. I too want to associate myself with your comments regarding Dr. Lander. The question before this committee this morning is whether to create a new agency, ARPA-H, partly driven by the growing concerns as to the culture at NIH. Given Dr. Lander's sudden resignation last night, it only raises more questions in my mind as to what is really going on at NIH, and the culture at NIH.

I too want to thank the second panel for their flexibility in being -- appearing before this committee earlier than you first anticipated.

We are discussing the proposal to address and create the Advanced Research Agency for Health, ARPA-H. It is a new biomedical research agency with the initial price tag of 6.5 billion over 3 years.

We are all proud that the United States is the leading nation leading the world in biomedical research and innovation. Still, millions continue to suffer from diseases that do not have any treatment. I have been a long-time supporter of NIH. I have supported doubling the funding at

NIH. I have supported projects like the Brain Initiative, intended to speed scientific research necessary to accelerate cures for neurologic diseases. But I do have some concerns with this particular proposal, and I want to address it in three main areas.

Its intent ignores actions by the Biden Administration and Speaker Pelosi that will destroy medical innovation, such as the government price controls.

NIH is not cooperating or being transparent with Congress on how existing research funded by taxpayer dollars is being spent, especially in China.

And lastly, many questions about the ARPA-H proposal itself remain unanswered.

Regarding innovation, my colleagues and I will send a letter to Secretary Becerra today to detail how the proposed national coverage determination for all biologics targeting amyloid for Alzheimer's will devastate innovation, and hurt patients who rely on it. Bipartisan members of this committee have also written in opposition to the Administration's decision to repeal a final rule that would have provided Medicare coverage for FDA-approved breakthrough medical devices.

I am concerned that innovation-crushing decisions like these are a preview of how the Administration would abuse its power under government price controls. If innovation is

truly what ARPA-H is about, re-proposing the NCD for Alzheimer's patients and innovators, giving them hope, reinstating the innovative medical device regulations, and abandoning government price controls are reasonable steps we should all take.

Second, I am not convinced that a brand new agency is the answer to or will be able to overcome the institutional, cultural, and bureaucratic barriers that are present at our Federal scientific agencies. Our COVID-19 origins investigation has revealed that NIH has failed to do proper oversight and ensure accountability over research dollars, especially the risky research in China. Right now NIH has a long way to go to build trust. It should start by providing complete transparency by complying with congressional oversight.

Before we give the executive branch more authority and resources, let's make sure that we get the answers on what is being spent today, and why.

Onto ARPA-H itself. There is a fundamental question about the role of the private sector and the role of the Federal Government. Right now ARPA-H seems to lack a clear mission. I have asked for clarity from passionate advocates, researchers, the Biden Administration, Dr. Collins. I asked Dr. Lander the last time we spoke. Everyone has a different answer. How can we hold an agency accountable for success

without clear, measurable goals?

I am concerned about duplication. In 2006 the NIH launched the Common Fund Program using a venture capital framework to tackle high-risk, milestone-driven projects to remove roadblocks in medical research that impede basic scientific discovery. In 2021 the program received over $640 million. In 2011 a new NIH center for biomedical science, NCATS, was established to "catalyze a generation of innovative methods and technologies.''

In the 21st Century Cures Act Congress established the Cures Acceleration Network to reduce significant barriers between research, discovery, and clinical trials. 21st Century Cures gave NIH other tools to advance biomedical research, such as funding opportunities for young investigators, a specific program called High-Risk, High-Reward Research, and funded the Cancer Moonshot and the Brain Initiative, the Regenerative Medicine Innovation Project, and the All of US research program. Are these existing programs not working?

Let's do the oversight. A new agency brings a lot of other costs.

Again, I am totally supportive. I want America to lead in innovation and medical research, but let's make sure that we are doing the job we need to do, this committee oversight of existing programs.

[The prepared statement of Mrs. Rodgers follows:]

**********COMMITTEE INSERT**********

*Mrs. Rodgers. I yield back. Thank you.

*Ms. Eshoo. The gentlewoman yields back.

The chair would like to remind members that, pursuant to committee rules, all members' written opening statements will be made part of the record.

Now this is one of the best parts of the hearing, is to introduce our witnesses. And we -- colleagues, this is really a sterling panel of witnesses.

The first, Dr. Keith Yamamoto, and he is here with us in person. He is the vice chancellor for science policy and strategy, director of precision medicine, and professor of cellular and molecular pharmacology at the University of California, San Francisco.

Welcome to you, Dr. Yamamoto. It is an honor to have you with us.

Virtually we have Dr. Esther Krofah. She is the executive director of FasterCures and the Center for Public Health at the Milken Institute.

Thank you to you for being with us.

Dr. Geoffrey Ling, here in person, is the CEO of On Demand Pharmaceuticals, a Johns Hopkins School of Medicine professor, and John Hopkins Hospital attending physician. Dr. Ling also served as the founding director of DARPA's biological technologies office, and is a retired colonel with 21 years of service as an Army medical officer.

It really is difficult to abbreviate your backgrounds. So, colleagues, I am just giving a snapshot. But if you go into the testimony and the bios, you will be reading, single space, for quite a while. Our country is blessed with the leadership of each one of these individuals.

Dr. Brett Giroir has served as the assistant secretary of health at HHS. He has testified many times at our committee, the acting FDA commissioner, director of the defense sciences office at DARPA, and admiral in the U.S. Public Health Service Commissioned Corps.

Welcome to you, Dr. Giroir. It is good to have you with us once again.

Dr. Brian Miller is here with us in person. He is a practicing hospitalist, and an assistant professor of medicine and business at the Johns Hopkins University School of Medicine.

Welcome to you.

So to each one of you, we are proud to have you here. We are grateful to you. We look forward to your testimony.

For those that are here with us in person, you are probably familiar with the system of lights here in front of you. You have one minute remaining when the light turns yellow, and I think everyone knows what a red light is signaling.

So, Dr. Yamamoto, thank you again. You have five

minutes for your testimony.

STATEMENT OF KEITH R. YAMAMOTO, PH.D., VICE CHANCELLOR FOR SCIENCE POLICY AND STRATEGY, UNIVERSITY OF CALIFORNIA SAN FRANCISCO; ESTHER KROFAH, EXECUTIVE DIRECTOR, FASTERCURES AND CENTER FOR PUBLIC HEALTH AT THE MILKEN INSTITUTE; GEOFFREY SHIU FEI LING, M.D., PH.D., CEO, ON DEMAND PHARMACEUTICALS PROFESSOR OF NEUROLOGY, JOHNS HOPKINS MEDICINE; BRETT P. GIROIR, M.D., ADMIRAL, FORMER ASSISTANT SECRETARY FOR HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND BRIAN JAMES MILLER, M.D., M.B.A., M.P.H., PROFESSOR OF MEDICINE, JOHN HOPKINS MEDICINE

STATEMENT OF KEITH R. YAMAMOTO

*Dr. Yamamoto. Good morning, Chairman Eshoo, Ranking Member Guthrie, and members of the subcommittee. It is also nice to see my friend, Congressman DeGette, here, as well. And it is an honor to present a statement before you today.

I shall address two questions: first, why at this moment of spectacular discoveries about biological mechanisms and disease, most of them NIH-sponsored, should Congress be establishing another agency, ARPA-H; and second, why should Congress ensure that ARPA-H is fully independent, with a culture and practices that seem almost polar opposites to NIH's successful model?

First, why ARPA-H now? The policy framework for Federal

support of U.S. science and technology was set in 1945 by President Roosevelt's science adviser. Government would fund basic research -- that is, discovery of new knowledge -- and training of future generations of scientists. Industry would then develop the new knowledge into products from which they would profit, and the American people would enjoy a happier, more secure quality of life.

In the case of health, for example, we needed basic research to understand biological processes, how molecules collaborate to make cells, tissues, organs, and healthy human beings. Basic research has to be untargeted. We don't know what we don't know. So NIH created a competitive funding program giving university scientists freedom to let their curiosity, ingenuity, and expertise determine which biological processes they wish to study, and how they would study them.

NIH's funding apparatus is driven by peer review. Working scientists serve on committees to decide which proposals submitted by their colleagues will win funding. With many scientists each pursuing whichever biological process intrigues them, the gaps in our knowledge are being filled.

Now, peer review is not perfect. Dr. Francis Collins, just retired as NIH director, acknowledged that the NIH process "is a little slow, a little conservative, not

necessarily going to embrace the transformative projects.'' Yet this curiosity-driven model is, by any measure, the world's greatest knowledge discovery engine for biomedical research. For example, 99 of the 230 Nobel Prizes ever awarded in chemistry, physiology, or medicine have gone to 163 NIH-supported scientists. Astonishing dominance.

However, new knowledge alone is insufficient to motivate industry to develop applications. Among the 9,000 known human diseases, there are approved treatments for only about 500. And among the 24 most impactful drugs on the market, the median time between the key bit of knowledge discovery and FDA approval was 32 years.

Clearly, biotechs face many barriers: economic risk too high, near-term markets too small, scope too broad for any one company to realize profit, industry alone unable to do the job. Thus, Federal science and technology policy needs a revise. Government support is required to de-risk industry participation, and government coordination and management are required to set and meet audacious goals. That is ARPA-H.

So question number two, why should Congress endow ARPA-H with a drastically different culture and operating model? Consider first ARPA-H's distinctive goals. Its starting point is NIH's endpoint: discovered knowledge is the foundation for ARPA-H development of platform technologies, devices, therapeutics. It seeks applications, rather than

discovery of knowledge to demonstrate feasibility of transformative concepts, de-risking development.

Next, look at the ARPA-H operating model, which draws on DoD's DARPA, which Drs. Ling and Giroir will discuss, and may have been mentioned here already. Support and manage program-specific, transdisciplinary, multi-sector partnerships and teams to meet contract goals set in and enforced by ARPA-H program managers. Embrace bold approaches, tolerate failure, create advanced technologies, computational tools, novel materials, imaging methods all leveraged on chronic and infectious diseases, and on countless rare diseases which afflict millions, but receive scant attention due largely to market size concerns.

None of this looks like NIH, so ARPA-H needs to look and act differently. At the same time, though, NIH must continue to thrive for ARPA-H to succeed. Thus, Congress should install safeguards to prevent ARPA-H funding from supplanting NIH investments or threatening its culture.

For ARPA-H itself, Congress should provide independence to construct a flat, nimble operating model that supports program managers, each overseeing a daunting health challenge and a bold path to its solution. Congress should grant the director and program managers authorities, flexibilities, and, yes, appropriations for hiring, diversity, contracting, broad partnering, and ethical and efficient IP and tech

transfer.

Importantly, ARPA-H should be authorized as an independent agency within HHS, rather than as a component of NIH. Dr. Regina Dugan, a renowned former director of DARPA, puts it this way: "An organization like the ARPA-H exists to challenge conventional wisdom. Don't put it inside the very organization that holds the conventional wisdom.'' Creating a new culture and operating model is always difficult, but creating it within a very different and long-established one is likely impossible.

Thus, the actions of Congress in authorizing these agencies will influence, if not determine, its success or failure. Thankfully, the legislation developed by Chairwoman Eshoo and all of you wisely recognizes the critical elements of independence, authority, culture, policy, and practice that will place ARPA-H on a positive trajectory.

ARPA-H repairs a weakness in our Federal science and technology policy. ARPA-H will consolidate new scientific knowledge and devise strategies and tools that improve and extend lives for all, including those long disadvantaged.

This concludes my testimony. I would be pleased to answer any questions. Thank you again for the opportunity to –

[The prepared statement of Dr. Yamamoto follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. Thank you, Dr. Yamamoto. Next we will hear testimony from Ms. Esther Krofah.

You have five minutes for your testimony.

STATEMENT OF ESTHER KROFAH

*Ms. Krofah. Thank you, Chairwoman Eshoo, Ranking Member Guthrie, and members of the Subcommittee on Health, for the opportunity to provide input on the proposed Advanced Research Projects Agency for Health, ARPA-H. My name is Esther Krofah, and I am executive director of two centers of the Milken Institute: FasterCures and the Center for Public Health.

FasterCures is driven by a singular goal, to save lives, by speeding scientific advancements to all patients. We like to say our name is our mission. With an independent voice, FasterCures is working to build a system that is effective, efficient, and patient centered. During the pandemic we have witnessed the rapid development of effective COVID-19 vaccines in under a year, and development of therapeutics and diagnostics that demonstrate how critical scientific discovery translated into real products and interventions save lives. But many patients are asking, if it can be done for COVID-19, can it also be done for my disease condition?

This morning I speak to you as my father is fighting stage four cancer, hoping for some more time so that he can see his children and grandchildren achieve their dreams. ARPA-H holds the promise to work at the cutting edge of science to take risks and achieve breakthroughs that can

improve lives like my father's, but countless others.

FasterCures has long supported NIH DARPA-like authorities and capabilities for more high-risk, solutions-oriented R&D. So we are gratified that this concept is being seriously considered at this time.

My comments today will be in the following areas: the structure of the proposed new agency, including its location, leadership, authorities, and funding; second, its activities, including priority setting and coordination with other agencies and sectors.

Some have questioned whether ARPA-H should be housed within NIH, as currently proposed. There is, of course, a more recent example of the DARPA model that has been stood up and can be looked to for lessons learned. And that is ARPA-E, which resides within the Department of Energy, but employs an operating model like DARPA's. We have seen with ARPA-E that an entity like this can exist within a larger Federal agency, and still foster a different culture and operating model with the right toolkit and key ingredients. As such, we do not see a reason ARPA-H could not be situated within NIH and still accomplish its mission, including advantages to having easy access to other NIH infrastructure, personnel, programs, and expertise.

We would like to emphasize that this new entity should not be considered as a substitute for the National Center for

Advancing Translational Sciences, NCATS. NCATS has a broad remit to support the whole field and discipline of translational and clinical research. That needs to remain distinct and well-supported.

Who leads a new ARPA-H entity will be critical, especially as its first leader, and should be selected by their visionary capacity and ability to inspire and empower a new team, directing milestone-driven initiatives. ARPA-H will need to ensure expertise from the private sector is engaged, both internally and externally. It should ideally have a leader with experience outside academia, with a proven track record of success and managing through failures. It will need an external advisory body comprised of patient organizations, industry, academia, and other non-profits to inform the agency's priorities.

Representatives should also include those from under-served minority communities, defining problems that are most important to be solved.

DARPA's program managers are a critical asset, and should also be for ARPA-H. Ensuring key people are recruited for those positions is central to the culture necessary for the success of this effort. This is likely to require freedom from the usual constraints of the Federal hiring process, in order to bring in the right people for limited durations, do it quickly, and pay them appropriately.

Perhaps more important than the exact budget number is a consistency of funding and sustainability over time. This needs to be a multi-year commitment of effort and funding. It is bigger than a three-year budget line item.

Collaboration with other Federal agencies is necessary for the success of ARPA-H. FDA is, obviously, a critical link in the process that gets exciting new science and products into the hands of patients. We need to make sure they have the resources and expertise to keep pace and effectively regulate new technologies coming to them for review through efforts like ARPA-H.

There also needs to be active and regular engagement with other agencies critical to advancing solutions to patients, such as CMS and CDC.

ARPA-H should develop a data-driven and transparent process for setting priorities, including and prioritizing conditions with high unmet need and low innovation activity.

In creating this new entity, we should heed key lessons from the COVID-19 pandemic. Investment should be prioritized in platform technologies [inaudible] infrastructure.

I would like to conclude by thanking you for the opportunity to offer input. I am happy to discuss these ideas with you further [inaudible] any questions you may have.

[The prepared statement of Ms. Krofah follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. Thank you for your testimony.

Next the chair recognizes and thanks Dr. Geoffrey Ling for being with us today in person.

You have to know that this is some -- it is a treat for us to have people here in person. It has been a rarity now for two years. So welcome to you, and you have five minutes for your testimony, Doctor.

STATEMENT OF GEOFFREY LING

*Dr. Ling. Thank you, Chairwoman Eshoo. Good morning, Ranking Member Guthrie and distinguished members of the Congress. I have to tell you that -- you have been thanking us, but I have to thank you. This is a life memory for me. So thank you all.

My name is Geoffrey Ling, and I want to start by saying I am an Army officer. So the way I talk, please forgive me, because I spent 21 years as a military officer. I served in the United States Army. I served in Afghanistan. I served in Iraq as a military physician.

I was fortunate, since leaving government service, to be able to go ahead and become CEO of my own company called On Demand Pharmaceuticals. I am also a professor of neurology at the Johns Hopkins, where I still practice medicine on occasion. I am getting kind of old for it, but it is what it is. So my comments are my own, please. They do not reflect that of Hopkins, On Demand, or U.S. Army.

Relevant to this hearing, I was the founding director of the biological technologies office at DARPA, and I served at the agency for 11 years. Also relevant to this hearing, I served for the NIH for 14 years. I was on advisory councils and study sections. So from this perspective, I am going to address my comments.

DARPA was found in 1958 in response to an existential threat: Sputnik. ARPA-H is being considered in the shadow of a real threat, COVID.

But in adversity, there is opportunity, there is a real chance to do something new, do something special, do something bold, and that is create an agency that says yes. Everybody else looks to say no. No is the easiest answer. It means you don't have to do anything, it means you are happy with the status quo. It means that you are just fine to go back to do what you were doing.

But you want an agency that says yes, yes, I will go after autism; yes, I will go after Alzheimer's; yes, I will go after glioblastoma multiforme, a brain tumor. And it is just not saying yes, it is knowing how to say yes. It is not about more money, it is about how to spend the money. Not what to spend the money on, but how to spend the money on.

When I was at DARPA we recognized that this is taxpayer money, not my money. This is not the investigator's money, it is taxpayer money, the people work every doggone day who expect you to perform against it to deliver something for them. And how do you do that? You do that by making sure that everybody knows what they are trying to accomplish.

This is about affirming, changing, or rejecting current clinical care. If you are not doing one of those three things, you are not doing the job. You want to affirm it,

you want to reject it, you want to change it. You have got to come to work every day, knowing that. You have got to come to work thinking that you have autism, or your child has autism. When we looked at DARPA performers, we expect them to have that level of commitment.

And what was given in return? DARPA program managers -- ARPA program managers will work with those groups from end to end. It is not about doing the science. That is the first step. You have got to get through regulatory. Then someone has got to make it, then somebody has got to distribute it. And then the patient community has to embrace it. It is an end-to-end solution. Programs are meant to address all of these.

At the start of a DARPA BTO project, it is not just the scientists. It is the scientist who has been reviewed by, not peers, I am sorry, but they are reviewed by NIH officers, DoD science officers, FDA science officers. Why the FDA, you would ask? Because the FDA should be there at the beginning, because you got to get through them. It is a fact of life. If they are not there at the beginning, they are not going to be there at the end.

You have to resource these performers, give them the people they need, give them the equipment they need, give them the money they need. But do not give them the time they ask for. Time is the worst enemy we have. ARPA-H is going

to be like DARPA. Hold them to time. You are going to say -- a lot of people are saying, "Oh, I need more time, I need more time.'' Those are not the people you want. You want the person who says, "Put me in, Coach. Put me in,'' and recognize that it is not a gift. It is taxpayer money. If they are not delivering, fire them, get somebody else.

