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Hearing on NIH and the National Center for Advancing Translational Sciences (NCATS)

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Thank you, Chairman Rehberg and Ranking Member DeLauro, for inviting me to testify on the National Center for Advancing Translational Sciences. I am a PhD neuroscientist and CEO of The Michael J. Fox Foundation for Parkinson's Research. Our Foundation has a single, urgent mission: fund research that will speed a cure for Parkinson's disease.

The structure of our drug development system fundamentally impacts every American at some point in their lives. And because our Foundation has a great deal of experience with the complexity of this system, I thought I could be most helpful today by sharing some key learnings from our short history.

Since our launch in 2000, our Foundation has had a hand in developing more than 100 Parkinson's therapeutic targets, pushing dozens of these closer to the clinic and practical relevance in patients' lives. We have built a staff of PhD-trained neuroscientists, each paired with business-trained project leaders. Sitting at the global hub of Parkinson's research, this team comes to work each day with the single-minded purpose of prioritizing limited resources for maximum impact on patients' lives in the nearest possible term.

Our work requires us to expertly navigate the complicated journey of drug development. We work with 500 scientists and review 800 proposals a year. We fund research in the United States

and abroad. We work with academic researchers and NIH as well as small and large companies, public and privately held. We have funded about $285 million in research to date.

To produce one new drug for Parkinson's disease takes upwards of 15 years and one billion dollars — and the timeline and costs remain unknown for the development of a disease-modifying therapy, because we don't have one yet. We've found it helpful to use the alphabet as an analogy for the complexities that result in such high costs and long lead times, and specifically for illustrating the different kinds of expertise needed at different stages of the process, to move ideas from lab bench to pharmacy shelf.

In the first part of the alphabet — say, letters "A to F" — there are the early-stage questions, the "a-ha" moments, where a scientist in an academic setting looks at some aspect of biology and asks herself: Could this be important? A lot of money gets spent in this stage asking additional questions to illuminate basic biology; discovery science is the backbone of all drug development. In fact, our Foundation's impact is possible because we strategically build off of the federal government's ongoing investment in discovery via NIH. But to be clear, when it comes to developing cures, questions at this level are the proverbial first step of a thousand-mile journey.

The next chunk of the alphabet — say, letters "G to P" — is translational research, applied work where scientists home in on discoveries from the "A to F" phase, looking for disease-specific effects. This series of questions must be asked and answered before we take the critical leap of faith to test a potential therapy in a human. The problem is, it's far easier said than done. In the medical research system as it stands today, few natural handoffs exist to shepherd promising findings from researcher to researcher, institution to institution, or discipline to discipline — let alone from academia to industry. This phase has famously been dubbed the "valley of death"

because of the chronic funding and expertise gap that is crying out to be addressed by an institute like NCATS. For now, unfortunately, this is where potential treatment breakthroughs go to die.

The very few novel approaches that do make it out of this middle phase still have to navigate the final part of the alphabet — call it "Q to Z" — which is largely handled by the private sector. Capital in this final stage, where potential new drugs initiate clinical testing phases and ultimately seek regulatory approval, is becoming more and more risk-averse. To come this far, potential drugs have succeeded against astronomical odds and have tapped into the very, very deepest pockets of a funder willing to develop the drug. If they succeed here, the next stop can be regulatory approval and practical relevance in patients' lives.

As I mentioned, our Foundation is approaching the 300-million-dollar mark in research funded, approximately 90 percent of which has gone straight to translational research. Compared to the unfathomable sums poured into the medical research enterprise, our resources may look like a drop in the bucket. But we believe that getting to patient-relevant results isn't about spending more money — it's about spending money more effectively. I'd like to share a few learnings from our model that may be helpful in defining the future of NCATS in this space.

First: The research enterprise is made up of multiple well-intentioned but differently incentivized stakeholders, all working toward different interim goals. For an academic researcher, success means publication; for industry, it's patentable assets; for patients, it's a new treatment. No one is streamlining and orchestrating the efforts of the different players on the field. As Michael J. Fox has said, there is no "Department of Cures." In the absence of such a department, progress requires a conscious decision to elevate translational research — including an appreciation for what it is, why it is vital, and what strategies can help foster success. Translational research is

bigger than any single disease and it is bigger than any single disease stakeholder, such as a Foundation like ours. Based on my experience of what can happen when substantive investments are made in translation, the total contributions NCATS can make to drug development may well be greater than the sum of the parts.

Second: Our Foundation realized early on that to drive Parkinson's breakthroughs, we needed to make investments in applied biology to transform basic discoveries into practical treatments. As a society, we benefit every day from the investment we make in "engineering" to leverage our early-stage investments in "physics," which ultimately transforms the world as we know it — advances in everything from the cars we drive to the bridges we drive them over. But there is no parallel investment made in "biology" and "applied biology." In other words: American taxpayers are funding the greatest discovery engine in the world. But we are failing to convert the fruits of our early-stage investment into practical therapies that can benefit the people who urgently need them.

The tough truth is that our system largely fails us right where it should be working the hardest. A successful NCATS would make a tangible difference by concentrating and building the right pools of expertise where they are most needed, at the "G to P" phase, by supporting creative, higher-risk approaches to drug development and leveraging relationships and collaborations with academia, patient and disease organizations and industry. This would ultimately move the best projects from "A to Z" faster and more efficiently for the benefit of all Americans.

Third: At the core of our Foundation's daily work lies a single purpose: We must allocate resources as wisely as possible to benefit Parkinson's patients in the near-term. NCATS can seize the opportunity to represent patient-relevant investment on a larger scale, potentially

impacting the lives of countless Americans. In real terms, this means not only orchestrating work within the translational stage but also stepping in to champion promising projects at risk of languishing because they hold no incentive for a for-profit entity to get involved. It means investing in agents that show treatment potential but can't be patented. It means working to reposition existing drugs if they hold promise for untreated diseases; and investing in pre-competitive research tools with potential to move the entire field forward.

Fourth: This panel will no doubt hear from those who believe that the private sector alone bears responsibility for bringing new treatments to market. In our experience, this is a misguided way of looking at the problem. The challenge is not inducing the private sector to pick up a promising idea that has already overcome the considerable odds to make it all the way to letter "Q." The challenge is getting it that far in the first place, particularly when economic realities and research challenges are making it harder, not easier, for companies to invest in high-risk science. With quarter-to-quarter decision making and stripped-down R&D programs, profit considerations often don't align with patient needs. Big Pharma remains risk-averse and requires greater and greater prior investment as a prerequisite for involvement. This is not a sustainable model for drug development or for patient benefit.

The drug development system impacts generations of Americans. I hope the core values for translation I've shared today —

- aligning and convening stakeholders to enable better handoffs from one stage of research to the next,
- adequately investing in applied studies,
- maintaining a patient-oriented perspective, and

- reducing risk as an idea moves along the drug development pipeline to carry promising treatments forward to the private sector —

are helpful in shaping the future of NCATS. It is one of our greatest hopes that we will have the opportunity to work with NIH and NCATS leadership to usher in this new institute devoted to improving the lives of Americans not only with Parkinson's, but across all diseases.

I'd like to thank the committee for the opportunity to be here today. While a great deal of work remains to be done, our Foundation believes without fail that we are making progress. As Michael J. Fox has said, the answers we want aren't going to fall out of the sky. We have to get ladders and climb up and get them. Thank you and I would be happy to take any questions.

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