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BEFORE THE

Subcommittee on Health

Committee on Energy and Commerce

U.S. House of Representatives

HEARING ON

ARPA-H: The Next Frontier of Biomedical Research

February 8, 2022

Good morning, Chairwoman Eshoo, Ranking Member Guthrie, and distinguished members of the Subcommittee. It is truly an honor to appear before you today, and I am grateful for the opportunity to discuss the Advanced Research Projects Agency for Health (ARPA-H)— an exciting new agency that the President has proposed to drive breakthrough advances in health and get them to patients quicker than ever before.

The Biden-Harris Administration is proposing ARPA-H because we stand at a remarkable time of scientific possibilities. The biological and biomedical sciences have made some remarkable advances over the last couple of decades. For example, we have learned how to train our own immune system to fight cancer and how to harness the power of cellular instructions, mRNA, to rapidly develop safe and

effective COVID-19 vaccines. And those are just a glimpse of the types of medical breakthroughs — from the molecular to the societal — that are possible.

Despite the progress, there is still tremendous need for medical breakthroughs. During the many listening sessions that OSTP and NIH hosted about ARPA-H, we heard powerful stories about individual patients with serious diseases — ranging from pediatric brain cancer and pancreatic cancer, to Parkinson's and ALS, to a host of rare diseases – where, despite the medical advances in recent decades, breakthroughs are still desperately needed. There are many such stories among my own family and close friends, and I know there are many among yours as well.

We also need breakthroughs to address inequities in care, inequities experienced in rural areas, inequities experienced by communities of color, and inequities experienced by the disability community, among others.

The combination of human needs and remarkable possibilities challenges us to ask: *What <u>more</u> can we do to speed and revolutionize medicine — to lay the foundation – to improve the health of <u>all</u> Americans? And, how can we also drive innovations that transform healthcare access, equity, and quality, and reduce disparities?*

What might be possible? For example, one idea would be to use mRNA vaccines to teach our immune systems to recognize the 50 most common mutations in cells that drive cancers, so that our bodies would recognize and eliminate early cancer cells before they ever create a tumor. Another idea is to develop molecular 'zip codes' that would deliver drugs into only the specific types of cells where they are needed; this could greatly increase the efficacy of drugs and avoid side effects. But, transformative innovation can occur not only at the level of cells, but also across healthcare. A third idea would be to apply innovation to our Nation's efforts to address health inequities across America, particularly in underserved and low-income communities. We could bring together community health workers and

cutting-edge health technologies to create effective systems that could help people manage chronic health conditions — with the goal of demonstrating rapid impact on health predictors, such as predictors of stroke and diabetes. We want to be able to encourage and to seize hundreds of ideas like these. ARPA-H can help us do that.

An important question to ask is: *Why do we need a new kind of research agency, ARPA-H, to drive this? Don't existing mechanisms suffice?*

The current biomedical research ecosystem in the United States is truly amazing. It consists of two components. The first is pathbreaking, curiosity-driven, *fundamental* research, largely supported by the National Institutes of Health (NIH), as well as other agencies, focused on understanding how the body works in health and disease; the NIH is recognized around the world as the crown jewel of biomedical research. The second is a vibrant biopharmaceutical industry focused on taking research through the development pipeline to bring vaccines, therapies, and devices to patients.

Unfortunately, the current system has gaps. Bold ideas that could make a big difference for patients can fall into these gaps, because they don't fit well within our mechanisms for supporting either fundamental research or commercial products. These ideas are often "use-driven" research — that is, research directed at solving a practical problem. They don't fit into existing mechanisms because they may be so risky, so costly, so broad in scope, so applied, so long-term, or so complex — in terms of requiring complex coordination across different groups— that they aren't suitable for basic research grants and also aren't suitable commercial projects.

Let me emphasize: The goal for ARPA-H is to fill an important gap. It's not to duplicate work that NIH already does. And, it's not to crowd out private sector efforts. The goal is to test transformative ideas that can have wider, faster impact than could happen through existing mechanisms — in the spirit of endeavors like the Human Genome Project or Operation Warp Speed.