If you look at national baseball teams, who makes it to the World Series? It is the people who recognize that the inside infielder may not be the one you started with, may not be the one you are going to end with, because at the end of the day you are trying to get into the World Series. It is not about who, it is about the what. It is about the mission. Get the mission done.

So when I -- when you ask, should there -- an ARPA-H exist, of course. I am not going to go through all of the wonderful things that all of my friends have said. I agree with them completely. This is about how it should be constructed.

It should be independent. It needs to be independent, because you need people there who are going to have the determination, have the drive, have the urgency to get the job done, end to end. And it means, at the very outset, the scientists, the regulators, industry, and the patient advocacy groups, and the clinicians. If you don't have them all there at the beginning, and you don't have them

throughout this, you will have the valley of death the congresswoman -- Chairwoman Eshoo, you are right.

We cross that by bridging it at the beginning. Look at how DARPA does this. The model exists. You are not looking for another model. It exists. All the authorities needed have been -- already been awarded by the Congress. Just institute them in this agency of ARPA-H.

We talk about U.S. losing ground. Let me tell you right now, U.S. will not lose ground. I tell you why that is. Because of this. No totalitarian government would ever set up a DARPA, ever. Put smart people, fund them, turn them loose? Who in heaven's name would do that, if you were a totalitarian dictator? You wouldn't. You would only do it in our kind of environment.

So at the end of the day, I want to thank the committee for allowing me to speak. But I say that now is the time, and make it -- please make it independent.

[The prepared statement of Dr. Ling follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. Spoken like a general in the Army. Thank you very much.

Next the chair is so pleased to recognize Dr. Brett Giroir.

You have five minutes for your testimony, and welcome again to the subcommittee.

STATEMENT OF BRETT GIROIR

*Dr. Giroir. Chairwoman Eshoo, Ranking Member Guthrie, subcommittee members, thank you for the opportunity to testify at this historic moment in American history, the creation of ARPA-H.

Long before I became assistant secretary for health, DARPA was my passion. In 1998 I joined a technical assessment council sponsored by DARPA to probe scientific frontiers, and recommended new DARPA initiatives. Five years later, I formally joined DARPA as the deputy director, and then director of the defense sciences office, where I had the honor of working with Dr. Ling. I was the first physician to lead an office at DARPA in its then-50 year history.

On numerous occasions I have assessed concepts for organizations modeled on DARPA. Frequently, these have failed to achieve their potential because of fatal flaws that condemn them to mediocrity. America cannot afford to have a mediocre ARPA-H.

There are two overriding principles that must be the foundation of the agency.

First, at all costs, ARPA-H must nurture a culture of the innovation, where the staff seek transformational advances, not incremental change; where there is no disincentive for failure, only for not being bold enough;

where conventional wisdom is generally rejected in favor of novel approaches; where the power of ideas is always more important than a proposal -- proposer's institutional brand; and where the goal is to create interactive collaboration, rather than stovepipe competition.

Second, program managers will make or break ARPA-H. The director must have the ability to motivate, attract, hire, and enable program managers from the government, academia, non-profits, and industry. Program managers must be diverse, entrepreneurial, and excel across multiple scientific disciplines.

Next, let me address a few specific issues.

One, I believe it would be a fatal mistake to organize ARPA-H within the NIH. To a great degree, we need ARPA-H because the NIH cannot maintain a culture of radical innovation, disciplined execution, specific accountability, and streamlined processes that are essential for ARPA-H.

Don't misunderstand me. The NIH is outstanding at what it does, but it will never be DARPA or ARPA-H. As such, I strongly support that ARPA-H be independent of the NIH, and that the director report directly to the Secretary of Health and Human Services.

Two, ARPA-H must have rapid, streamlined, and non-burdensome processes to make financial awards within weeks, not months or years.

Three, ARPA leadership must be able to select performers based on the overall likelihood of the program's success. They must be empowered to select diverse technical approaches and manage overall risks.

Four, with the exception of core business and legal components, ARPA-H staff must have term limits.

Five, like DARPA, ARPA-H must employ disciplined execution. Awardees' progress should be reviewed weekly by program managers, quarterly by office directors, and annually by the director. There are milestones and timelines, and if these are not met the entire agency must address the root causes and attempt to remedy them.

Six, the ARPA-H director must have deep technical knowledge in a field, but by definition cannot be expert in everything that ARPA-H will address. More importantly, the director must be strategic, visionary, and able to recruit the best and the brightest. And needless to say, the director's ability to communicate is paramount.

Seven, the initiatives at ARPA-H must be informed by national priorities, but they must also intersect with scientific opportunities. It may not be possible to "cure stage four cancer next year,'' but it is possible to develop systems for extraordinarily early diagnosis of multiple cancers at home on a rapid test, enabling early treatment.

In the short term, I believe it is possible for ARPA-H

to develop systems to monitor improved health equitably in the home, to prevent falls among the elderly, to dramatically lessen maternal mortality, to develop a new paradigm to solve neurodegeneration, and to shield our nation from future pandemics.

In conclusion, when the Soviet Union launched Sputnik, the United States channeled its shock into action: DARPA. DARPA has changed the world: the Internet, GPS, stealth, NASA, microelectronics, autonomous vehicles, the bionic arm developed by Dr. Ling, and mRNA vaccines. Much like our nation's Sputnik moment, it is time for America to admit that the health of our nation is intolerably poor, that health disparities have worsened, and that we spend far too much to get so little in return. ARPA-H is our best opportunity to catalyze a healthier future for all Americans.

Thank you, and I look forward to your questions.

[The prepared statement of Dr. Giroir follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. Thank you very much, Dr. Giroir. You really offered compelling testimony to my colleagues and myself.

Next, the Chair is pleased to recognize and welcome Dr. Brian Miller. Dr. Miller -- I introduced him earlier, but we love the word "practicing,'' practicing hospitalist.

So we are delighted to have you -- honored, actually -- and extra pleased, because you are here with us in the hearing room. You have five minutes for your testimony, Doctor.

STATEMENT OF BRIAN MILLER

*Dr. Miller. Thank you, Chairwoman Eshoo, Ranking Member Guthrie, and distinguished members of the Subcommittee on Health for inviting me to share my views on biomedical research and ARPA-H, the question for today.

As you mentioned, I am a practicing hospitalist, and my other hat is actually as a health policy researcher. I run a 15-person group, and have experience at 4 regulatory agencies, which are sometimes barriers to innovation or, at other times, they facilitate it. Today I am here in my own capacity, and my views don't represent those necessarily of Hopkins or Johns Hopkins Medicine.

I think we all know that innovation -- and no one would disagree that innovation is important to us -- as consumers or patients, as citizens, as clinicians, and as a country. That is why we spend over $70 billion in taxpayer funds across 10 agencies -- more than that, actually; there is quite a list -- and $31 billion through the NIH's Extramural Grant Program. The private sector accompanies us on this journey, and spends around $89 billion annually, and venture capitalists join us with an additional $36 billion.

ARPA-H, as proposed, has multiple challenges, as I see it.

The first is structural. We are duplicating core

functions, administrative and otherwise.

The lack of a clear scientific mission and a strategic plan, to me, is most concerning. I have heard all kinds of good visions about things that we can and should do, and agree that we can and should support innovation. However, after meeting with 5,100 stakeholders, the White House should release a clear report identifying the scientific and medical research gaps, along with a strategic plan, before, as my colleagues mentioned, we spend taxpayer money to the tune of $6.5 billion.

I do agree with all of my colleagues that the basic principles of tenure-limited leadership, and program managers' managerial independence, and minimal bureaucracy are to be applauded. And in fact, we could think about applying them to some of the existing agencies.

But ARPA-H, even before this, is not enough. China is a rising threat. The biopharmaceutical company market cap of Chinese companies rose from 3 billion to 380 billion, a 100-fold increase over the last 5 years. There were 23 Chinese bioscience IPOs in 2020, and of the world's largest bioscience IPOs, 7 of 10 were from China. China has more researchers than we do, and more patents granted it. The Chinese Communist Party has made research and development -- and, in fact, dominance thereof with specific GDP targets -- a national priority, representing political risk for us. The

Thousand Talents program, launched in 2008, recruited 7,000 scientists, and even featured an ad in Nature Magazine.

So ARPA-H is really not enough if we are going to respond to China. We need to protect our greatest achievement, which is our biomedical research industrial complex. Instead, we should apply the principles that we are talking about here today for ARPA-H to part of a program that we already fund, the NIH Extramural Grant Program, where we invest $31 billion of taxpayer funds every year.

Let's look to change part of the NIH and the Extramural Grant Program into ARPA-H. Let's have transparency and accountability for indirect costs. Let's have indirect cost reforms to find more funds for researchers without an additional burden on taxpayers, who already face inflation. Let's decrease investigator administrative burdens and, most importantly, that sort of enthusiasm and the three shots of espresso that my colleague Dr. Ling had, as did I, probably, this morning, let's get that into the NIH Extramural Grant Program.

We talk about problems. Well, we all admit that there are problems there. Let's address them.

I also want to say that, in addition to looking at the Extramural Grant Program and just the innovation overall, we can't, you know, ignore regulatory burdens such as the Medicaid Drug Rebate Program or the need for new FDA

regulatory pathways for software-driven medical devices and other potential future states.

Thank you, and I look forward to your questions.

[The prepared statement of Dr. Miller follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. Thank you, Dr. Miller.

Okay, we have heard from all of our panelists, and the chair recognizes herself for five minutes for questions.

Dr. Yamamoto, you have spent and continue to -- I mean, you have an illustrious career working with and around NIH. Why do you feel so strongly that ARPA-H should be located outside of the agency?

And I would also like to have Dr. Giroir and Dr. Ling answer that question.

*Dr. Yamamoto. Thank you for that question. The --

*Ms. Eshoo. Perhaps, Dr. Yamamoto, if you could, it would be interesting if you would rebut Dr. Miller.

*Dr. Yamamoto. Excuse me? I am sorry, I missed what you said.

*Ms. Eshoo. To rebut Dr. Miller, whether you agree or disagree, helpful to us.

*Dr. Yamamoto. But you asked specifically whether -- the argument why it should be located outside of NIH. And I think that the main force of that argument is that the mission and goals of ARPA-H are different.

NIH is a masterful agency at discovery of new knowledge, but does not actually extend to being able to develop applications for that new knowledge. And the route for being able to do that has already been cast and demonstrated extremely well in DARPA and in ARPA-E.

*Ms. Eshoo. Thank you.

*Dr. Yamamoto. And so I think that is the reason that it should be outside. Setting up that new culture and operating model within the culture and operating model of NIH, as successful as it is, right, would be challenging, at best. And my fear is that the agency would actually fail, if it were to try to be within the NIH.

*Ms. Eshoo. Dr. Ling?

*Dr. Ling. I was actually --

*Ms. Eshoo. You need to turn your microphone on so we can hear your commanding voice.

*Dr. Ling. I never want to go ahead of a ranking officer.

So anyway, I do believe that ARPA-H needs to be independent.

As we had -- we have talked about the construct of this new agency, ARPA-H. To put it inside of NIH -- which does its job and does it well -- it has created a certain structure, a certain organization, and, of course, a certain culture. That culture has been successful for what it does. We are asking ARPA-H to do something completely different, to take a bold, initial view of things, to do an end-to-end type of approach towards building capability. That is A-number-one. The goal of ARPA-H is to create capability. The role of NIH is to create new knowledge, which it does beautifully.

So when you ask an agency that exists, does their job well, and you subsume another one underneath it, it is going to lose its identity, it is going to lose its structure, it is going to lose its way. So ARPA-H, if it is going to be something new, something bold, something innovative, then it needs to be set free to do exactly that.

And I would point out that we are not doing something brand new, never heard of before. It is following a model that has worked, DARPA. DARPA's model has worked. So that -- and so that is really why I feel passionately that, for ARPA-H to work, it needs to follow the same model.

*Ms. Eshoo. Thank you.

Dr. Giroir?

*Dr. Giroir. I completely agree with my colleagues. Tom Brady may be the best quarterback in history, but probably would not have been a good linebacker. The NIH is outstanding at what it does, but it does not have that type of culture, execution, and methodology that an ARPA-H does need.

And look, at DARPA we frequently work with the NIH investigators, right? These are the foundations of the knowledge, that one little glimpse to say yes to people funded by the National Science Foundation, by the Office of Naval Research. These are very complementary and synergistic organizations, but you can't fuse them because you lose the

culture of both if you do that.

And again, you cannot condemn ARPA-H to mediocrity from the moment it is born. I feel really strongly, as my colleagues do, that being independent but highly interactive with all the basic research agencies is the way to do this.

*Dr. Yamamoto. Doctor -- Eshoo, Ms. Eshoo, if I may.

*Ms. Eshoo. Yes, Dr. Yamamoto?

*Dr. Yamamoto. If I may, I would just comment on one point made by our colleague, Ms. Krofah, that ARPA-H would be able to work well within the NIH because of the demonstration of ARPA-E being -- existing within DoE. And actually, these are non-parallel situations. And Regina Dugan, former DARPA director, has made that point and I think that others have, as well, that the focus of the mission agencies is narrow and really tightly defined.

And so if ARPA-H were in the NIH, it would be like -- would be much more like DARPA being within the Air Force. DARPA in the DoD, and so we are talking about ARPA-H being within the HHS.

*Ms. Eshoo. The HHS, mm-hmm. Thank you, that is very helpful.

Now I would like to recognize the ranking member of our subcommittee, Mr. Guthrie, for your five minutes of questions.

*Mr. Guthrie. Thank you very much.

And first to Dr. Krofah, my prayers are with your father. You said your father is -- in your testimony -- struggling with stage four cancer. And you are saying that he hopes that he lives long enough to see his children and grandchildren live their dreams. My guess, if he is watching his accomplished daughter this morning, heavily credentialed, testifying before Congress, he is living one of his dreams. So our thoughts and prayers go with you. And people's personal stories matter, and they bring us forward.

So when we were going to have a previous witness from the White House -- and I talked to him this week -- one of my questions that we wanted to answer is why was ARPA-H needed, and where should it be, in NIH or outside, and which we are talking about today. And so when we compare DARPA and Sputnik, it appears to me -- I wasn't around in the 1950s. I was a child of the -- born in the 1060s. But there was really no private sector doing Sputnik, or those types of things.

And so, all of a sudden, we had to put all forces of government to move forward, and which we did this summer with COVID-19 and the mRNA vaccine. And I know that Pfizer and BioNTech used their experience to develop mRNA cancer vaccines to create vaccines for COVID. So this is for Dr. Miller.

In fact, the company announced in October 2021 they

would begin phase two trials in U.S., Germany, Spain, and Belgium to use technology to create colorectal cancer [sic]. And so the -- and in the ARPA-H concept paper, they use this as an example, said if we have ARPA-H, we are going to be able to use -- take NIH's research and use mRNA vaccines, an example of transformative projects.

So the question is that is happening in the private sector, and I think Dr. Yamamoto said that we have NIH doing basic research, which we all agree, and then it is executed. That is when we need ARPA-H to execute that research. And so my question, Dr. Miller, is that being done in the private sector? And do we need another government agency to do that? And we are just trying to get to the bottom of that.

*Dr. Miller. Thank you. I agree wholeheartedly. I think that this highlights that we need to actually define what the gap is.

So we have the NIH spending $31 billion, industry spending 89 billion, the life sciences venture capital community -- largely California Research Triangle Park -- spending $36 billion. What are the specific disease targets? What are the specific platform technologies that we see as gaps? We haven't really seen that. I have seen clear suggestions that ARPA-H is a good idea, but not yet a clear strategic priority.

And of course, on top of this, if we are actually going

to occupy with a government agency that translational enterprise, we are potentially going to crowd out private sector investment.

*Mr. Guthrie. So I think an 83 billion in resources through the private sector alone was invested in 2019. How do you see the marketplace, as you just kind of got to, currently adapting to unmet clinical needs?

And what -- so there -- what we are trying to find -- when we talked with Dr. Lander before, it was we have NIH, as we talked about here today, then we have a gap, and then we have the execution in the private sector. So what is the gap? And then, is the gap -- how can the gap be filled?

*Dr. Miller. I think the gap is already being filled by the private sector, frankly, and industry. If we look at orphan indications, rare diseases, we now have gene therapy, we have the accelerated approval pathway, which allows early market entry for oncologic therapies for products and disease indications, which people previously had no hope.

I think, if we want to change how we do research, we should think about getting more money out of the indirect costs that we already spend at the NIH in the Extramural Grant Program, rather than burdening taxpayers further.

*Mr. Guthrie. So Dr. Yamamoto and Dr. Ling, or one of the two of you who have advocated for ARPA-H, would you argue why our -- why the private sector isn't filling that, and why

ARPA-H is needed to fill the gap? Because you are, obviously, arguing there is a gap. And so why there is a gap, and why the private sector is not filling it.

*Dr. Ling. There is a gap. There is a gap. There are 10,000 known diseases, there are only 700 cures and treatments. That is a pretty big gap. I am a practicing physician, also. And I am a neurologist, which is the worst. So there is so much in the gap in terms of what I am able to provide patients: Alzheimer's Disease, you can go down the list. I am not going to do that.

There are some very simple things that an ARPA-H could do that do -- where the private sector is not filling. The private sector is actually quite conservative. And the point is that early government investment can yield a huge amount of private industry pull.

The trick is going through the valley of death. We have talked about that again and again. And so that is why I am saying that this construct of an ARPA-H is to create that end-to-end, going-forward type of approach. That is really what is needed. You have to de-risk it at each step of the way. We do this at DARPA all the time. You have to de-risk it at each handle. You have to de-risk it for the FDA. You have to de-risk it for the industry. You have to de-risk it for the patients and the clinicians. There is de-risking along the way.

Government support -- government, being that they don't have the constraints that the private industry has, for example. I mean, I am a CEO of my own company that I founded. There was a lot of elements to it that government funding does, in fact, really help.

But I will give you a tangible example, a very tangible example, all right? And forgive me, this may take a little bit more than two --

*Ms. Eshoo. Yes, you need to summarize, Dr. --

*Dr. Ling. I will summarize it --

*Ms. Eshoo. -- so Dr. Yamamoto can give his answer --

*Dr. Ling. I will tell you what. I will just yield to Dr. Yamamoto.

*Ms. Eshoo. Okay.

*Dr. Ling. I am just going to yield to Dr. Yamamoto, an old friend.

*Dr. Yamamoto. Thanks, Geoff.

There is a gap. I mentioned the fact that the time between the basic science observation that eventually leads to an FDA-approved drug is 32 years, median time. That is a gap, right? We need to fill that gap, because patients are sick and dying in that -- during that period.

*Mr. Guthrie. Okay, I guess I will yield back, and just say I know that some of the 10,000 diseases are still -- are at the NIH level, and not moving forward. So I mean, not

saying they won't get to the private sector to move forward, as well, and the gap. But thank you so much for your answers, I really appreciate it.

Sorry I went over. I apologize. I yield back.

*Ms. Eshoo. You don't have to apologize. Everything that is being discussed is important, and there are so many facets to this.

So the gentleman yields back. The chair is pleased to recognize the chairman of the full committee, Mr. Pallone, for your five minutes of questions.

