GLOBAL
DOWN SYNDROME FOUNDATION®

Chairman Aderholt, Ranking Member DeLauro, thank you for the opportunity to testify today.

My name is Michelle Sie Whitten, and I am the co-founder, President, and CEO of the Global Down Syndrome Foundation ("GLOBAL") and the mother of two, including a 21-year-old who happens to have Down syndrome. Like other parents of children with Down syndrome, our family considers Sophia a gift who has transformed our lives and the lives of those around her for the better.

The genesis of GLOBAL is the result of NIH leadership acknowledging that its medical research priorities do not necessarily align with medical research needs. Former NIH Director, Dr. Elias Zerhouni, encouraged me to work to build a pipeline for science and establish an academic home for Down syndrome (DS) medical research. He encouraged this because researchers discovered that the extra chromosome in people with Down syndrome gives them a radically different disease profile compared to the general population with people with Down syndrome highly predisposed to certain diseases and highly protected from others:

- This is the largest population with a genetic predisposition to Alzheimer's disease;
- 50 percent of babies born with Down syndrome have congenital heart defects and have a predisposition to autoimmune disorders such as celiac and autoimmune thyroid disease.
- People with Down syndrome are also highly protected from developing solid tumors. For example, it is extraordinarily rare for someone with Down syndrome to have breast cancer or prostate cancer; however, they are highly predisposed to two blood cancers: acute megakaryoblastic leukemia and acute lymphoid leukemia.

All to say, people with Down syndrome have complex yet manageable and treatable health needs that involve almost each of NIH's 27 institutes and centers.

GLOBAL's goal since its founding has been to elongate life and improve health outcomes for children and adults with DS by overhauling NIH's approach to funding DS research. When GLOBAL was formally established in 2009, DS was the least funded genetic condition at NIH, receiving $22 million dollars out of an NIH budget of more than $31 billion dollars in Fiscal Year 2010 despite DS being the leading cause of developmental delay in the U.S. and globally.

We were fortunate that Chairman Cole and Ranking Member DeLauro, who led the House LHHS Subcommittee in 2017, recognized the immense potential of Down syndrome research. After testifying before this subcommittee about NIH funding for DS research, there was bipartisan consensus from the hearing that NIH was significantly underinvesting in DS research. Chairman Cole concluded that while Appropriators are very careful about intruding too deeply with NIH in terms of making decisions and how to spend their resources, he said "there are times when there are gaps" and Down syndrome research was one of those gaps.

Members also recognized that sustained investment in DS research impact would extend far beyond improving the health outcomes of this specific population, offering hope for all individuals affected by some of the most physically and financially devastating chronic conditions, such as Alzheimer's and cancer. This led to the creation of a transformative NIH DS funding project (later called the INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) Project) to catalyze new DS research investments.

The INCLUDE Project is a real-time example of how effective and efficient NIH can be when research priorities and plans are developed in a collaborative, multi-institute, centralized approach rather than occurring in silos and being isolated in the field of childhood development.

Before INCLUDE, NIH's approach to DS was better, faster, detection and you saw that bias in the way that research dollars were funded and spent. DS research occurred almost exclusively within the National Institute of Child Health and Human Development, whose major research focus is reproductive biology; embryonic development; maternal, child, and family health. Today, because of INCLUDE, 18 of NIH's 27 institutes are involved in DS research with 11 institutes participating in Down syndrome research for the first time ever and supporting scientists at universities and research institutes across the country.

A few examples of the research happening that has implications for people without Down syndrome include:

- Researchers at the University of Alabama Birmingham are researching Optic Nerve disorders associated with Down Syndrome as the prevalence of optic nerve hypoplasia among individuals with Down syndrome is more than ~100 folds higher than in the general population and it is the leading cause of childhood legal blindness in developed nations.

- Researchers at the University of Michigan are working to identify the molecular regulators of the comorbidities in Down syndrome, which will offer insights into the development of therapeutic treatments that target these conditions and provide molecular and cellular insights into other neurological disorders, such as intellectual disabilities, epilepsy, and ASD.

- Scientists at Vanderbilt are researching fundamental questions of why children with DS have an increased risk of ALL and how their leukemia differs from that of children without DS.

- Texas A&M researchers are using INCLUDE funding to understand whether bone regeneration holds the key to helping people with Down syndrome recover from fractures. Findings from the project will also aid treatment development for people with limb loss, which is expected to be more than 4 million people by 2050 because of the increase in vascular diseases like diabetes.

- University of Florida researchers are examining the significant genomic variants underlying congenital heart disease in DS patients, which could lead to advancements in personalized medicine for conditions that affect DS individuals and the general population.

In just the six years since the INCLUDE Project was established, scientists have a better understanding of the health needs of people with DS and have measurably improved health outcomes and quality of life for people with DS. The universe of scientists now involved with DS research has also increased significantly, ranging from top cancer researchers, Alzheimer's and dementia specialists, neurologists, immunologists, endocrinologists, cardiologists, and more.

We can already point to advances in research and concrete outcomes resulting from INCLUDE:

1. Clinical Trials. Prior to INCLUDE there were few if any Down syndrome clinical trials and most clinical trials excluded people with Down syndrome from participating. There are now at least 12 clinical trials that include repurposed drugs to treat autoimmune diseases, Alzheimer's, cognition deficit, and Regression Disorder, and more.

2. Data Coordinating Center: INCLUDE established the Data Coordinating Center under the leadership of Dr. Joaquin Espinosa that now has more than 9,000 participants, 4,000 whole genome sequences, hundreds of molecular data sets and other data sets that can launch the career of investigators interested in Down syndrome medical research.

3. Alzheimer's Research: INCLUDE has funded the Trial-Ready Cohort-Down Syndrome under the leadership of Dr. Mike Rafii who runs the Alzheimer's Therapeutic Research Institute at the Keck School of Medicine.

4. Down Syndrome Registry. INCLUDE now houses the important Down syndrome registry, called DS Connects that was essentially directed by Congress into existence in December 2010 when GLOBAL and the NIH were required to organize the first-ever Down syndrome research conference at NIH looking at databases, registries, and biobanks.

5. Down Syndrome Clinical Cohort Coordinating Center. INCLUDE recently put out an RFA for the DS-4C with a centralized biobank. The establishment of such centers has been a GLOBAL goal since 2006 and to see it coming to fruition is very exciting and rewarding.

As a population with a unique health profile that is more susceptible to certain conditions and diseases while protected from others, people with DS benefit by INCLUDE's goals to streamline the current structure of NIH research to better support a holistic life stage approach rather than by specific diseases, conditions, or organs and the proposed restructuring reflects what science has learned about the interconnectedness of health.

We are entering a new era when it comes to valuing people with Down syndrome. We are seeing a renaissance for Down syndrome research and witnessing the great promise and tangible results from this program. We look forward to working closely with the new NIH Director, Dr. Bhattacharya, and our champions in Congress, to ensure U.S. leadership in life sciences, and in continuing to advance cutting edge research to improve and elongate the lives of Americans with Down syndrome as well as millions of Americans without Down syndrome.