Advancing these kinds of ideas requires a different approach to supporting biomedical research — one that exists in other areas of research and development — notably, at the Defense Advanced Research Projects Agency (DARPA).

As you know, DARPA is the legendary Defense Department agency that laid critical groundwork for the Internet, GPS, and much more. Launched in the wake of Sputnik, DARPA's mission is clear — to make pivotal investments in breakthrough technologies for national security. And it has been successful by pioneering a model that smartly blends boldness with discipline. For example:

- DARPA aims to be a lean and nimble organization with a fair amount of autonomy. It focuses on mission-driven research that could offer extraordinary returns, and program managers are empowered to take on bold, transformative ideas.
- At the same time, DARPA also brings discipline, including by placing limits on a program's duration and on staff's tenure. Program managers are appointed to short terms — typically around 4 years. Its director also serves for a limited period.

ARPA-H proposes to apply a similar model to propel bold projects in the biomedical and health ecosystem. The President's vision is to create a new kind of entity for biomedical research that will have the autonomy, authorities, and resources to boldly tackle big challenges facing human health. It will aim to benefit the health of *all* Americans by catalyzing health breakthroughs that cannot readily be accomplished through traditional research or commercial activity. It will support transformative programs that enable the emergence of new technologies, new capabilities, and new platforms to drive progress – across a broad range of diseases.

In doing so, programs supported by ARPA-H will focus on practical solutions through use-driven research that aims to foster breakthroughs ranging from the molecular to the societal scale — including advancing both individual health and health equity for all Americans. Because equity will be an essential

element of ARPA-H, it will be key to its practices, including in hiring program managers with diverse perspectives about health challenges, in selecting programs that aim to fulfill a diverse range of needs, and in building interdisciplinary teams with unique expertise to accomplish program goals.

Echoing many elements of the DARPA model, ARPA-H will embrace urgency, nimbleness, and innovation, while also ensuring discipline. To do that, ARPA-H's culture will be key to its success. Like DARPA, it will have a flat, dynamic organizational structure — and the director and program managers will serve for only a limited time.

ARPA-H program managers will be given broad autonomy and the authority to drive innovation and be creative with their programs. They will each bring ideas about areas that are important and ripe for progress, and they will then solicit bold proposals in these areas. Adopting the DARPA model for review, ARPA-H program managers will use expert reviewers to evaluate whether the proposals hold great promise and meet the needs of the program, and then they will have the authority to assemble portfolios of projects and teams to tackle important goals. Through this model, DARPA attracts remarkable people to come into the federal government for limited periods of time to try to make a big impact; ARPA-H will aim to do the same.

We should be clear: Some ARPA-H programs will fail. That's not only OK — it's an essential feature of the model. To take on potentially transformative ideas, one must accept some degree of failure. If no ARPA-H programs fail, then ARPA-H is being too risk-averse.

ARPA-H will need to work across a wide range of sectors, including having close relationships and collaborations with patient groups, industry, academia, NIH Institutes and Centers, and other federal agencies. It will also need to work across a wide range of disciplines, including those that don't traditionally engage in biomedical research, to draw them in. ARPA-H should avoid areas of research that are already well-supported by research stakeholders, unless it can bring a very different approach.

In addition to having a distinctive culture, ARPA-H needs flexibility—for example, concerning how it hires program managers, how it reviews proposals, and how it makes funding decisions. And, it's critical that the ARPA-H director have complete independence and autonomy with respect to scientific direction and program selection.

We look forward to working with the Congress on how best to design ARPA-H, because I know we all want to get it right.

In summary, I believe that ARPA-H has the potential to revolutionize how we prevent, treat, and cure a range of diseases that impact Americans' health and quality of life. The DARPA model is not the right approach for all challenges, but it's a powerful approach for driving certain kinds of innovation — including the kind of innovation we need for health, transforming the seemingly impossible into reality.

Matthew Might, a patient advocate and computer scientist who lost his son Bertrand to an ultra rare disease, put it like this, "For all lives lost for failing to move as swiftly as possible, establishing ARPA-H honors their memory." The time to act is now.

Thank you Chairwoman Eshoo, Ranking Member Guthrie, and all the Members of the Subcommittee for your consideration of this critical issue. I look forward to addressing your questions.