*The Chairman. Thank you, Madam Chair --

*Ms. Eshoo. And thank you for allowing us to have this hearing.

*The Chairman. It is a consensus.

Dr. Ling, over the course of your career you have participated in and led biomedical discoveries that have transformed medicine, notably your work at DARPA. And you -- the stated goal of ARPA-H is to expedite cross-cutting technologies and discoveries like the Genome Project not every 20 or 30 years, but every 5 to 10.

We have seen the success of programs like DARPA and ARPA-E. But yet engineering systems are not direct comparisons to human biology and complex diseases, so I just want to better understand why ARPA-H is the appropriate model for achieving biomedical breakthroughs, and why now is the

right time.

And my first question really expands on what you have already said today, which is, you know, the -- what is the gap between the fundamental research and commercial sectors that ARPA-H seeks to fill?

*Dr. Ling. No, thank you, Congressman.

The -- what ARPA-H offers is the opportunity to leverage against the successes of the NSF and the NIH and other agencies that do fundamental research. Biology is not engineering, that is true. But the way to do research can follow a model that does work in engineering.

So a timeline-driven, a milestone-gated, with clear deliverables at the end of a performance period are, in fact, good ways to fundamentally support advancement of R&D so that it can get into and across the valley of death. That is the most important thing. It is not a question of if it is biology or is it chemistry or physics or engineering. It is really of how to manage the research, and how to manage the research dollars.

As Dr. -- I gave you an outline of -- DARPA takes a very disciplined approach to it, much like ARPA-H must do, as well. To differentiate itself, it must take a very disciplined approach on how the dollars are spent. Milestone-driven, timeline-limited, with clear deliverables: those are the essential elements of success in an ARPA-like

construct. And therein lies -- so it is not really a question of is this amenable, it is the -- it is how the dollars are managed. That is very, very important.

The accountability of that money has to lie with the program manager. The accountability of the program manager lies with the director. And a director's accountability lies, of course, with the Congress, as well as the Secretary of the HHS. There has to be accountability to the money.

*The Chairman. Okay. Now, let me just combine my second and third question, which are how will ARPA-H be more effective at advancing cures and treatments for the medical field's biggest challenges, and why is ARPA-H additive, rather than duplicative of existing programs addressing translational research, such as NCATS, if I could combine those two?

*Dr. Ling. Again, it comes to exactly what I said, it is the process.

So one of the things that, when we set out to do the robot arm that you had heard about, the prosthetic arm, it was that it had to be delivered within four years. There were clear gates to go through it, and so on and so forth. We then achieved it. But at the beginning of that program we had NSF science officers and FDA officers helping review the program, and being part of the program so that, by the time, at the four-year mark, it was ready to transition over to

going through the FDA regulatory process, we got the arm regulated, fully approved, within eight years of start of program. Eight years, not thirty-three. Eight years. And that arm is now with the Veterans Administration.

So again, we involved the Veterans Administration early on, too, so that they had clinicians and they had patient advocates already going through the steps. That is one example. There is many others, but I don't want to take up your time, Congressman. But I think that that is the point, is that you have to start at the beginning, where you are going to go through all these gates. Plan for them, structure it into the process. And it is the how you spend the money and how you design the program and -- to make it a contractual obligation to the performers.

*The Chairman. I appreciate that. I also appreciate your enthusiasm. I can't help thinking about the Super Bowl. Like -- you seem like you are, you know, organizing a football team here. It is really great, the energy. Thank you.

I yield back, Madam Chair.

*Ms. Eshoo. The gentleman yields back. It is a pleasure to recognize the ranking member of our full committee, Representative Cathy McMorris Rodgers.

You have five minutes for your questions.

*Mrs. Rodgers. Thank you, Madam Chair.

Leadership matters, accountability matters, character matters, people who do the right thing when nobody's looking, that matters. Unfortunately, I am fundamentally concerned that NIH is not responding to Congress right now. So I will set that aside, because we are focused on ARPA-H right now.

So, Dr. Lander, Dr. Giroir, I would like to start just better understanding how you view what currently is happening at NIH, some of the programs that exist that are intended to be innovative and cutting edge. Congress is funding the Common Fund; the National Center for Advancing Translational Science; High-Risk, High-Reward Program; the Accelerating Medicines Partnership. And that is just at NIH. I would just like to hear you share with me, to share your insights with me as far as are these programs not working, if they are working. Do we still need ARPA-H? And if they are not, should they be eliminated, and these dollars spent part of promoting ARPA-H?

That was Dr. -- oh, Dr. Miller. Dr. Miller, sorry. Dr. Miller and Dr. Giroir, if you would answer those questions, please.

*Dr. Miller. Thank you. I guess my question even before that is, you know, with Dr. Ling's comment about program managers and these gated timelines, we have these other programs at the NIH. It sounds like they are not doing that. Why don't we make those NIH programs do that, and

transition funding from indirect costs to make a mini-ARPA-H at one of those other programs that are already there?

It sounds like the NIH is also not being responsive. If we think that we have gaps -- and there are gaps, and it does take a long time to develop a drug or a device -- we should use the existing programs that we have, rather than make a whole new program because we say that the other programs aren't working well. It seems sort of like common sense.

*Mrs. Rodgers. Okay, thank you.

Dr. Giroir?

*Dr. Giroir. Thank you for that question, and it is a very important one.

ARPA-H is going to be -- if so authorized -- is going to be a major part of the ecosystem. But it is not the entire ecosystem. As Dr. Ling and others have said, ARPA-H will rely on the basic discovery and ideas that occur at the NIH, at the National Science Foundation, funded by the Gates Foundation, the Leap Fund at Wellcome Trust.

It will also need the kinds of advanced translation that comes out of ARPA-H. ARPA-H will never cure pancreatic cancer; it will create the technical abilities, the novel approaches, de-risk that, so it could be translated and transition to the private sector, and potentially other aspects of NIH, like --

*Mrs. Rodgers. Okay, if I could just clarify, why do

some of these existing programs, that I believe are intended for that same purpose, are not working as intended?

[No response.]

*Ms. Eshoo. Dr. Giroir, we lost your audio.

*Dr. Giroir. Sorry. I am going to say that I don't feel I have the ability to comment, you know, extensively on any of these programs currently.

*Mrs. Rodgers. Okay, okay.

*Dr. Giroir. I certainly have been involved with them, but I can't comment negatively on this program.

*Mrs. Rodgers. Okay, thank you.

*Ms. Eshoo. Yes.

*Mrs. Rodgers. And I hear that this agency will be accountable to Congress, yet it is a presidential appointment without any congressional oversight.

*Dr. Giroir. So --

*Mrs. Rodgers. Another question, Dr. Miller. Are there things that we can reform at our existing science agencies, such as NIH and BARDA, to change the culture and the risk tolerance without eroding their core missions?

*Dr. Miller. Absolutely. That is an excellent question. I think having tenure-limited program managers and leadership in various parts of the NIH, in conjunction with making that decision with the NIH director and/or oversight, would be an important transition to happen over time.

Indirect costs, which represent billions of dollars at the NIH, lack of transparency and accountability, and we should demand from funded institutions where that comes -- where those dollars are spent.

*Mrs. Rodgers. Okay, thank you. Well, and I will attempt one more for Dr. Giroir.

I appreciate your perspective here. You know, we are talking about ARPA-H, and that the rules should not be to implement and bring to the market preventions or cures, it should be to develop and prove the viability of these concepts. Can you explain why ARPA-H should be a proof of concept agency?

*Dr. Giroir. Because it really fills -- it does fill that gap, it bridges that gap. This is not meant to supplant the private sector or anything down the line, but that gap is real. It needs to de-risk to create new approaches. We don't even have a paradigm for neurodegeneration now. These are the things that it needs to do.

And let me just make a comment. My last year at DARPA I did 113 meetings and briefings. About half of those were to Congress or professional staff, and about half of those were within stakeholder groups. You know, ARPA-H has to have that degree of responsiveness and interaction for it to be successful, and I share your concern about that, and that should be an expectation.

*Mrs. Rodgers. Okay, thank you. I have more questions, but I have run out of time.

I will yield back. Thank you.

*Ms. Eshoo. The gentlewoman yields back. The chair is pleased to recognize the gentlewoman from California, Ms. Matsui, for her five minutes of questions.

*Ms. Matsui. Thank you very much, Madam Chair, and thank you to everyone who is joining this hearing today to think critically about the future of the biomedical technology pipeline.

Now, there is an ongoing and healthy debate on the appropriate placement of ARPA-H. Generally, there is a consensus that ARPA-H will need an independent structure and novel culture to deliver innovative ideas in health and medicine.

Dr. Giroir, you mentioned ARPA-H needs to be independent, distinct from the traditional NIH institutes and centers. Can you elaborate on how your experience at DARPA helped shape that perspective?

*Dr. Giroir. Thank you very much for that question, ma'am. As Dr. Ling said, it is the whole process of how you do business. It is the whole process and thought process of accountability, but also sort of being a counter-cultural organization that doesn't go with the flow, that doesn't rely on your peers for incremental change.

It relies on teaming, where we bring academia, together with industry, with non-profits, and teams of teams. Nobody really competes against each other. They are competing all for the same goal.

Look, I am a big fan of the NIH. The NIH has done remarkable things for this country. But it could never create the culture that is needed at DARPA. We have a model, as Dr. Ling has said. I do believe it needs to be independent, but it does need to be housed within HHS, the same way as DARPA is within DoD, ARPA-E is within Energy, and ARPA-H should be within HHS.

*Ms. Matsui. Well, can I say this, though? HHS is still a massive agency, with its own levels of bureaucracy, as we know. And acceleration is a key to ARPA-H's mission to transform and improve health care. Now, placed at HHS, how can we ensure that ARPA-H has that capability to move quickly and efficiently?

*Dr. Giroir. It really depends on your authorizations. And as I put in my written testimony, I think the legislation by Chairwoman Eshoo has deep insight into the authorities that are needed to make sure that this happens. Picking the first director is going to be critical, allowing rapid contracting, having term limits, being able to hire the best and brightest program managers, and having that independent culture: I really think that legislation provides the basis

for what is needed.

This -- reporting to the Secretary does not mean the Secretary runs the agency, but it is vital that the director report at the highest level, and I do believe the Secretary is the appropriate level for that.

*Ms. Matsui. Okay. Well, thank you very much, Dr. Giroir.

Talking about necessary authorities, DARPA is a unique agency that benefits from numerous special authorities. For example, DARPA can capitalize on flexible hiring and procurement authorities, including grants, contracts, and cooperative agreements, and other transaction authorities. Ms. Krofah, can you explain why special contracting authorities are needed for ARPA-H, and provide an example of when they are best applicable?

[No response.]

*Ms. Matsui. Ms. Krofah?

*Ms. Krofah. [Inaudible.]

*Ms. Matsui. Yes?

*Ms. Krofah. Thank you, thank you so much for that question. And you know, I want to make a comment, in terms of some of the prior conversation, to say that the momentum for which we are seeing the acceleration and the need for driving innovation is coming out of COVID-19. And we have seen NIH be successful, particularly with a RADx program, in

being able to stand up a collaboration with public and private quite quickly.

In terms of your question with other transactional authorities, that is an example where you can leverage such authorities to do hiring, to do contracting in a way where you are not going through significant levels of delay or barriers. That type of authority also needs to be embedded within ARPA-H, including leveraging other hiring practices such as FDA, in bringing top-notch scientists outside of government to play a role in regulatory approval processes.

*Ms. Matsui. Okay. Well, that is very good, Ms. Krofah.

I want to quickly touch on a related issue of the critical role that indirect cost recovery associated with NIH grants plays in supporting research at the University of California. From building labs, to quickly processing data, to keeping patients safe, there are indirect but essential costs of conducting research and the Federal Government's support is vital to advancing the research mission.

Dr. Yamamoto, I know you have a long history of helping Congress understand the importance of indirect cost issues. Can you please provide some insight into why research institutions like UCSF receive indirect cost recovery?

Quickly.

*Dr. Yamamoto. Indirect costs are part of supporting

research. Direct costs pay for salaries of the investigators, the equipment that is needed, and so forth. Indirect costs help the institutions to be able to support the infrastructure required for that research to be -- take place, whether it is buildings, providing distilled water and electricity, or having administrators who will oversee the grants and make sure that they are managed properly and come into compliance.

So those -- so indirect costs have kind of a -- have a funny ring to them, because it seems like it is not related to what the investigators are doing. But in fact, those are -- those things are crucial. And so they are an important part of allowing the research enterprise to go forward. Institutions do not recover their full costs of supporting research. Indirect costs provide a portion of that. That is essential.

*Ms. Matsui. Okay, thank you very much, Dr. Yamamoto.

I yield back.

*Ms. Eshoo. The gentlewoman yields back. The chair is pleased to recognize the gentleman from Michigan, Mr. Upton, former chairman of the full committee, and one of the authors of Cures 2.0.

Five minutes for your questions.

*Mr. Upton. Well, thank you, Madam Chair.

Nine thousand diseases, five hundred remedies. Every

disease group that is out there is looking for that breakthrough therapy. They have got to have the hope to help.

We have got some real champions, bipartisan, on both sides of the Capitol, looking for ARPA-H, knowing that DARPA was so successful, and mainly because they cut through the chaff. They got the job done.

I am not from the Sputnik generation either, but I do remember Lee Iacocca. "Lead, follow, or get out of the way.'' That is exactly the charge that this organization needs.

So the appropriators have already funded it to billions of dollars if we end up getting out of a continuing resolution. Dr. Giroir, how do we ensure that ARPA-H runs like DARPA? How do we cut through the chaff to make sure that that happens?

*Dr. Giroir. Well, thank you very much, and you are exactly correct.

And I will make another comment. It is not -- the money is necessary, but it is not sufficient. You could allocate 10 times that amount of money and not achieve the goal, if you don't create the right authorities, the right culture, the right director, the right program managers. I was hired as an IPA from academia, where I was a full professor [inaudible]. These are critically important. But sir, it is

all about the culture, and it is all about execution and creating that environment. And that is going to require this committee to protect that environment and the program managers, so they can do exactly what you [inaudible], because that is exactly where it needs to be.

*Mr. Upton. So that is why, to me, that is why we need more than just an appropriation. We need to have the proper oversight and controls to make sure that it runs the way that Lee Iacocca would. Coming from Michigan, he was a good Michigander.

*Dr. Giroir. Yes, sir.

*Mr. Upton. Ms. -- he was a great Michigander.

Ms. Krofah, I am so glad the Milken Institute is here. And for those that are watching, or those members that weren't here when we did 21st Century Cures, the Milken Institute just did a wonderful job for us to tap them for ideas to include in 21st Century Cures.

So one of the things that we are looking on in the next version 2.0, is the pandemic response and drug development. I am worried a bit by the current state of the drug development incentives to prevent future pandemics. As you know, Diana DeGette and I are huge proponents of encouraging new antibiotic developments, and we included our colleague Mr. Doyle's PASTEUR Act in legislation this summer, calling 2.0.

The use of real-world evidence, RWE, has been a big priority. And as -- you, as -- I want to ask if you are concerned, as I am, about the lack of new antibiotics in the pipeline. And if so, how might RWE or other components of the agreement before us help search for new cures as we look to the -- stop a future pandemic?

*Ms. Krofah. Thank you so much, Mr. Upton, for your question. And absolutely, a delight to be here and to partner with you on 21st Century Cures 1.0, and now very supportive of 21st Century Cures 2.0.

I am glad that you brought up the antibiotic issue because, as many of us say, [inaudible] silent [inaudible] that is happening right now. So many are losing their lives to drug-resistant infections.

We do believe that inclusion of the PASTEUR Act is going to play a critical role because, as you know, the market is broken, in terms of [inaudible] process for new antibiotics. On the one hand, we want to use fewer antibiotics. On the other hand, because of drug resistance, we need more antibiotics that are able to cut through those particular bacteria.

The challenge, of course, is that we don't have a marketplace that will reimburse innovation at the levels that are needed. PASTEUR will go a long way in ensuring that we are de-linking volume and value, eventually providing

incentives along the way that we are supporting innovation tied to the value of those antibiotics, not just prescribing more.

At the same time, we need more than just PASTEUR. We need to ensure that the private sector can be brought in, as well. The Milken Institute has been doing some work around creating innovative financing mechanisms to ensure that we are tying the private sector investment dollars, as well as other incentives such as PASTEUR to make sure it is a level playing field.

You also talked about the [inaudible] evidence. We need to collect that wherever they may be found. We need to ensure that [inaudible] regulatory grade where they can be used, from decision-making perspectives. So we welcome what we saw during the COVID-19 pandemic. We do think there is much more we need to do to learn from that [inaudible], and ensure that we are capitalizing on that antibiotic R&D pipeline.

*Mr. Upton. So do you think we can get to where we ought to be in the next 5 to 10 years?

*Ms. Krofah. Absolutely, if we make sure that we put these incentives in place. We need to make sure that we get PASTEUR over the finish line, absolutely. We need to make sure that we are continuing to invest in these companies upstream. They are doing their best right now, but they are

not going to be successful -- of course, we saw bankruptcy [inaudible] in the antibiotic space. We don't want to continue that trend, so absolutely we [inaudible]. We need to make sure [inaudible] is on the same level as other pandemic preparedness initiatives.

*Mr. Upton. Thank you.

I yield back.

*Ms. Eshoo. The gentleman yields back. I just would like to say that it is the intention of the chair that we move to, you know, legislative and markup on Cures 2.0 and ARPA-H. They are highly complementary of one another.

And you know, when you use the figures 9,000 diseases, 500 solved, we have our work cut out for us, and the people across the country, families, are -- they deserve to have hope. Every life is a valuable one. And we always, you know, offer our -- not only our sympathy, but our caring to one another when we know something has stricken the family of one of our colleagues. So this is as real as our getting up in the morning and doing our work.

So I think that Congress has the capacity to do this, the wisdom to do it, and that we work hard together to refine whatever needs to be refined, but we should not be in the way of what I just described. So thank you for allowing me the time to say that.

The chair is really pleased to recognize the gentlewoman

from Florida, Ms. Castor, for your five minutes of questions.

*Ms. Castor. Well, thank you, Chair Eshoo, and good morning, everyone. And thank you to our witnesses for their insights today. And I really want to thank Chair Eshoo, and Representative DeGette, and Representative Upton for their leadership. And I look forward to working on this very exciting concept for advanced research projects, the whole initiative that will help us build on the existing research, so that we are not leaving innovative discoveries, treatments, and cures on the table.

But we have to set up this endeavor for success, and I think that includes transparency and accountability. Because, unfortunately, what we have seen over the past two years, data evidence and interventions to address the pandemic have often been met with distrust, outright distrust, and misrepresentation. It has led to poor uptake in the effective and lifesaving interventions such as the COVID-19 vaccine. So for ARPA to succeed, we are going to need to build trust among the public and all of the stakeholders out there.

Stakeholders have specifically requested that ARPA-H be transparent about the selection criteria and the decision-making process for its broader investment goals, as well as the selection of individual research projects. So Dr. Ling, what is your perspective on how ARPA-H can be both

transparent and accountable?

*Dr. Ling. Thank you, Congresswoman. It absolutely should be transparent and accountable. It needs to be transparent and accountable at every level, and it begins with the performers. It begins with the scientists and the engineers.

Again, the structure of it is very DARPA-like. And in this case there -- it is not a DoD type of project, but it is a health project. So transparency is -- absolutely, should be built within the system fully.

So let me be more specific. The performers should be accountable to the program manager. The program managers have the authority to move money around, as well as move the investigator pool around, as well. That program manager is accountable to the office director, and the office director up to the director, and then for -- ultimately, the director to the Congress, as well as to the Secretary.

In this whole construct is that -- we said before it is going to be a timeline-driven, milestone-regulated process. Those milestones should be very, very transparent. Those should be published, actually, so that you know exactly what the taxpayers dollars are spent on and, in fact, how well they are doing against those milestones, those phase gates, as it were. And money is tied to it. I will be blunt, money is tied to it. So if they don't perform, they don't get the

money. It is real simple.

The other element of this is the engagement. As I said to you before -- and I really reiterate this point -- engagement has to be just not the investigators. The science is not the end of this. You still have to get through regulatory, you have to get through industry, and you have got to get to the consumer groups, which in this case are the patient advocacy groups, as well as the clinicians that support them.

So at all stages, they have to be engaged from the very beginning, and they have to be engaged throughout the entire process. So that is, in fact, how you build in accountability and how you build in trust, quite frankly. You don't want to bring something in the eleventh hour and say, "Here it is.'' You want them to be part of the process from the get-go. And in fact --

*Ms. Castor. Great.

*Dr. Ling. -- that is how -- again, we have a model. It is called DARPA. That is the model, if you look at the BTO, how they do a lot of their medically-related portfolio --

*Ms. Castor. Right.

*Dr. Ling. -- because it is a small part of their portfolio. It is still a Defense Department agency. That is why an ARPA-H, which is only devoted to health, is really

something that we need here and now.

*Ms. Castor. Okay, thank you.

And Dr. Yamamoto, I was very enthused to see in President Biden's concept paper for ARPA-H he explicitly mentioned the idea of using mRNA vaccines to prevent cancers as an example of potential transformative projects for the new agency. We know the -- about the success of mRNA for COVID. Most traditional vaccines take years to develop. Here was a medical miracle, really.

And back home I represent the Moffitt Cancer Center in Tampa, and they are -- the researchers there tell me that the mRNA cancer vaccines could potentially be the most -- some of the most cost-effective methods for preventing recurrences in the high cost of cancer care. Do you agree, and what do you see as the future here for immunotherapy treatments and prevention?

*Dr. Yamamoto. Thank you for that question, Congresswoman.

The mRNA vaccines do represent a really revolutionary breakthrough that depended upon years of basic research that came before that to understand the elements that drive stability of messenger RNA, you know, the -- inside the cells to be able to create the little packaging molecules that protect the RNA on the way in. And so it was a great victory in that sense.

And your colleagues in Tampa are correct that the potential promise of cancer -- mRNA-driven cancer vaccines is enormous, and DARPA had a role in these RNA technologies. So I think that that is correct, and is worthy of all of the excitement that has been generated.

If we step back -- and I think it is worth making an explicit point about how the kinds of -- the collaborations that come together that drive the kinds of advances we are talking about. There are about two dozen Federal agencies that are doing science and technology. There is nothing -- except for the ARPA models, there is nothing in the mission statements or goals of those agencies that drives them to work together and collaborate.

It is not -- there is nothing explicit in the ARPA agencies that say that they should be out talking to all of the agencies around to find out what the capabilities are that could come together to -- that would allow them to really make advances. But instead, it is the mission of the program managers and the director that say, "How are we going to get to this really hard point?'' And they realize that the only way they can do that is to bring together the talents of other agencies, to bring together -- bring in the private sector, and research foundations, and so forth, academia and so forth, to be able to accomplish these goals.

So it is not in the mission statement of the ARPAs to

drive collaborations. But the directors know that that is the only way they are going to get there. It is the only way that it is going to work. And so the -- so this is a aggregating, convening force that actually does something that no other science agencies in the Federal Government do, to bring together these talents and skills to accomplish hard things.

*Ms. Castor. Very helpful, thank you.

*Ms. Eshoo. The gentlewoman's time has expired.

Colleagues, I think you have already noticed that I have been very generous with time on both sides of the aisle. But there are excellent questions that are being asked. They deserve to be asked. But we have brilliance here, in terms of our witnesses, and their answers to these questions are just so important. So thank you for indulging my generosity, which I will continue to put out there. How is that? Okay.

The chair is pleased to recognize the gentleman from Virginia, Mr. Griffith, for your five minutes of questions.

*Mr. Griffith. Thank you very much, Madam Chair. Innovation and medical research has been a priority of mine since I arrived in Congress. I believe there is a role for both the Federal Government and the private sector in this space, and that Congress has a responsibility to fund these activities.

My line of questions that was originally written out

said, "Okay, tell me why we need a new agency. Let me get my head around this.'' You all have answered those questions to a certain extent already, so I am not going to be redundant on this occasion.

But Dr. Ling, you caught my imagination in the spirit of trying to create something new and different. And you said, you know, if we are trying to build -- and you used the baseball analogy -- if we are trying to get to the World Series, we might like that person a whole lot, but if they are not getting the job done, if they are not performing, we should fire them. But firing people is very difficult at the Federal level, as you know.

So I am interpreting -- and I want you to confirm, yes or no, if you agree -- I am interpreting that you think, when we pass this legislation, we need to have specific language on, if they are not meeting the requirements of their particular contract, that that contract will be terminated and they will be fired. Is that correct? Did I understand you?

Mike, so that everybody in the world can hear you.

*Dr. Ling. Correct, Congressman. In DARPA there is a phrase. It says, "At any time, for any reason, without prior notice, this contract may be terminated at the decision and -- of the United States Government.''

*Mr. Griffith. And I appreciate that. And Ranking

Member Cathy McMorris Rodgers pointed out, okay, well, what are we talking about with accountability? We need to have some accountability language in there, as well, not just for the executive branch, but also for the congressional branch. Would you agree with that, as well, Dr. Ling?

*Dr. Ling. There needs to be accountability throughout the system. Exactly, Congressman.

*Mr. Griffith. And that would be both executive branch and, two, the Congress of the United States.

*Dr. Ling. Absolutely. And all the way down to the performer level. They need to feel accountable. This is not their money, it is the taxpayer money.

*Mr. Griffith. And we are trying to make sure we get big things done. And if we are going to create a whole new agency inside of our NIH, or inside of whatever we are going -- wherever we are going to put it, we need to make sure that they are performing and getting that research done for the American people. I appreciate that very much.

Dr. Giroir, I know you said some good things about the NIH, and I agree. I am involved in some stuff with the NIH. I think they do a great job in their lane, and so forth. But one of the concerns we have had of late is it appears that, through third-party contractors, there is a lot of money being funneled to China. Do you think that we can stop that with ARPA-H?

And should we put some specific language in there that this research needs to be done on American soil?

*Dr. Giroir. Thank you for that. You know, I do believe that the NIH investigators do need to -- well, the NIH program managers in NIH offices do need to be more accountable.

In general, if you are an NIH grantee, you get your grant, you put a report together at the end of a year, you send it in, and that is it. And you really don't become accountable until every five years, when that is renewed. Contrast that to DARPA, where, literally, every week the program manager is reviewing the performer. Every month the office director is reviewing all the programs, and every year the director reviews every single [inaudible].

I can also say that, when I was at DARPA [inaudible] to your staff and the appropriations staff, or from the Defense side, I briefed every single program in my office, what they were doing, and what they were accountable for. That is the degree of transparency and accountability.

So yes, I agree. I do believe the NIH needs to raise the accountability, particularly for overseas investigators, without being burdensome on U.S. investigators. But ARPA-H would be accountable at every level [inaudible] transparent. That is the nature of the beast.

*Mr. Griffith. Well, one of the frustrations that I

have had is, in trying to figure out what was going on at the Wuhan lab with American money, was getting answers, and they won't give us the answers. And the -- well, I never expect to get answers from the Chinese. And so that creates a problem.

If we are going to spend this money, Dr. Miller, you said, you know, the Chinese are ahead of us on research, they have got all these extra people doing research, and that the United States needs to catch up, and we need to be doing this research, too. What is the point of putting this money into ARPA-H or anything else, if we are then just going to subcontract with the Chinese?

Don't you think we ought to be doing that here, in the United States?

*Dr. Miller. I agree wholeheartedly.

*Mr. Griffith. That is what I like, a short, quick answer.

[Laughter.]

*Mr. Griffith. Do you -- and so we would be a whole lot better off if we were doing that.

And then, if there is some kind of a question of accountability, you would agree, Dr. Miller and both -- and Dr. Ling -- it is a whole lot easier to get it if we are dealing with people who are in this country and who are answering to us directly, as opposed to a government that

does not have any reason to show us anything, or give us any information?

*Dr. Miller. Yes.

*Mr. Griffith. Dr. Ling?

*Dr. Ling. We should only be working with trusted allies and, of course, the United States citizenry. That is exactly what it should be.

*Mr. Griffith. Well, and I would say I think it needs to be mostly American. I suppose, if we had a trusted ally that we could actually trust, but when we can't get answers on what happened at Wuhan with American money, I have serious problems about expanding any program that doesn't have language to protect us.

I yield back.

*Ms. Eshoo. The gentleman yields back. The chair is pleased to recognize the gentleman from Maryland, Mr. Sarbanes, for your five minutes of questions.

*Mr. Sarbanes. Thanks very much, Madam Chair. I appreciate the hearing, and I thank the witnesses for their testimony.

There were, I think, 15 listening sessions that were conducted last year, broadly, to invite input around the proposal of ARPA-H. I had a chance to listen to a kind of wrap-up session of that that took place in October. And some of the themes there in describing ARPA-H included positive

disruption, establishing benchmarks so that this high-risk, high-reward ambition could be deployed through the opportunity to fail fast. Equity and diversity was a big part of the description of what is being sought through ARPA-H. Use-driven, not curiosity-driven, was a phrase, as well. Measuring success, not through publication, but health improvement for the public, not duplicating existing initiatives, et cetera. And I assume that these are features and characteristics that we saw in DARPA, as well, when it was being developed and obviously now, that it has been deployed.

I wanted to ask Dr. Ling -- you and Dr. Yamamoto -- to comment on -- to put the Human Genome Project and Operation Warp Speed in some context relative to this discussion of ARPA-H, are those efforts ones that, if an ARPA-H had been in place, would have resided there, or would it have been sort of the tip of the spear for those kinds of efforts?

Or are they different in the sense that they were assembling on, at least in the case of Operation Warp Speed, assembling in a kind of emergency fashion existing resources across many different agencies, and therefore they should be distinguished from the kinds of projects that we will see in the ARPA-H space?

But it would be useful to me, as a kind of reference point, for you to make some observations about what ARPA-H

would look like, how it would operate, et cetera, against that idea of the Operation Warp Speed or Human Genome, or both.

So why don't we start with Dr. Yamamoto and then Dr. Ling? I would be interested in hearing from you.

*Dr. Yamamoto. Thank you for that question. Important -- an important one.

My view on this is that the two examples that you gave, the Human Genome Project and Operation Warp Speed, if the ARPA-H office had been established, might well have been projects that were carried out under that aegis.

If you remember the way that the Human Genome Project ran, first of all, it took a long time. And second, it turned into this sort of kind of entertaining competition between a private company and the government effort. If ARPA had been in place, that collaboration would have been formed early on, and the progress on the Human Genome Project would have gone much faster. Instead, you had these two camps that weren't communicating with each other, they were collaborating -- they were not collaborating, and the work went more slowly.

Operation Warp Speed worked pretty well, and it was in -- as you said, in response to an urgent need, right. But Francis Collins himself has said that it was a difficult lift because the culture and practices were not in place at the

NIH to really make it work well.

So those examples are actually good examples of things that I think an ARPA structure could be able to accomplish, accomplish well, accomplish better.

*Mr. Sarbanes. Dr. Ling?

*Dr. Ling. Yes, I fully agree with Dr. Yamamoto, that the -- if there was an ARPA, the opportunity there would have been leveraged much, much earlier.

Let me talk specifically about Operation Warp Speed, which was really -- if you take a look at the mRNA vaccines, DARPA had actually invested in this program. It was called the ADEPT program run by my colleague, Dr. Dan -- Colonel Dr. Dan Wattendorf, bought back in 2010. And the two performers that he chose was Moderna and GSK. So they were -- already, industry was being brought into this 10 years before anybody knew that there was a COVID threat around, and they were doing it to develop vaccines against Ebola, actually, at that time.

And so the beauty of this was that they brought in a public-private partnership already at the very beginning, in 2010, 2010 -- that -- look what it yielded here, now, in 2020, when COVID finally reared its ugly head. And that is why we are talking about -- you want to say good gravy, we are really lucky to have an ARPA investment at that time. I think that speaks loudly for it.

And again, let me point out that it was a true private-public partnership. They -- it involved laboratories, of course. It involved the FDA, of course. But Moderna and GSK, Moderna and GSK, they were performers in this program.

*Mr. Sarbanes. Let me ask you, Dr. Ling, since you are speaking now, and I have only got 25 seconds here. But on this discussion around where ARPA-H should be situated, whether it should reside formally inside of NIH or more broadly inside HHS, should it be in the orbit of NIH, either physically or organizationally, be somehow tethered there?

Or do you see it as, in a sense, free-floating within HHS? Can you comment on that a little bit?

*Dr. Ling. I believe it should be a separate, distinct, and independent agency, just like the CDC is, the FDA is, the NSF, and the NIH. So they are all complementary. They all work together, but they are separate and distinct, and they each have their own chain of command. That is very, very critical.

*Mr. Sarbanes. Thank you. I yield back.

*Ms. Eshoo. The gentleman yields back. The chair is pleased to recognize the gentleman from Florida, Mr. Bilirakis, for his five minutes of questions.

*Mr. Bilirakis. Thank you, Madam Chair, and I thank all of you for testifying today. Thank you for your patience.

Dr. Miller, you talked in your testimony about the

critical need for our nation to have a strong response to China in the area of biomedical research, and I agree. Rather than focusing on ARPA-H, you say we need to transform the NIH's Extramural Grant Program, which consists of an almost $32 billion-per-year budget.

One of your reform proposals is to improve accountability and transparency of taxpayer dollars by specifying where indirect dollars go for extramural projects. I couldn't agree more, which is why I introduced the Protecting Integrity of our Biomedical Research Act, which would require disclosure of participation in foreign talent programs as a condition of receiving Federal extramural biomedical research grant dollars.

This was in direct response to cases where -- you probably know this -- where NIH-funded research had concealed support they had received from the Chinese Government. In fact, the GAO has issued reports stating the need for NIH to address undue foreign influence and increased transparency through disclosure. Despite its direct relevance to research integrity and combating Chinese influence, I am disappointed that the majority decided to ignore my comments in this proposal, and not place it in the COMPETES Act.

Dr. Miller, can you elaborate how adding more transparency requirements to NIH extramural grants will ensure the appropriate use of funds?

And can you give additional ideas of how we can protect against inefficient project selection, please?

*Dr. Miller. Thank you. First and foremost, the average indirect cost rate is around 52 percent. Originally, when the NIH started, it was around eight percent. The Gates Foundation pays 10 percent, and the European Union pays 20 percent. It is unclear to me why our average would be twice that of the EU, or five times that of the Gates Foundation. If a billionaire is getting a better deal than the U.S. Government, that is not exactly a great look for us.

Ways to fix that would include putting a cap, and having tiers, and having a tier tied to your three-year prior rolling average, meaning that universities that get more money are in a lower indirect rate group -- say, 10, 17.5, 25 percent as an example.

I think the important thing to emphasize is that the current distribution is highly inequitable, where HBCUs and a lot of public schools in the plain states and also the southeast and the southwest don't receive a lot of NIH grants. It is not because there aren't great researchers there, there are. It is just, if you are getting a lot of NIH grants, and you have a lot of administrative funds, you build a massive grant-making apparatus. And then that apparatus helps your researchers compete and comply with the 154-page, I believe it was, guide for NIH extramural grants,

right? That takes a lot of infrastructure to respond to that.

So I think that sort of breaking that cycle is a way that we could promote innovation and growth, and also free up funds for direct research funding.

*Mr. Bilirakis. Thank you. My next question is for Dr. Miller and Dr. Giroir.

I have spent much of my time here in Congress advocating for policies that encourage medical innovation by removing red tape, and incentivizing companies to develop cures as fast, as safe -- and safely as possible, particularly for rare diseases. Because of the nature of the 7,000 known rare diseases affecting small patient populations, it often falls through the cracks, unfortunately.

Can you provide examples of how ARPA-H could fill in these gaps and prioritize rare disease research, especially without a specified strategic plan before its creation?

And again, for Dr. Miller and Dr. Giroir.

*Dr. Giroir. Well, thank you --

*Dr. Miller. I will be brief, thank you.

[Pause.]

*Dr. Miller. I was going to say, I will be brief.

We should have a list of what those priorities are before we fund it.

*Mr. Bilirakis. Thank you.

Dr. Giroir?

*Dr. Giroir. I think, for rare diseases, ARPA-H could be incredibly important.

I am a pediatrician. For example, genetic cures can be remarkable in the future. But if they cost 2 or $3 million per cure because we have limiting technologies, they are not going to be equitably accessible across the country. So DARPA investing in core types of technologies that can dramatically increase access in an equitable way across a number of rare genetic diseases is just one example that really is biology, but it has an engineering flair, and it is completely [inaudible].

We can drive down the cost of cell-based therapies from a half-a-million and a million dollars down tenfold, so we increase the access. So these kind of platforms, as opposed to just an individual [inaudible], is where ARPA-H can make an enormous contribution.

*Mr. Bilirakis. Thank you very much.

I yield back, Madam Chair. Thank you.

*Ms. Eshoo. The gentleman yields back. Let me just say to the gentleman the points that you have made about your legislation, which I was not aware of, we will work with you on that, because I think that there are some really important elements relative to transparency and the other things that

you raised. So I would be happy to do that.

The chair is pleased to recognize the gentleman from Oregon, Mr. Schrader, for your five minutes of questions.

*Mr. Schrader. Thank you very much, Madam Chair. I really appreciate this hearing. Very timely, very critical. COVID is shining a light, as some of our witnesses have showed us, on the need for this type of program, going forward, in this very complex world we live in.

I guess the biggest concern I have is, like I said -- comment to Dr. Yamamoto -- is how do we assure that ARPA-H is not, frankly, just doing the research that industry would do anyway?

I mean, how do we make sure that we are complementary, and assisting, and getting to what industry cannot afford to do, that high risk beyond which they draw the line? How do we evaluate that?

*Dr. Yamamoto. I think this really depends on the wisdom and insights of the program directors, program managers, to be able to identify de-risking opportunities, areas where industry can't afford to go, or feel that there is not an open -- not a big enough market, or that the challenge for getting to -- across the valley of death is too great to risk, economically.

And those opportunities are actually all around us. They are really at the heart of why it takes a median time of

32 years to move from a basic research discovery to an approved drug. And so we will be able to find within ARPA-H the program managers that that have identified or maybe even lived those barriers. And it will be -- come into ARPA-H.

You know, these program managers, by the way, get their jobs by competing with each other to come to the director of the agency and say, "I have a problem that I think really needs to be solved,'' right? "And I have a way that I think it can be solved, and here is what it is going to take to get there,'' right?

And a part of that evaluation and -- that the director will make is, you know, what is unique about this? There is something called the Heilmeier Catechism that says, what is unique about this, where it is not being done elsewhere? And what is it that you think can be done that makes it specifically an ARPA-like project?

*Mr. Schrader. All right, very good. Thank you. I guess that brings up a second question I had.

I guess Dr. Ling or whoever, I -- the question of intellectual property. Would the collaboration between the government and -- you know, government equals taxpayer -- and industry, which equals shareholder and, you know -- how do we allocate the intellectual property rights in those types of collaborations? What has been done?

Mike.

*Dr. Ling. That has already been legislated, Congressman: the Bayh-Dole Act of 1980, and then the -- you know, the Federal regulations, the contract for Federal regulations, are very clear. They -- the IP belongs to the private entity. The U.S. Government doesn't make anything. They don't own any factories. So the intellectual property actually belongs to the private entity --

*Mr. Schrader. Even in case where we are going beyond just basic research?

I understand that argument with basic research. But now that we are going into applied research, should that still apply, in that --

*Dr. Ling. To my understanding, it does, Congressman.

The one thing that I would point out, though, in all contracts -- contracts, not grants, but contracts -- is march-in rights. The U.S. Government reserves the right to march in. They can create exceptions that allow them march-in. They can march in because the private partner did not, you know, commercialize it within an X period of time --

*Mr. Schrader. What, march in, meaning they can acquire those rights?

*Dr. Ling. Oh, absolutely. They can call -- we -- at DARPA, we used to call it clawback.

*Mr. Schrader. Okay. Okay, very good. I guess my last question is for Dr. Krofah.

That discussed a little bit about we need both NCAT and ARPA-H. They seem -- what is the difference, and why do we need both?

*Ms. Krofah. Well, as I mentioned earlier, the broad portfolio for NCATS is actually quite diverse in terms of their reach and activities.

A large part of their portfolio funds the CTSAs. These are the academic institutions that are quite focused on translational research, and that needs to continue. It is about 80 percent of NCATS budget. They help to talk about issues such as de-risking, [inaudible], but really [inaudible] significant way that affects the entire sector, the entire industry.

NCATS also has a program, for example, the [inaudible] program [inaudible] for example, and they also have programs for rare diseases. Some of these programs [inaudible] appropriate for an ARPA-H-like entity, and others may not be necessarily appropriate for an ARPA-H-like entity. But when we are talking about the point of high-risk, high-reward projects that would be captured under an ARPA-H, those types of projects are quite distinct [inaudible] supporting the overall [inaudible] example of translational sciences, which includes things like [inaudible] inventory, which happened during COVID-19.

Those [inaudible] mentioned also contributed data into a

platform called [inaudible] C3, which allowed all of that data that is being generated in these trials and studies and academic settings to be [inaudible] COVID-19. Those kinds of programs ought to continue [inaudible], and may not be the right types of projects for ARPA-H.

*Mr. Schrader. Very good. Thank you, and I yield back, Madam Chair.

*Ms. Eshoo. The gentleman yields back. It is a pleasure to recognize the gentleman from Indiana, Dr. Bucshon, for your five minutes of questions.

*Mr. Bucshon. Thank you, Madam Chairwoman. I think most of the questions about ARPA-H have pretty much been answered, so I am going to focus on research, in general.

And in a September letter from numerous biotech and venture capital executives to President Biden, Secretary Becerra, and bipartisan congressional leadership, the executive state -- and this is a quote from the letter -- "As written, Build Back Better would cause investors and researchers to de-prioritize small molecule drugs for diseases predominantly covered by Medicare, including many cancers and Alzheimer's.''

Although many of the small companies represented by signatories to this letter will feel that shift in priorities immediately, it will take years for the public and Congress to see the impact of this mistake on the kinds of new drugs

that do and don't come to the market. We can assume that it will take a long time for Congress to come around to fixing its mistake, so BBB could cost us decades of small molecule progress. And I know all too well, as a physician, that eliminating any -- even one drug is -- has substantial consequences.

So on one hand, some members are stressing the need for additional research and development -- and a new department, in fact, or agency -- while on the other hand actively working to potentially curtail the industry's efforts to find new cures through price control-type policies.

So Admiral Giroir, as you know, President Biden recently relaunched his Cancer Moonshot, which I agree with. Considering small molecule oral cancer drugs account for a significant percentage of the biotech industry's oncology pipeline moving forward, do you share some of the concerns raised by the biotech research and investment community in this letter?

*Dr. Giroir. Well, thank you for the question. I think we have to listen to the biotech community in the letter. Of course, this needs to be overseen by Congress, and really ask the probing questions.

But we cannot -- we can absolutely not bias the system against any class of therapeutic, whether it be large molecules, small molecules, biologics, vaccines, types of

vaccines. The aperture has to be completely open, and the competition needs to go forward.

So again, I can't comment specifically on -- but you need to listen to industry, and generally -- and to ask the right questions. But I -- by the fact that they raised it and raised it in such a passionate fashion, I think we need to be very careful about that, because ARPA-H will need to develop small molecules. And in general, they are a lot cheaper, easier to manufacture, and easier to keep on shore than other types of interventions.

*Mr. Bucshon. Thank you. And more broadly, just broadly, do you think that drug price controls will take us backwards in cancer research and innovation for patients, and potentially could result in fewer cures discovered if we set Federal-level drug price controls on the industry?

*Dr. Giroir. You know, I am going to give you my own personal feeling here. I think there is a balance that needs to be set, right? There is a balance that needs to be set, that -- and it can be set. It is hard to set it, but, you know, if you have drugs that are too -- are not affordable, and people can't have them, it is no use having the drugs. On the other hand, we have seen -- and particularly in antibiotics that were brought up -- if there is not the proper incentives on that side, then no one will develop it. I do think it is a balance.

Unfortunately, I am not going to give you a simple answer, because it is not a simple answer. Both sides are very valid points, I believe, in my opinion. And this is exactly why we have a committee like yours to work out that balance, because there is [inaudible].

*Mr. Bucshon. Yes, thank you for that. I mean, it is a difficult policy discussion to have. And you know, the Trump Administration proposed some price control-type things that I disagreed with from that Administration, and I disagree with price controls in general proposed in BBB.

But on the other hand, of course, as you mentioned, patients should have access to drugs, and we need to strike a balance here, and figure out what policies that we can put in place, like some of the bipartisan ones we passed in the last Congress, that can get drug prices down.

I mean, obviously, I am an avid supporter of innovation, and have spent my time in Congress advocating for increased funding for research and development, including at the NIH and other agencies. I think it is important to examine all the different government-funded programs, in addition to the work currently taking place at the NIH, and see how we can, you know, pull or pool our resources together to stretch taxpayer dollars further through better collaboration and assurance that more of the money actually goes towards R&D for innovative drugs, and not towards indirect costs at

agencies.

I yield back.

*Ms. Eshoo. The gentleman --

*Dr. Giroir. May I -- okay.

*Ms. Eshoo. Excuse me, did you have something else you wanted to add, Doctor?

*Dr. Giroir. I just wanted to say, from the ARPA-H point of view -- and that relates to cost -- remember Moore's Law for semiconductors, that every year the capability goes up twofold and it drops by half. That is why your laptop is so relatively inexpensive.

ARPA-H could absolutely do things -- like the cost of a genetic cure, just the cost of goods, are a million dollars now. That is why you have to charge $3 million. ARPA-H could have a program to lower that to 100,000, to decrease that by tenfold, thus increasing access, lowering costs, and helping everyone out. Those are the kinds of things that DARPA -- ARPA-H could easily do as part of its mission that will help take the, you know -- as an orthogonal approach to drug prices, yes, we need to do what you are doing, but let's lower them across the board by making them more inexpensive because of technologies.

*Ms. Eshoo. Thank you, Dr. Giroir. And thank you for quoting my constituent, Moore's Law.

It is a pleasure to recognize the gentleman from

California, Mr. Cardenas, for his five minutes of questions.

*Mr. Cardenas. Thank you very much, Madam Chairwoman, and I would also like to thank Ranking Member Guthrie. I really appreciate both of you for having this ARPA-H hearing. It is really important for medical innovation and for progress.

Biomedical research is absolutely critical to understanding our most insurmountable medical challenges, and ARPA-H is a particularly exciting opportunity, because it will allow our researchers to investigate with more flexibility, and take on more risk than they can through our more conventional processes.

To me, one of the greatest promises of ARPA-H is its potential to address so many conditions that disproportionately impact communities of color and poor people in America. As we come up on three years of a pandemic that has shown an even brighter light on the glaring health inequities in our country, I am hopeful that ARPA-H could provide a lifeline in the form of treatments, medical devices, and even cures for so many diseases out there.

Dr. Ling, again, thank you so much for sharing your valuable perspective on ARPA-H's incredible potential for a biomedical -- for biomedical innovation. How can ARPA-H be leveraged to focus on bridges -- bridging the gap in health outcomes across different demographic groups?

*Dr. Ling. Thank you, Congressman. I would say that it is about what ARPA-H should be about, which is developing capability. Developing capability, that is how you are able to help broadly across the enterprise of not only specific diseases, but also of groups that have been under-represented, you -- by being what -- the goal of an ARPA-H is not a thing, but a capability, not a particular piece of knowledge, but a capability.

So for example, if you had a much better imaging capability beyond that of MRI, it helps everybody. It helps all diseases. Those are the kind of things that should be an investment of an ARPA-H. DARPA always created capability, and that led to all the other wonderful outcomes that we see today.

*Mr. Cardenas. Thank you, Dr. Ling. Also Dr. Ling, is it possible or actually happening out there, where a pursuit of finding a cure could be a company -- a private entity could spend $10 million, $100 million, or even more, and then, oops, find out that they got at the end of their research and they couldn't find a cure and have to shelve it? Has that happened? Does that happen out there?

*Dr. Ling. Yes, it does. So the -- there is always risk in any endeavor such as this. But the way you manage that risk is through the process.

So we had a saying at DARPA, which I think would apply

equally to ARPA, which is, "Fail early, fail fast.'' And what you do is, by having this gated milestone approach, you can see how you are progressing. You don't want to find out that you are going to lose the race at the end of the race. You want to know along the way that it is not possible to get there.

What it allows you to do is pivot. You don't have to abandon the pursuit of that cure. You might have to pivot. You may say that, oh, a small molecule may not work, I might have to use a large molecule. I may not have to use a large molecule. Surgery, may be more -- whatever. But the point is, by having this phased-gate approach, as opposed to just throwing money at the problem, you now have a way of monitoring accountability of the money, and accountability towards achieving the goal, which is, as you point out, the cure.

But remember, in any of these journeys, if you push the knowledge forward as you do this -- you want to push it as fast as you can -- you can build on it, even if it looks like you are not going to get there.

*Mr. Cardenas. Dr. Ling, it is unfortunate, in my opinion, that in America today some of these innovators, some of these companies, private entities that are investing 100 million, in some cases even $1 billion, and don't bring something to market, that there is something evil about that.

What is the reality and practicality when an entity has just invested 300 million, 400 million, 600 million, 700 million, and they are just not getting the results to find that cure, for example? Is -- does that make them evil for having to figure out maybe it is time to shelve it, and then let's focus on other things?

*Dr. Ling. Sometimes the science is not there. Sometimes the way it was conducted. There is many reasons for so-called failure, and I think that is --

*Mr. Cardenas. So therefore, in our limited time, Dr. Ling, so therefore, is it that ARPA-H will actually help create more opportunities where those investments are -- the willing of -- the will of those investments can actually result in more cures, more results, more positive results, as you mentioned earlier, having the ability to have this support system, and then shift, and then continue, rather than abandon?

*Dr. Ling. Absolutely. Absolutely, you can -- you -- when -- we learn mostly from our mistakes. We learn mostly from our failures. It is the pivot and move that becomes very essential. And that is, in fact, the model of an ARPA. An ARPA does exactly that.

*Mr. Cardenas. Yes, thank you very much. That is why I have my wife, she definitely reminds me when I make mistakes, and then I learn, and then I [inaudible].

Thank you so much. I yield back.

[Laughter.]

*Ms. Eshoo. Dr. Yamamoto, you were nodding. Did you want to add something to this, briefly?

*Dr. Yamamoto. Yes, I did. Thank you. I would just like to say that the other way that ARPA can contribute to solving the problem that you raised -- and a very important one -- of a company making a huge investment and coming up with failure, is getting back to capabilities.

Something that Dr. Ling and I talked a lot about when he was founding the BTO was being able to use big -- was having DARPA be able to generate computational tools that would allow us to evaluate massive amounts of data that could then be serving, in the case that you are raising, to changing the nature, the size, and the composition of clinical trials.

The more we know about the mechanism behind a given disease that -- which can be gathered by, in fact, pulling together lots of data, including real-world evidence -- that was raised earlier -- the better we are able to be able to construct patient cohorts in clinical trials that actually have a bigger chance of having the tested drug be successful.

There is great examples of this, but in breast cancer medicine, for example, the first precision medicine drug, if you will, call Herceptin, the drug made by Genentech, a biotech -- a small, relatively small, biotech company at that

time -- was able to structure a clinical trial based on what they knew at the molecular level about the cause of a certain kind of metastatic breast cancer. And by being able to limit the size of that cohort, they were able to carry out a small clinical trial that went relatively rapidly, and succeeded, and Herceptin came out as a drug.

If they didn't have that information, if they hadn't collected that data, they would have had to put together a big trial, with many more patients, and it would have lasted longer. And in fact, we know from Sue Desmond-Hellmann, the president of product development at Genentech during that time, they would not have carried out the trial because it cost, as you said, hundreds of millions of dollars, and it would have failed.

So one of the things that ARPA-H can do is to be able to carry -- put together capabilities of that sort that would, in fact, lead to clinical trials that are more -- that are successful, and lead to drugs that are successful.

*Ms. Eshoo. Thank you. The gentleman's time has expired.

Dr. Yamamoto, it is nice to hear Susan Hellmann's name raised and mentioned.

The chair is now pleased to recognize the gentleman from Pennsylvania, Dr. Joyce.

*Mr. Joyce. Thank you, Chair.

*Ms. Eshoo. Five minutes.

*Mr. Joyce. Thank you, Chair Eshoo, for yielding, and to our witnesses for appearing --

*Ms. Eshoo. And happy birthday to you.

*Mr. Joyce. Thank you for the birthday greetings.

*Ms. Eshoo. Happy birthday from all of us.

*Mr. Joyce. Thank you, I appreciate that.

Thank you to our witnesses for appearing here today. This is an incredibly important topic.

Dr. Ling, thank you for your passionate testimony on this subject. You have worked at Johns Hopkins. You have worked in academic medicine there. You have worked in the military, and you have worked in the private sector. I think the many prongs that you bring into this equation are very important.

We recently saw a controversial coverage decision from a government agency regarding a breakthrough treatment for Alzheimer's disease, specifically related to amyloid and the deposition of amyloid. How would you envision this ARPA-H agency working with and complementing work being done already with the private sector, and not being resistant to private sector innovation?

*Dr. Ling. Thank you, Dr. Joyce, and -- Congressman Joyce. The drug that you are speaking of, I believe, is the Biogen drug Aducanumab, which was for Alzheimer's, and one of

the first to actually show some efficacy against this horrible disease.

So again, I am not privy to understanding the reimbursement decisions, or anything like that, but I can simply say this, is that comes back to what Dr. Yamamoto just said, and that is developing those capabilities that you can work with a company like Biogen, or you can work with a company like GSK and these others, so that they can better use the data that is available to make it better and easier for them to conduct their clinical trials to be able to save the money up front, to determine more quickly what, in fact, is the benefit.

Because to my understanding of the study right now, is it is -- the question is it doesn't work for everybody, but it is very effective in some. And so how do you identify those "some'' that could do well? So -- because that is true for cancer, that is true for infections. There is always a cohort that seems to do much better from that therapy than, say, another, for whatever reasons it may be.

And elucidating those reasons using new computational capabilities, perhaps using new diagnostic capabilities, all these things within the purview of an ARPA-H to build that capability, Dr. Joyce, so that it can be brought to bear so that then these decisions will have much better evidence to work by, that is the way an R&D agency such as an ARPA would

be able to contribute in a positive way to the point that you are making.

*Mr. Joyce. Dr. Ling, you mentioned the research that is necessary. What do you believe can be taken from DARPA and ARPA-E when it comes to securing that research, securing the confidential and sensitive nature of research from nefarious foreign actors?

And how can we do that successfully, while being able to work with the private sector and the academic researchers, all at the same time?

*Dr. Ling. No, the point you raise is very, very important. You know, these are investments made by the American taxpayer, by the citizenry of our country, and they should be, first and foremost, be to the benefit of the United States.

And I said to you before, and I say it again, that what we are proposing is something a totalitarian government would never propose. That is, having a free and independent agency that would be able to work on behalf of the citizenry. That is totally against what a totalitarian government, such as the adversaries of which we speak of.

As we come back to ensuring that they do this, I think we can take the model of the Department of Defense and DARPA. DARPA agonizes over this all of the time. DARPA agonizes that the things that they create will work their way into an

adversarial's arsenal, quite frankly. And so, in many ways, we can learn to use those safeguards and to use those processes that already exist by the model agency that we are working on right now to incorporate them back into an ARPA-H, much as it is in an ARPA defense, which is what DARPA is.

*Mr. Joyce. And I thank you, Dr. Ling, for mentioning the time restraints to achieve these goals, to listen to industry, and we, as Members of Congress, to be responsible stewards of the taxpayer dollars.

Thank you, Madam Chair. Thank you for holding this incredibly important meeting, and I yield the remainder of my time.

*Ms. Eshoo. And the chair thanks you, always, for your thoughtful questions and the -- such a respectful way of presenting them. I think we all appreciate that.

The chair is pleased to recognize another one of the doctors -- we are blessed, because we have several doctors as members of this subcommittee, and we benefit from their membership here.

Dr. Ruiz from California, five minutes of questions.

*Mr. Ruiz. Thank you, Madam Chair, for holding this important hearing.

Over the course of the last two years, the COVID-19 pandemic has exposed the magnitude of health inequities plaguing our country. As a doctor who grew up and practiced

medicine in a medically underserved community where health inequities are rampant, I am encouraged that these disparities are at the forefront of our policy conversations. It is imperative that, as we consider the structure and implementation of the ARPA-H program, that we prioritize health equity.

Ms. Krofah, the Administration is committed to promoting and prioritizing health equity in every decision made by ARPA-H. How can this be achieved, and should such a directive be included in statutory language authorizing ARPA-H?

*Ms. Krofah. Congressman, thank you so much for raising that. You know, when I think about the last two years with the pandemic, it has been absolutely devastating on communities of color, while at the same time there are essential health care workers that were suffering disproportionately.

And the issues around health equity are not new, right? We have known these issues for many, many decades, but we have not galvanized the full attention both of government, but also all of our private sector, non-profit sectors, and others to really address this problem. I think we have the unique opportunity to do so now, and I absolutely agree with you that ARPA-H is a model and a vehicle that we should use to really start to understand what is different in the

underlying biology of diseases that may affect some populations differently than another.

You know, an analogy that was used the other day that I really appreciated is that, when we think about our clinical trials, it is like testing a car down a straight road and expecting that it is going to perform when conditions change. What we really need to do is to test our products on windy roads, for all populations, to understand when they may not work for subsets of populations.

*Mr. Ruiz. Well, I appreciate you saying that, because I have a bill specifically to do just that, Diversity in Clinical Trials Act. Do you think that we need to add statutory language authorizing ARPA-H to do the health equity work?

*Ms. Krofah. I think we need to give the program managers and ARPA-H the flexibility. However, I do think that we need to have a patient advisory board that really provides the diverse representation. That should be written in, where there is consultation in which projects are prioritized.

*Mr. Ruiz. And how can we -- how can ARPA-H ensure that its workforce is sufficiently diverse?

And how do you see workforce diversity play a role in ARPA-H supporting projects to advance health equity?

*Ms. Krofah. I would agree we need diversity in the

program managers, we need diversity in even the director of ARPA-H, and, particularly given that it is time-limited, who those directors will be over time.

We know, particularly at the provider level, that patients are more likely to see people who look like them. We need program managers who look like the communities that are suffering from the burden of disease. So I absolutely agree that part of the considerations for hiring needs to include diversity, and that should be embedded in the legislation.

*Mr. Ruiz. Thank you, Ms. Krofah. I am a man of science. I like to measure things. And if you can measure it, then there is a way you can improve it. So how can we measure societal improvements in health equity catalyzed by ARPA-H?

*Ms. Krofah. We need metrics. Earlier we talked about we need a strategic plan. I would add that we need metrics. We need specific metrics for programs that are identified, for which populations may benefit, and for what outcomes we are looking for.

*Mr. Ruiz. And how would ARPA-H guarantee that products developed through their pipeline are made available and affordable in an equitable manner to all consumers?

*Ms. Krofah. You know, that is the role of the private sector. We talked a bit earlier about what the private

sector offers. They offer that manufacturing, they offer that end to end.

What we need to ensure early on with these high-risk projects with ARPA-H is that we have the ability to reach communities that we are not reaching already. Let's talk about capabilities --

*Mr. Ruiz. Well, currently -- you know, I understand it is the private sector, but current -- in the private sector, often times people who can't afford a certain price are left out of lifesaving remedies that -- they have no choice over whether they live or die if they don't get the lifesaving remedy. So government has a role in influencing and incentivizing equity and promotion.

So I hope that, as -- Ms. Krofah, that ARPA-H can help advise on ways that we can promote equity like the Biden Administration has done in purchasing some of the vaccines and incentivizing the pharmaceutical companies to use 40 percent in underserved communities.

And with that, I yield back my time.

*Ms. Krofah. Yes, I will just --

*Ms. Eshoo. The gentleman yields back.

*Ms. Krofah. -- comment, just one more --

*Ms. Eshoo. Oh, I am sorry.

*Ms. Krofah. -- comment on that last point, which is just to say that the regulatory piece of the collaboration

with ARPA-H is quite critical. We need FDA [inaudible] responsible for the review and approval of those products to make sure participants are diverse, and that is what I would add to that.

*Ms. Eshoo. Thank you.

The gentleman from Georgia, Mr. Carter -- oh, you want to take Mr. Curtis first? Wonderful.

Mr. Curtis, good to see you. You are recognized for five minutes for your questions.

*Mr. Curtis. Thank you, Madam Chair, Mr. Ranking Member.

Well, those who know me know I am excited to have another chance to brag about the community in Utah, and our advances in life sciences, and the great things that we are doing there. The Utah BioHive and Utah Health Care System is very active and very healthy. As a matter of fact, BioHive is made up of about 14,000 companies across the State of Utah, and I am really confident that it has been a really dynamic and powerful combination of public-private investment and success.

And I have got to tell you, I am just really pleased with the panel that we have had here today. I have really enjoyed the discussion, and I feel like there is a strong sense that we all want to do something, and we all want to do the right thing, and that we are here to have a thoughtful

discussion about what that is. And from the tone of my questions, I wouldn't want anybody to imply that I am opposed to ARPA-H. I just have questions that I want to have resolved in my mind.

Maybe, Dr. Miller, if I could start with you, I am reminded, as we talked today about a famous quote from Ronald Reagan that he made famous, "The most terrifying words in the English language are 'I am from the government, and I am here to help'.'' And it feels like sometimes Congress wants to solve all our problems by throwing a lot of money at it, and instead of analyzing maybe what we could be doing to more facilitate what is happening in the private sector.

So I wonder if we should also be talking about less regulation, faster approval process, how removing incentives like I think H.R. 3 does impacts less giving away of IP, as I think we have done with COVID, and less competition. And if I understand some of what has happened today, it almost feels like ARPA-H could come into Utah and compete with some of my private investors, right? Maybe in an IP or otherwise.

So could you just talk about is that a possibility, and what could we be doing to -- Dr. Ling, I loved your passion when you talked about unleashing this power, right? But I got to tell you, having spent most of my time in the private sector, I feel the same way about the private sector.

And what can we do, Dr. Miller, to fully unleash the

private sector?

*Dr. Miller. Thank you, Representative Curtis, for that question, and good to see you. A couple of things.

First of all, a $6.5 billion investment in biomedical research does not counterbalance the threat of administrative pricing in drug markets. So the -- that doesn't really compute for me.

I think you are right, all -- this could potentially, actually, misplace -- displace the private sector. I hear phrases like "time-gated'', "performance metrics'', "fail early,'' holding program managers responsible. All that sounds like is what I hear my colleagues from pharmaceutical companies and device manufacturers saying. So I worry that ARPA-H will be potentially directly displacing them.

I think we have to look at regulatory barriers, as you said. The Medicaid Drug Rebate Program is one, for example. We have these high-cost, million-dollar therapies, and we want equitable access to them for everybody. Well, the Medicaid Drug Rebate program means that, if you have a value-based contract, and your pharmaceutical company doesn't meet the milestone, and the value is zero dollars, that means the price for your drug is zero dollars. So I think we need to address barriers like that.

*Mr. Curtis. Thank you. There has been a pretty healthy debate, but I would kind of like to give Ms. Krofah a

chance to weigh in on this, or any of you that would like to, this concept of is the best place for this under NIH.

And I have just got to tell you, from a -- here again, from a business perspective, you typically would not put an organization that you wanted very different -- under an organization that the culture was so different. So, Ms. Krofah, you seemed to disagree with that. I would love to hear from you, and any of the -- else that want to weigh on that that haven't had a chance to express your thoughts on that.

*Ms. Krofah. Yes. Well, thank you so much, Congressman. And I do seem to be in the minority view [inaudible] on this topic. So I do you appreciate you pointing that out.

My perspective comes from a few different places. One is I just experienced coming out of the COVID-19 pandemic. I absolutely agree, in terms of the culture, NIH really is a culture that allows us to [inaudible] discovery. What we saw differently during COVID was NIH put together public-private partnerships through active [inaudible] that helped us achieve in, really, a tremendously short amount of time, movement in vaccine therapeutics that really translated into saving of lives.

If we can take [inaudible] and leverage those learnings, there is an opportunity for ARPA-H to succeed and do well

within NIH, but with safeguards. We talked earlier that we need -- absolutely we need those safeguards. We need –

*Mr. Curtis. I --

*Ms. Krofah. -- that there is a level of independence, which --

*Mr. Curtis. I regret that we are out of time, so I am going to cut you off before I get cut off.

I -- once again, before I end, I would just like to thank -- the discussion, I think, has been healthy and vibrant, and I appreciate being part of it. Madam Chair, I yield my time.

*Ms. Eshoo. The gentleman yields back. The chair is now pleased to recognize the gentlewoman from Washington, another one of our wonderful doctors, Dr. Schrier.

*Ms. Schrier. Well, thank you, Madam Chair, and thank you to our panelists for coming today. I am very excited to talk with all of you about the prospect of ARPA-H. And I think I can speak for all of us when I know just how remarkable it was when the power of the Federal Government joined with private industry to rapidly roll out -- develop and roll out coronavirus immunizations. And we had shots in arms in less than a year, and that was remarkable, and it is this sort of power that we are looking to harness in ARPA-H.

This presents such tremendous opportunities, specifically for my home state of Washington, for the

researchers who are working on things like CAR-T gene therapies, and precision medicine, and more. And in my state innovative researchers spent more than eight years pioneering personalized cancer immunotherapies for patients with lymphoma that hadn't responded to traditional treatment, and that CAR-T therapy represents not just another treatment or the last ditch effort, but is a cure, as we have seen recently, as that immunity lasts a lifetime, and will continue to kill any residual cancer cells that might arise.

I will tell you that another brilliant Washington researcher is studying the ways we might be able to tailor medicine according to individual genomes and phenoms. So using genetic information, coupled with environmental factors, this theory can inform, even from infancy, a child's lifetime risks for disease, and give parents -- and then that child later -- the tools to mitigate those risks and keep them well.

So, Dr. Yamamoto, I wanted to ask a few things, if you wouldn't mind answering briefly about how ARPA-H could impact just everyday people in Washington State. Like, in your opinion, would ARPA-H be a catalyst for expanding CAR-T gene therapy, maybe to see if it will work in solid tumors?

*Dr. Yamamoto. Thank you. CAR-T therapy is, in many ways, is powerful and amazing and important, as it is. This is really the tip of the sword for being able to do cell

engineering. It enables us to use -- develop cell therapies that deliver new therapeutics to the point of action, to the exact cells that are responsible for the disease, for example.

And so I think that there is every possibility that, under an ARPA-like management, that cell therapies could be developed that will definitely be able to serve people throughout your state, and throughout the country, and the world, in fact, because they are -- they provide the kind of targeting that allows for early diagnosis, for highly effective therapy early in the state -- in disease. And that sort of detection and treatment is really what is needed in order to really counter disease --

*Ms. Schrier. That is great. And --

*Dr. Yamamoto. -- early detection and focused, targeted treatment.

*Ms. Schrier. And speed is of the essence, right? I mean, eight years to get CAR-T, it is remarkable in one sense, but with the force that we put into Operation Warp Speed, imagine what we could do for, say, pediatric solid tumors, brain tumors, and they just don't have time.

Also, I --

*Dr. Yamamoto. I will just add that, as a matter of fact, there is a project that UCSF -- actually being undertaken right now to be able to use CAR-T therapies in

glioblastoma, a very important and devastating brain disease.

*Ms. Schrier. That is phenomenal. Thank you. I wanted to also ask, in your opinion, as we talk about precision medicine -- and I think of this, as a doctor, and who is enrolled in studies. We had to work really hard to get a diverse population in vaccine studies. I was wondering how precision medicine could make a difference, specifically for how health outcomes for women and people of color.

*Dr. Yamamoto. It is essential that -- so precision medicine, as you know, really capitalizes on being able to aggregate and integrate and analyze vast amounts of data about many, many different individuals, right, to be able to gain the knowledge that will allow us to be able to then take a focused approach to a given disease. And collecting that data then, in a way that is equitable, is very -- then becomes very essential.

Clinical trials in this country have not been carried out in an equitable fashion, and it is -- and it is the reason that we have found, at the end of the day, disparities that are very damaging. And at the root of them is the failure to be equitable in collecting the information and analyzing it.

*Ms. Schrier. I only have 10 seconds left, so I just want to say, as a pediatrician, how exciting all of this as I think about my patients, patients with autism, patients with

threatening diseases [inaudible] for them we can find cures through something like ARPA-H. So thank you very much. I yield back.

*Ms. Eshoo. Thank you, Dr. Schrier. Now, who is next?

Okay, the gentleman from Georgia, the pharmacist on our subcommittee, you have five -- the only one, too, that is right -- you have five minutes, Mr. Carter, for questions.

*Mr. Carter. Okay, and thank you, Madam Chair, and thank all of you for being here.

I want to start -- and bear with me here, before I get into my questions -- but it seems like we have a bullying problem with this Administration. I mean, our first witness that was supposed to be here this morning is not here because he resigned last night because of supposedly bullying.

Dr. Fauci, another example of bullying, bullying us into having to take vaccines and having to wear a mask. All examples of bullying.

You look at Dr. Kestner and Dr. Levine bullying governors into not using monoclonal antibodies, which have been proven to be effective, and then limiting the supplies of those.

The Administration bullied Americans into not using Ivermectin, calling it a horse de-wormer, when actually it has worked for many people, been effective.

And then you have got U.S. Trade Representative

Katherine Tai, who has tried to bully American pharmaceutical companies into giving their intellectual property, free of charge, to China.

You know, it just -- there is a common theme here, and it is bullying, and it needs to stop with this Administration.

Now that I got that off my chest, Dr. Miller, I want to ask you. You know, we have got a lot of serious public health challenges in this country. There is no question about that. And I recognized that in my 30-plus years of practicing pharmacy. And we need innovation, we need treatment innovation for lymphedema, cancer, hypertension, and all kinds of things. But I am especially concerned about the prevalence of antimicrobial resistance, and the need for new medications. ARPA-H proposals suggest an entirely new department is needed to address the lack of cures and treatments for these issues.

And, I don't know, one of our colleagues on this committee, Morgan Griffith, had recommended a book, "The Perfect Predator.'' I don't know if you have read that or not, but I am right in the middle of it, and it is a fascinating, true story, a fascinating read. But I will tell you, NIH gives out billions of dollars every year to different agencies, to different companies. And I get it. I understand what their role is, and what they are supposed to

be doing here. But sometimes you have to wonder if we are getting the return on our taxpayers' money that we should be. And it looks like there is a lack of transparency and accountability at the NIH, and it is concerning to a lot of us.

Dr. Miller, what can Congress do, what could we do to reform and modernize the NIH and its mission for advanced research before opening an entirely new department, as is being proposed?

*Dr. Miller. Thank you. I think this brings just a couple core questions to us about sort of how to run a research enterprise. Like my colleagues have all said -- and I agree with -- you want to minimize bureaucracy, right?

So just blowing that bureaucracy away, why is the grant guide 154 pages long? I mean, that is longer than most people's grants. Could you imagine writing a grant in response to that?

So I think blowing that away, creating a culture of risk tolerance, and that culture of tolerating failure and supporting failure as we think about platforms, as we think about new big ideas, all these principles that my colleagues are mentioning are principles that we should try and integrate into the NIH, and we need to change that culture.

*Mr. Carter. Well, thank you for that. Let me ask you, again -- Admiral Giroir, is he with us?

*Dr. Giroir. Yes, he is.

*Mr. Carter. Yes, thank you. I wanted to ask you, I have mentioned my concerns about the prevalence of antimicrobial resistance, the drugs that are currently on the market, and I have certainly witnessed this in my practice of pharmacy throughout the years in the overuse of antibiotics, the lack of pharmaceutical companies investing into research and development for new antibiotics. I believe it is like the early 1980s, the last that we had, and we need to address that. We have got to address that in this country, and I would rather government stay out of it, but at the same time I don't know how we are going to afford not to. We have got to stimulate this in some way.

But looking back on your time at HHS, Admiral, I wonder if you can fill us in on why BARDA and other Federal agencies aren't equipped to address these needs. Is there room for reform at BARDA and NIH and other research programs in the Federal Government to address these type of gaps?

*Dr. Giroir. Well, thank you, and it is good to see you again. And, you know, I am a big pharmacist fan, and I think ARPA-H could do a lot to support pharmacy and distribution of care.

These are fundamentally different organizations. BARDA has turned into -- and it is fine -- a truly advanced development group on a limited mission set that is for

biodefense. So you see investments being made like taking an underlying technology that might have been developed by DARPA, and making sure it gets approval for influenza, or making sure it gets approval for COVID. So it is in a fundamentally different operating space, and I would say its processes are highly bureaucratic, and not really that quick, agile type of program.

On the other end, you have the NIH, which we have discussed very much, so there is, of course, room for reform across the board. But that bridging of the gap that ARPA-H can do -- not to displace the private sector, but to empower the private sector -- to decrease risk for the private sector, to create technologies that [inaudible] rising tide will raise all boats, this is all the kinds of things that ARPA-H will do.

And let me just say, in terms of equity, we talk a lot about cures. Just as you and I talk so much about distributing health care by using pharmacists, I think the explicit goal of DARPA should be to get care and prevention in the homes, particularly of the underserved in the world. That may not be as sexy as curing stage four cancer, but it is vitally important, and is along the lines of distributing equitable health care and meeting people where they are.

*Mr. Carter. Thank you, Admiral.

And I thank you for your indulgence, Madam Chair, and I

yield back.

*Ms. Eshoo. Let me just say we have two votes that are up on the floor, so we are going to have to go over to vote.

We have two, four -- Mr. Crenshaw came in, that is five, plus a waive-on. Let's take two more members, and then we will recess. I think the -- our witnesses need a break, as well. And then we will come back to take the questions of members that have not been recognized yet.

So at this point I will recognize the gentlewoman from New Hampshire, Ms. Kuster, for her five minutes of questions.

*Ms. Kuster. Thank you, Madam Chair, and I want to thank all the witnesses for being here today, and for this hearing. I want to take some time to discuss ARPA-H's relationship to existing efforts by the National Institutes of Health.

The NIH has run large, complex programs before, using DARPA-like approaches to drive highly-managed, use-inspired, breakthrough research. For example, the NIH Rapid Acceleration of Diagnostics, RADx, initiative utilized an innovative funnel approach to rapidly advance promising COVID-19 diagnostic technologies. Other NIH programs have similar goals to ARPA-H, such as the National Center for Advancing Translational Sciences and the Accelerating Medicines Partnership. The ARPA-H program, then, will need to complement NIH's existing research portfolio, rather than

duplicate it, as we have heard in this hearing today.

Ms. Krofah, can you explain how you see ARPA-H complementing NCATS and other research programs at NIH, and how can its structure avoid redundancies to existing programs?

*Ms. Krofah. Thank you so much for that question. And in fact, you just referenced some good examples from NIH about use-driven research that would be applicable in the ARPA-H context.

I referenced in my prior talk that we need to look at RADx, and the model that was used in RADx, as a potential for what ARPA-H could mean and be in an NIH context. So I agree with you, that those particular case studies -- learning from NCATS, learning from AMP, learning from RADx -- are absolutely great examples in terms of NIH has performed these types of activities before, and they could be successful in the future, again, with those guardrails that we talked about and the independence that is needed.

*Ms. Kuster. Great. Now, one of the cornerstones of Federal support of research has been around the use of peer review, which plays a critical role in determining project merit and, ultimately, whether a project is supported.

Dr. Yamamoto, can you speak to how peer review will be leveraged at ARPA-H, and how is it different from the process leveraged by NIH and other Federal agencies?

*Dr. Yamamoto. Well, if we learn from DARPA, what we know is that there is not actually peer review there, but it doesn't mean there is not review -- there is extensive review -- and that one of the powers of an ARPA agency will be that it will gain expertise and input and advice, not just from peers, those that are actually carrying out the kind of work that is being proposed, but from across the research spectrum, looking -- getting experts from different agencies within the Federal Government, something the NIH doesn't do, and being able then to being able to establish a judgment about the kinds of programs they will undertake, and being transparent about it.

So there will actually be extensive review within the ARPA agency. This is what we have learned from DARPA, very powerful mechanisms that work very, very well.

*Ms. Kuster. Do you think it will be more of a collaboration approach, is that what you are saying?

*Dr. Yamamoto. Collaborative in the sense that you are bringing voices in from different groups that are not -- voices that are not tapped in the NIH peer review system. Remember, that it is an important, I think, distinction to make, that what NIH is trying to do is knowledge discovery, and that -- and that the -- really, the best way to do that, we now know from many decades of experience, is to give working scientists their own head in -- with the problems

that they choose to study, using their -- the drive of their curiosity to understand something, to do that.

And so peer review of just calling on other fellow scientists to make a judgment about the merits of a given proposal actually works very well. It is -- and as Francis Collins has said, it is -- does tend to be conservative, because peers are the ones that made the existing paradigms that are going to be defended. They will choose things that are relatively high feasibility, so higher-risk projects are not as well celebrated within the NIH. Those are problems. They are problems that I think can actually be solved by modifying the peer review system.

But the ARPA system actually depends on being able to cast a wide net, get out into the communities, and listen to what is needed, and what is available, and what is possible in order to bring together groups to build the kinds of capabilities that Dr. Ling talks about.

*Ms. Kuster. Well, I think your testimony has been so helpful and important for us today to understand that collaboration is going to be essential, and it is distinct from the other NIH efforts, and I think that is an important distinction.

Thank you, Madam Chair, I yield back.

*Ms. Eshoo. We thank you.

Let's see if we can get two more in. Is that all right

with you, Brett?

Okay, the chair is pleased to recognize the gentleman from Texas, Mr. Crenshaw, for your five minutes of questions.

*Mr. Crenshaw. Thank you, Madam Chair, and thank you to the ranking member. Thank you to the witnesses for being here for this really important subject. It is fascinating to all of us and I think there is certainly broad agreement that we need to do more to help biomedical innovation and health care innovation. There is a lot we can do.

I do have concerns about the ARPA-H proposition, that it may be duplicative, and that it doesn't address some of the problems with innovation, the core problems with CMS, with the FDA. You know, I wonder if that valley of death is really lack of funding or problems with the FDA and CMS not agreeing to pay for a particular project or treatment.

For Dr. Miller, if ARPA-H will cover investment when the private sector fails, we have to ask the question: Why is private sector not investing in a particular product?

Okay, so why wouldn't they want to invest in a particular project?

*Dr. Miller. Thank you, Representative Crenshaw. I get proposals from biotech companies and device manufacturers probably every week, and I read them, and usually my answer is no, this isn't going to go anywhere. And it is not necessarily because it is not a good scientific idea, but

because, one, there is usually not a payment policy framework for it.

I mentioned the Medicaid Drug Rebate program earlier. That is a common barrier for these sort of curative dream-type therapies that we would like to see that can cure rare diseases.

I think other things are, like at the FDA, we don't have a pathway for software-driven medical devices. And so you are not going to develop that product, because there is no path to market. If we want to turn into the Borg -- which, you know would be great, I could run faster, I wouldn't have to worry about getting a knee replacement eventually, and other things -- those products aren't there, and no one is going to create them, because you invest hundreds of millions of dollars, years of time, untold thousands of human hours of labor, and then you don't get FDA clearance because the FDA says, "Oh, am I going to evaluate this as AI? Am I going to evaluate this as machine learning? Am I going to evaluate this as software as a medical device? Am I going to evaluate this as a traditional medical device? And should it go through all four offices before it gets cleared?''

So I think a lot of these are regulatory barriers, and we have to address them.

*Mr. Crenshaw. And maybe I will move the question to Dr. Ling.

You know, is there anything in these proposals that would change that?

I mean, what assurances could ARPA-H give to therapeutic developers that their product might be greenlit by regulatory agencies?

*Dr. Ling. Well, that is a wonderful question, Congressman. Thank you for it.

Part of it, again, comes from -- is that there needs to be innovation at all levels. CMS needs to innovate. FDA needs to innovate. CDC needs to innovate. NIH needs to innovate.

*Mr. Crenshaw. Okay.

*Dr. Ling. Within these different groups. to keep up with the 21st century -- because that is where we are right now, facing 21st century problems -- in fact, you are correct, across the enterprise this needs to be done, but this is where ARPA-H could be very helpful.

*Mr. Crenshaw. I -- and I agree. Like, I think there is places for that. But it does seem like the -- you know, we might be putting the horse before the cart here, or the cart before the horse. The horse does go before the cart.

[Laughter.]

*Mr. Crenshaw. Anyway, you know what I mean.

Maybe -- and help us paint a picture, Dr. Ling, of, if ARPA-H was created right now, in your perfect vision, do you

have any examples of some projects that it could immediately undertake?

I mean, who out there, what startup out there right now, is just waiting for investment, but just can't get any?

*Dr. Ling. Thank you, Congressman. One project I think that would be very helpful, to be illustrative, is what I came back to before, is imaging.

So right now -- in the 1920s, we came with X-ray, great. In the 1960s we came up with CT scan, great. In the 1980s we came out with MRI, super duper. What has happened since then? Nothing.

So an ARPA-H project would be get me an imaging platform that would have performance metrics at least an order of magnitude better than MRI. Boom. Make it so that it has to operate at room temperature. That drives cost down. Make it so that it is not using ionizing radiation, much as X-ray and CT do, so it doesn't hurt patients. What technologies can bring to bear that you can do this right now?

And I am a geek, all right? So, for example, quantum orbital resonance spectroscopy could be an example. What you want -- and there are small groups doing it right now, they can't get the money to do it. Siemens doesn't want to do it. Why? Because they sell MRIs. Why in heaven's name would they do that? So it is a white space. It is a technological solution.

Now, what would be the benefit of doing such a thing, you would ask, Congressman. Well, if you had an order of magnitude better performance, you could actually diagnose cancer earlier. And I don't mean just a cancer. I mean, all cancers. Then you now have the opportunity of treating cancers when in stage one and stage two. We may not have to invent new drugs. We may actually improve health because we are able to -- that is an example of building a capability.

Now, you talked about the regulatory on that. You need to drag the FDA in, right then and there, as we start, and say, "Look, this is coming. You need to come up with ways to regulate this. That is your job.'' But they -- but you can't bring it to them four years later, after it is done, and say, "Now you have got to do it.'' You have got to bring them in on day one. That is the point I am trying to make, is that that end-to-end solution -- and ARPA-H would call that -- as much as Dr. Yamamoto said, you have got to bring these groups together now, early.

You have got to bring the patients in, because they are not going to want to lie down in this thing if they don't understand what the heck it is. So you have got to bring them in early, early, early. You have got to bring them in at the very outset, Congressman. That is, in fact, how DARPA does it. It doesn't tell the Marines you are going to have this new thingamajig. They bring them in right away and say,

"Look, we are going to develop this thingamajig. You need to go -- how to figure out how to make it, and then -- and put it in to your combat system and your tactics.''

So you don't do -- you have got to do it from the beginning, Congressman. That is the how you do it.

*Mr. Crenshaw. I appreciate your answer, and I have gone well over.

Thank you, Madam Chairwoman. I yield back.

*Ms. Eshoo. The gentleman yields back. I am going to call on one more member, because she can't return when we resume the hearing -- is the gentlewoman from Illinois, Ms. Kelly, and then we will break for the two votes.

And what time should we say we will be back, Mr. Brett?

*Voice. Mr. Brett?

*Mr. Guthrie. Twenty minutes after the first vote -- after the last vote.

*Ms. Eshoo. Okay, but how long is that? Just to give the witnesses an idea.

Well, why don't we -- well, let's see what time we walk out, and then we will better estimate the time.

So the gentlewoman from Illinois, you have five minutes --

*Ms. Kelly. Thank you so much, Madam Chair and Ranking Member Guthrie, for holding this hearing on ARPA-H.

It is well-established that our country faces large gaps

in access to care, and that the color of your skin can determine the quality of your care and your health outcomes. Despite these inequities, Black and Latinx scientists who are well aware of the role these inequities play in their communities continue to be funded at low rates.

According to the NIH, in 2020 only 2 percent of funded NIH research project grant applications have Black or African American lead scientists, and 5 percent had Hispanic or Latinx-led scientists.

Ms. Krofah, how can ARPA-H prevent repeating the mistakes of the past, and fund a diverse pool of researchers working across biomedical and community-based settings?

*Ms. Krofah. Well, thank you so much for your question. It is a problem. It is exactly a problem, just as you have stated. And what we need to do is to make sure that we don't repeat the mistakes of the past, which is a nice to have, but not a must have.

What we typically say is, "Write a community action plan, and send us your ideas of how you are going to do outreach,'' but there is no accountability in the end.

I think we have the opportunity to take all of the learnings that we have gone through to really put that into place with ARPA-H. We should have targets. We should say, "What are the diseases that are affecting the most number of people that are bearing the highest burden of disease, and

how do we innovate there?''

We also need to make sure that we are hiring the right program managers from these diverse perspectives, and we need to set some targets, and we need to have a patient advisory council that is diverse. I think those are issues that we just should not shortchange.

We should not broaden into language that is not specific enough that we do nothing about. So I completely agree with you. I think we can write that in to make sure it happens.

*Ms. Kelly. So would you consider those to be metrics that would be used to determine if ARPA-H is funding a diverse pool of scientists, or are there other things you would suggest?

*Ms. Krofah. I do think that we need to make sure that we have metrics. Again, we do want to make sure that ARPA-H has the flexibility to pursue the science and the innovation, wherever that lies -- of course, understanding that there is a public health need at the end of the day.

Outlining a strategic plan that includes metrics and it is transparent -- what diseases, and why, for whom, to what benefit, and who are we bringing along -- during those research studies needs to be clearly outlined.

And that also needs to occur in partnership with FDA, because a regulatory approval process happens there.

*Ms. Kelly. As you know, some of the most successful

and innovative interventions to improve health come from within impacted communities. For example, community health centers, hyperlocal health care hubs serving marginalized patients are often the epicenter of new ideas and cutting-edge innovation, from community-based emergency departments to trauma-informed behavioral health care.

How do you envision ARPA-H partnering with local communities to build upon the wealth of community-based knowledge that really already exists?

*Ms. Krofah. I think the program managers need to go out, and not rely on the communities to come in. We have these models. We use mobile clinics to go out into the communities. We need to do listening sessions. We need to take the managers and those messages out, wherever they are.

We can leverage platforms that were used to communicate around COVID-19 vaccination, turn those infrastructure into opportunities to listen to the communities.

But if we are going to stay in ivory towers with program managers who are all located centrally, and expecting those diverse communities to come to them, that just will not happen. So I do agree with you --

*Ms. Kelly. Yes --

*Ms. Krofah. -- and I do think those messages need to be taken out on the road, and to have those listening sessions with broad and diverse communities.

*Dr. Giroir. Ma'am, if you will, at DARPA my program managers in my office needed to be in the office two afternoons per month. I want to reinforce how important it is to get out into the communities. They are not going to be cooped up, they are not going to be in an ivory tower. They can't be behind walls. They have to go interact.

And the second point -- and this is so important -- is if you have an NIH system that ranks proposals 1 to 100, and only the top 5 get picked, you are going to lose all the diversity, because they are not in the mainstream. They don't have the grantsmanship offices that Harvard or Yale or Hopkins do.

The whole goal of DARPA in the review process is maybe to take number 1 and 3, but to pick that diverse approach, number 25 that is not from, you know, Harvard. And I am just using that stereotypically, but it might be from a community health center, or it might be from an HBCU. They would never make it to a traditional 1-to-end review process, but having that -- diversity is a means to success. It is a goal in and of itself, but more than anything it is a means to success, particularly in the health realm.

*Ms. Kelly. Well, thank you both so much. Thank you for your patience. Thank you for being witnesses, and I yield back.

Thank you, Madam Chair.

*Ms. Eshoo. You are most welcome. I am glad we could accommodate you.

*Ms. Kelly. Thank you.

*Ms. Eshoo. All right. I think that -- well, we are going to go over to vote. We will recess, and we are going to try to be back here by 2:20. All right?

And then, I don't know, I know I have two members from our side of the aisle, and a third that wishes to waive on. But we will make that determination when we come back.

*Mr. Guthrie. Somebody can --

*Ms. Eshoo. Okay. Well, I am not -- no one is going to be penalized if they come back.

*Mr. Guthrie. I know --

*Ms. Eshoo. They should be heard.

Okay, the committee will recess until --

[Recess.]

*Ms. Eshoo. The Subcommittee on Health will now come back to order.

The chair is pleased to recognize the gentlewoman from California, Ms. Barragan, for your five minutes of questions.

*Ms. Barragan. Thank you, Madam Chairwoman, for hosting this important hearing today. This bold proposal to create a new agency exclusively tasked to drive medical breakthroughs is so important because, among the 9,000 or so known human diseases, there are FDA-approved treatments for only about

500 of them.

To date, more than 146 drugs have been tested for Alzheimer's disease and rejected. While the first new drug for Alzheimer's in nearly 20 years was approved -- recently approved by FDA, there is still a long way to go to truly treat and prevent the progression of Alzheimer's disease. ARPA-H has the opportunity to play a critical role in revolutionizing how we prevent, treat, and cure a range of diseases with unmet medical needs, like Alzheimer's, which affects millions of families across the country, including my own.

My first question is for you, Dr. Yamamoto. I am interested in how ARPA-H could help accelerate the discovery of Alzheimer's biomarkers as a means of tracking responses to potential Alzheimer's therapies and exploring the use of digital technologies for diagnosis, assessment, and disease monitoring, among other important research initiatives. Can you discuss how Congress can ensure there is transparency around ARPA activities, including data sharing and the open resources development of data and information?

*Dr. Yamamoto. Thank you for that question, and let me start by saying that my dad died of Alzheimer's, so I know something about that from -- at a very, very personal level.

Everyone knows that early diagnosis is probably the clearest route to being able to cure diseases, and

neurological diseases are kind of the king of the failure to be able to diagnose early. My dad died when he was 84. In retrospect, I can think back to not quite a decade before that, but a number of -- let's say, eight years before, when I could then, in retrospect, begin to think, oh yes, there was something going on, my dad. But we didn't know that.

But, in fact, right, there are things that are going on in the brain when the baby is born, or maybe before, right? We just don't know what they are. So the impact of being able to diagnose neurological disease early could go back to decades, seven decades. And think of the impact that we could have in being able to cure or prevent those diseases, if we knew what those early markers were. I think that ARPA has the capability -- can develop the capabilities to be able to achieve such early diagnoses.

As we said before, when -- what precision medicine does is collect enormous amounts of data about lots of people and experimental organisms, to be frank, that allow us to be begin to pool that information, and begin to perceive biomarkers, indications of what the diseases are. So I can easily see an ARPA undertaking a project where at least the access to information to be able to establish those early markers is there to say that they have -- a project manager could walk in and say, "I think the goal is that we want to diagnose Alzheimer's 15 years earlier than we can right

now.''

*Ms. Barragan. Thank you, Dr. --

*Dr. Yamamoto. I think we are beginning to pull together the data to be able to do that.

*Ms. Barragan. Thank you.

Dr. Ling, part of the proposed mission of ARPA-H is to make pivotal investments in breakthrough technologies and broadly applicable platforms, capabilities, resources, and solutions that have the potentially -- potential to transform important areas of medicine and health. This is a broad mission.

But what do you see as some of the greatest unmet needs facing human health, and how could ARPA-H help solve some of these unmet needs?

*Dr. Ling. Thank you, Congresswoman. I think that Dr. Yamamoto hit it right on the head.

One of the really ripe areas where a good period of investment could really make a big difference is the early diagnostics. And it is just not finding the widget that is going to identify the blood marker. It is also the analytical techniques that Dr. Yamamoto speaks of.

What does that mean? It means bringing in mathematicians and statisticians and physicists, potentially, into this discussion. It can't just be biologists and physicians. That is what an ARPA-H does. It brings in the

people who are not commonly in the ecosystem into the ecosystem, bringing the chemists, bringing the entomologists, bringing the marine biologists, bringing -- honestly no joke -- the meteorologist, who looks at data at a large ecosystem-level, with the techniques that they do, to do something straightforward as weather. Apply those to the data sets that we are talking about right now.

You don't have to rediscover the wheel; you have to readapt the wheel. That is what an ARPA-H could do. It could bring in and create a new ecosystem, Congresswoman.

*Ms. Barragan. Well, thank you all for your responses. I didn't get to any of my other questions, but hopefully I will submit them.

Thank you, Madam Chairwoman, I yield back.

*Ms. Eshoo. The gentlewoman yields back. The chair is pleased to recognize the gentlewoman from Delaware, Ms. Blunt Rochester, for your five minutes of questions.

*Ms. Blunt Rochester. Thank you so much, Madam Chairwoman, and thank you to the witnesses for sharing your testimony today. I am pleased that we are discussing the Advanced Research Projects Agency for --

*Voice. Are you ready --

*Ms. Blunt Rochester. -- ARPA-H, which will accelerate the development of lifesaving treatments and cures in this country.

Last week the House passed the America COMPETES Act, a comprehensive package of -- to bolster America's global economic competitiveness. And today we turn our attention to ensuring that the U.S. remains the leader in global biomedical innovation.

I am particularly interested in understanding how the interests of the American people can be protected, and how preventions and cures derived from the work of ARPA-H will be distributed equitably and ethically.

One of the goals of ARPA-H is to create platform technologies upon which others can build and innovate. Admiral Giroir, based on your previous experience with BARDA, how can the U.S. Government ensure that contractual agreements for the technology transfer and commercialization of products that use research sponsored by ARPA-H reflect the contributions of the American Government and the American people?

*Dr. Giroir. Yes, thank you for that question, and it is good to work with you again.

Number one, the agency needs the flexible contracting authority to put that in. One cookie cutter does not fit. And as we heard, again, other transactions, cooperative agreements, all of those things.

Number two, I would like to switch the paradigm a little bit. Instead of making sure that the next thing is

distributed equitably, we ought -- the next thing ought to be focused on equitable distribution as its primary goal, right?

So just as an early diagnostic could be, I could see a program that says we want to assure in the next five years that all the underserved communities have a projected life expectancy equivalent to those who are White and affluent. Now that is a big goal, but that is a DARPA hard goal. That is going to be prevention, preventing kidney disease, preventing hypertension, getting in the home.

So I think you have to design it from the start, not just do it as an afterthought.

*Ms. Blunt Rochester. I love that, and it gets to the disparities issues that we have been talking about for years.

What guardrails could be put in place so that technology developed within the U.S. Government research funding is not exported for manufacturing overseas?

*Dr. Giroir. You know, that is not going to be necessarily the purview of ARPA, but I think it is very important.

Now, we talk about ARPA-H, you know, that the things that are going to be developed are going to benefit the world, just like the vaccines for COVID. America is, literally, saving the world. But we want to do our best to keep that technology here, so it supports jobs here, it supports the infrastructure here, that we don't get it copied

by foreign -- you know, overseas, that we don't get hacked, and all that gets done away. Again, these are all vital things.

And again, as Geoff said earlier, DARPA has been managing this. You know, things that are developed now won't necessarily be public for 30 years. The technology needs to be protected. I think we have the model. I think we have to employ the model and adapt the model, but I think your concerns are incredibly right on target, ma'am.

*Ms. Blunt Rochester. Thank you. Thank you so much. And I am going to ask this question of the panel, and I will call you, and if I don't get to you, if you could submit it in writing, that would be great.

And how will we know if ARPA-H is successful, given the lag time between product development and commercialization?

And if we could, start with Dr. Yamamoto.

*Dr. Yamamoto. So I think that we want to be able to look at the nature of the projects that are undertaken, and think about the scope, the breadth of application that -- if the capability is developed. So we want things that don't focus on one disease, but things that will be effective for big clusters of them. I think that would be one measure that we could begin to apply to examining and evaluating the projects that ARPA-H comes forward with.

*Ms. Blunt Rochester. Great, thank you.

And Ms. Krofah?

*Ms. Krofah. Yes, I would say understanding the impact on health outcomes through an ARPA-H program or intervention. Have we actually seen a difference in a disease or classes of disease states and, in particular to what Admiral Giroir just mentioned, equitably, across different populations who suffer disproportionately?

*Ms. Blunt Rochester. Great, thank you.

And Dr. Ling?

[Pause.]

*Ms. Blunt Rochester. Microphone.

*Dr. Ling. I think that there are metrics that we can use that are in existence. How many patents is one of them. The second is how many have transitioned into commercial practice. That is number two. Number three is how many have transitioned into clinical use and adopted by patients.

These are all metrics that have existed. DARPA, for example, has metrics looking at the dollars that are invested, and the return on investment in terms of commerce-produced, and it is a 10-to-1 ratio if you don't include the internet. If you include the internet, then it becomes, you know, astronomical.

So there are metrics that we can use that at all different levels that can actually be brought to bear to look at metrics of success -- and failure, I might add.

*Ms. Blunt Rochester. Yes, my time has expired. But Dr. Miller?

*Dr. Miller. Yes, I think we have to look at measures that are clinically relevant. So did we change how people practice medicine? Did we change how consumers access health care?

And then I think we also need to measure if that is distributed fairly and equitably because, frequently, it is not.

*Ms. Blunt Rochester. Great, thank you so much.

Dr. -- or Admiral Giroir, we will get back to you later.

And again, thank you so much, Madam Chairwoman, for this important hearing. I yield back.

*Ms. Eshoo. Well, thank for your patience and for participating.

Let's see who -- oh, we have -- the chair is pleased to recognize the gentlewoman from Massachusetts, Mrs. Trahan, for five minutes.

*Mrs. Trahan. Well, thank you, Madam Chairwoman, and thank you to the witnesses here today. I am pleased that this subcommittee is holding important discussions on the establishment of ARPA-H.

Developing multiple vaccines within one year to effectively prevent serious illness and death from COVID-19 was unprecedented, and this outcome was made possible by

significant Federal investment and collaboration with the private sector. Seeing what we accomplished in such a short time to save lives from COVID-19, it only makes sense for the numerous research projects out there to receive that same level of investment and urgency.

Those increased levels of investment and urgency is critical for people like my dad, who has been living with MS for 25 years, and who will benefit from the next innovation or lifesaving cure. However, barriers and gaps exist within the public and private biomedical research ecosystem, which can lead to the stalling or failure of innovative projects.

So to address this research gap, the Biden Administration has proposed the establishment of ARPA-H, and I am a big fan of the DARPA model, which ARPA-H will follow, including the groundbreaking discoveries we all know so well: internet, GPS -- we could go on and on. So I am excited to witness the groundbreaking discoveries that will come out of ARPA-H.

Dr. Ling, how can we ensure the appropriate resources will be allocated toward high-potential projects?

*Dr. Ling. Again, it begins with the program managers and the construct of the agency itself. If we are following the DARPA model, which I totally advocate, completely and totally, what it is is that program managers develop the program that they think is appropriate.

Let's say, using Dr. Yamamoto's case, it is for a new analytical approach that could be applied broadly across a number of different diseases. That program manager will then construct the program. What are going to be the milestones? What, in fact, are going to be the performers staff? And then they ask for the money.

So the money isn't allocated initially. One program maybe gets $10 million. Another program might get $50 million, and another program might get $100 million. It is dependent upon resourcing properly the program, and what the program hopes to achieve. As I said to you before, the most critical element is proper use of the dollars. And that is -- it is the how. I always said it before, it is the -- how the dollars are spent.

And so what you want to do is be sure to adequately resource the performers to achieve the goals of the program, as they are outlined from the get-go. The one thing you don't want to give them is time. Time is the one resource that we are not going to want to give to the performers. We will give them money, we will give them people, we will give them equipment, but not time.

*Mrs. Trahan. I appreciate that.

Ms. Krofah, I am wondering if you could just expound a little bit on how we can ensure that, you know, profit will not be the main driver for the development of a device, a

treatment, or a technology, or a cure under ARPA-H.

*Ms. Krofah. Yes, thank you for that question. You know, what is the most important, as we think about these sets of challenges, is to go back to that patient perspective. Where are we seeing high burdens of disease? What are the issues that are affecting that high burden of disease? What is the role of technology? What is the role of analytics? What is the role of diagnostics? How do we address those sets of issues?

And then work backwards from there to really address the science and the innovation question. Once we do that, that should yield the results that we are looking for. And that is why we make sure that we translate that science into what can be accessible for those patients at the end of the day.

It is not about the money, it is not about the profit motives at the end, because that is the issue why we are not seeing particular types of innovation targeted to patients who are suffering on the ground from diseases that we all know very well that we have not made a difference in decades and decades.

*Mrs. Trahan. Great. And then, you know, my colleague from Delaware asked about metrics, and I think that is on all of our minds. How do we know if we are going to be successful?

I guess, once established, how long do you expect it to

take to measure the success of the new agency through some of the metrics that were mentioned?

And I know that the clock is ticking down, so, Ms. Krofah, I will start with you.

*Ms. Krofah. I think metrics should start from day one. How quickly does the agency get up and running?

And then we should go and talk about how quickly do the program managers get established, and how quickly do those projects get funded and get started?

And then, of course, what kinds of science yields the outcomes over time? This could be a year, it could be 5, it could be 10 years, but the metrics need to start on day one.

*Mrs. Trahan. Great. Well, I appreciate you all being here. I look forward to working closely with the Administration and the important stakeholders as the ARPA-H proposal comes into fruition.

Thank you so much, I yield back.

*Ms. Eshoo. Thank you. It is always enlightening to hear the questions that you pose.

Is Mrs. Fletcher with us? Is she poised to question?

*Mrs. Fletcher. Yes, Chairwoman Eshoo.

*Ms. Eshoo. Oh, there you are.

*Mrs. Fletcher. Yes.

*Ms. Eshoo. Okay, I am pleased to recognize you, the gentlewoman from Texas, Congresswoman Fletcher, five minutes.

*Mrs. Fletcher. Thank you so much, Chairwoman Eshoo. Thank you for allowing me this time to participate in this hearing, and thank you for holding this hearing on the proposed creation of ARPA-H. I want to thank all of our witnesses for being here today, as well. This has been a really interesting and informative hearing.

And I know I have said before on this committee one of the reasons I was so excited to become a member of this subcommittee was because of its jurisdiction over medical research, and that is because of the community that I represent in Houston, Texas. I -- my district lies just west of the Texas Medical Center, which is the largest medical center in the country. It employs more than 300,000 people, many of whom live in my district, including some of the researchers that have done this incredible research we have been talking about today.

I know Dr. Schrier was talking a little bit about CAR-T therapies earlier, and, of course, Dr. Jim Ellison, who won the Nobel Prize for his cancer research on this very issue lives in my district, and was my guest at the State of the Union two years ago. So I am just so proud to represent these incredibly creative, innovative, thoughtful, and really pioneering researchers in my district.

So I am very supportive of the ARPA-H proposal that is before us today. I am glad to have co-sponsored both

Chairwoman Eshoo's bill, the ARPA-H Act, and Congresswoman DeGette's bill, the Cures 2.0 Act.

And as we have discussed throughout the hearing, the agency is modeled on DARPA, which has led to key innovations like GPS and the internet, things that we now couldn't imagine living without. And it could be that ARPA-H leads us to that next medical breakthrough that will revolutionize health care as we know it.

But there are key differences between DARPA and ARPA-H, and one of them that is really notable is that DARPA has, one, major customers that helps set its priorities, right? The Department of Defense. Whereas, when it comes to the biomedical ecosystem, there are various players, ranging from scientists to pharmaceutical companies to patients that are setting the agenda. And all these players have a crucial role in developing biomedical solutions that improve the lives of patients every day.

So I am interested in talking more about and learning about your thoughts on the role that ARPA-H will play within this larger system, and I want to direct my first question first to Ms. Krofah.

You discuss how ARPA-H must be engaged with other agencies. We have talked about that throughout the hearing, engaging with CMS and FDA. And you know, these things are critical to advancing solutions for patients. How do you

envision ARPA-H working in a collaborative manner with these other agencies?

*Ms. Krofah. Thank you so much for the question. I mentioned in my written testimony and earlier this morning that I believe it is critically important that we have an advisory council and engagement with patients, engagement with industry, engagement with non-profits, engagement with academia to listen.

And of course, we need to listen throughout the country. We don't need to sit in the ivory tower, as I mentioned earlier before. I think that would be critically important to understand the kinds of issues that are motivating people to ask questions: What is holding back science for me, and why? And to bring forward their solutions to inform the program managers as they outline the proposals that they put forward to the ARPA-H director.

*Mrs. Fletcher. Terrific, thank you. You also mentioned in your testimony that the private sector will be an important partner for ARPA-H. Can you discuss -- and I know we have touched on it throughout the day, but with the kind of minute-and-a-half I have left, there varying opinions here, and we have heard some of our colleagues on the other side of the aisle really want to defer more to the private sector. But can you discuss why it is so important for the private sector and other stakeholders to help work together

to ensure that the project that ARPA-H supports ultimately lead to improvements in health for patients?

*Ms. Krofah. Yes, absolutely. The biomedical innovation is an ecosystem. It is not one actor. And each part of the ecosystem matters to all the other parts.

So when we talk about the totality that end-to-end solution set, as was outlined by some colleagues, we need R&D upstream to be connected downstream to where manufacturing occurs and, importantly, where those products end up going to patients. And that is really the role of the private sector. That last mile is an area where the private sector has significantly innovated the manufacturing capacity that we see.

Even when we got the COVID-19 vaccines over the finish line, we needed vast manufacturing capacity and capabilities in order for those vaccines to reach patients. And then the delivery points, right, the retail sites, the mobile clinics, outreach to the community settings. These are all the roles that we need to engage the private sector.

But also, importantly, they need to bring their expertise to bear. Many of these companies are also investing in different types of technologies. They can identify where the gaps are. Data analytics is a big gap. Our data ecosystem is quite siloed. We do not talk well to each other. If you are in one hospital setting, your data is

not carried over to another hospital setting. If you are in one pharmacy, your data is not carried over to the other pharmacy.

How do we break down these barriers in data silos? The private sector can come forward and say, "We may not be able to solve it as one company,'' but we can put forward a project like ARPA-H, where it can break down those issues and those barriers.

*Mrs. Fletcher. That is terrific. Well, thank you so much. I see I have gone over my time, so I just want to thank you for that explanation, and really reminding us all about the ecosystem, and how we can accomplish so much when everyone works together.

So Chairwoman Eshoo, thank you so much for bringing us together for this hearing, and I yield back.

*Ms. Eshoo. I thank the gentlewoman, and you should know that this big screen carries your beautiful face and voice. It is exciting, you know? We really get -- with the screen you get a real close-up.

[Laughter.]

*Ms. Eshoo. I am glad it is not of me, but it is wonderful to see colleagues on the big screen.

Now we welcome -- we are grateful to Congresswoman Diana DeGette. She is not a member of our subcommittee, but she is waiving on, an important member of the Full Energy and

Commerce Committee and one of the authors of Cures 1.0, now with 2.0.

And I want to restate my intent that ARPA-H and Cures 2.0, they are complementary, and the chair will seek to move them together so that we could advance the legislation not only through the full committee, but the full House of Representatives, as it is so important that we do.

And with that, welcome, Diana, and you have five minutes.

*Ms. DeGette. Thank you so much --

*Ms. Eshoo. And if you go over a little, it is okay, we are just about done.

[Laughter.]

*Ms. DeGette. Okay, thank you. Thank you so much --

*Ms. Eshoo. You have waited all day.

*Ms. DeGette. I will just be happy to bat clean-up. Thank you so much, Madam Chair. Thanks for letting me waive on, although I do consider myself to be sort of an adjunct member of this subcommittee, anyway. And I want to thank you for your commitment to working with me and Congressman Upton on both this important initiative, ARPA-H, and also Cures 2.0, which really, really have synchronicity and need to go together.

When Fred and I first teamed up in 2015 to draft the 21st Century Cures bill, we couldn't have imagined the

incredible success it would have for this country. And because of that Act, we have a better understanding of the human brain. We have made huge strides in regenerative medicine. We have increased funding for Alzheimer's research and cancer research. Congresswoman Trahan talked about Operation Warp Speed. Many people don't think we would have been able to get the vaccine that we did without the pathways that we had in 21st Century Cures. And, as Fred likes to say, it passed out of this committee 57 to 0. And of course, through the House and Senate.

And so I want to talk both about ARPA-H and Cures 2.0 today to hear how they can work together to have even more stunning advances in U.S. biomedical research. I would like to start with you, Ms. Krofah.

What are pathways and programs that were included in 21st Century Cures -- or why are they, like the Moonshot and the Breakthrough Devices program, critical to the continued success of technological innovation?

*Ms. Krofah. Well, thank you so much, Congresswoman DeGette, and I very much applaud the efforts for Cures 2.0, and certainly your commitment to 21st Century Cures 1.0 that passed a number of years ago. [Inaudible] tremendous [inaudible] to the biomedical innovation ecosystem.

You know, I will start by saying the role that patients have in providing their data towards medical research,

contributing their data into the ecosystem, was supported through 21st Century Cures, and continues to be [inaudible] on the landscape. At the same time, seeking opportunity for breakthrough therapies and breakthrough designations has allowed us to see many new therapies reach the market to treat conditions like cancer, and many different types of cancer we would not have seen, otherwise.

And as we think about ARPA-H and the potential to merge the proposals that are in Cures 2.0, [inaudible] ARPA-H model, [inaudible] is that close collaboration that is needed between ARPA-H and FDA, similar to what is in Cures 2.0, in terms of encouraging communication between FDA and [inaudible] to bring that regulatory science up front at the time of determining the program or project [inaudible]. And creating that regulatory [inaudible] throughout that process will create clarity through the breakthrough process, will enable us, ultimately, to get the product [inaudible] ARPA-H into products that are approved by FDA and, ultimately, to patients.

*Ms. DeGette. Great. So what you are really saying is you see Cures 2.0 and ARPA-H as complementary, not substitutes for each other. Is that correct?

*Ms. Krofah. That is absolutely correct.

*Ms. DeGette. And I -- Dr. Yamamoto, I see you nodding your head yes. Do you agree?

*Dr. Yamamoto. Absolutely, I agree. And I think the other -- the thing I would add to what you just heard is that I think that -- I said earlier that there is nothing in the Federal Government that incentivizes agencies with different focused missions to really cooperate and work together. And in many ways, Cures 2.0 -- and Cures 1.0, but also Cures 2.0 -- begins to do that. It doesn't --

*Ms. DeGette. Thank you.

*Dr. Yamamoto. It doesn't create the natural drive for collaboration that ARPA-H does, because that is what the -- the only -- the program managers know that the only way they are going to get there is to bring together different groups.

*Ms. DeGette. Right.

*Dr. Yamamoto. But --

*Ms. DeGette. And Dr. Ling, I saw -- I also saw you nodding your head. Do you agree with that?

*Dr. Ling. I fully agree with that. The ultimate goal here is to improve health care for everybody in this country, for every American citizen. And to do that you have to attack the entire problem in toto. ARPA-H is just a small piece. Cures 1.0, Cures 2.0, in fact, actually embrace much more of the health reform, the policy issues, working with FDA, and a number of other things that are absolutely essential to realizing this ultimate goal that we have.

*Ms. DeGette. And Admiral Giroir, I can't see you, but

I am hoping you were nodding your head, too. What is your view on that?

*Dr. Giroir. I actually could not agree more with you. These are not only complementary, but synergistic. They can't live without each other.

And I will just make one comment, as I do believe a significant minority of program managers at ARPA-H come from FDA or NIH, because they will have been frustrated at things they couldn't get done within their own agency, will come to ARPA to get it done, and then return richer and the country better for it.

*Ms. DeGette. Great, thank you. Well, thank you to all of you for your leadership. I appreciate it.

Madam Chair, I just would like to take a moment of personal privilege on something else. One of our colleagues was attacking Dr. Fauci earlier, and calling him names.

And I want to say that, for Dr. Fauci, for all of our research scientists and our public servants who have worked hard to get us through this pandemic, including all of you, I want to say I appreciate what you are doing. I appreciate the advice and the science that you are relying on. And I want to apologize on behalf of the U.S. Congress that many of you have had to get security details because you have been under the threat of violence and worse. So thank you. Thank you to all of our advisors and scientists for getting through

this. We will continue to do that.

And I yield back.

*Ms. Eshoo. The gentlewoman yields back. I thank her for her -- for not only her questions, but for -- to recognize the extraordinary service of people: Dr. Fauci, so many others.

You know, I often think that those that are in the public sector, like he is, like so many are, they could be making millions of dollars a year in the private sector. Millions, tens of millions a year, a year. He devoted an entire lifetime to serve the American people. And you know, whether we agree with each other or not, to -- that honorable servants of the people are attacked, that really has no place. That is not America. That just isn't America. So thank you for raising that.

I want to thank all the witnesses. I love hearings. I have to admit that. So if I sit here for seven hours, the only regret is that my -- or ranking member that I am dragging along with me, although he is a very, very attentive member -- you have, I think, filled this room, whether you were -- are with us virtually or in person, with very, very rich testimony, and very direct answers to our direct questions.

And so you have enlarged the issue that is before us. And your expertise, I think, whomever is listening in at

home, that they would really be applauding the experts that we have in our country. And that you have come forward to advise the Congress is your gift to our country, and you have added immeasurably to our thinking today and helped us to improve the legislative vehicle that is before us. So on behalf of all of the members of the subcommittee, we all thank you and applaud you.

Now I need to get a -- I request unanimous consent to enter the following documents into the record. Do you want me to read them?

*Mr. Guthrie. No, no. No objection.

*Ms. Eshoo. Oh, no objection? So ordered.

[The information follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. They will be entered into the record.

That -- our panel has completed their work today. And I think that you all deserve at least a martini this evening before dinner.

And members have 10 business days to submit additional questions for the record. So, to the witnesses, when we get those to you, please answer as promptly as you can to any of the questions that you receive. That is -- it is not just appreciated, but it is an important weighing in, and we always want members' questions to be answered.

So with great gratitude, at this time the subcommittee is adjourned.

[Whereupon, at 2:58 p.m., the subcommittee was adjourned.]