Importance of Pediatric Cancer Research Funding And Senate Bill 74

Testimony presented by:

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Good Morning. My name is Elizabeth Fox and I am a Pediatric Oncologist at the Children's Hospital of Philadelphia.

- I want to thank Senator Martin for sponsoring this legislation and Chairman Hutchinson for holding this hearing.
- I'd also like to thank Representative Benninghoff and Representative Caltagirone for sponsoring these important legislative initiatives in the House.
- Lastly, I'd also like to express my sincere gratitude for the invitation to speak to you today and thank the young people and their families that are here with us today, as well as children, families and advocates fighting cancer throughout Pennsylvania; thank you for your courage and inspiration.

For context, a bit about myself. Pennsylvania is my home. I grew up in the Lehigh Valley, attended Penn State Hershey Medical School and now live in Philadelphia, where, as Director of the Developmental Therapeutics in Oncology at the Children's Hospital of Philadelphia, I work every day to bring new treatments and clinical trials to infants, children, adolescents and young adults with cancer. I study how a child's body handles new drugs. It was 20 years ago that I completed the required education, training, and certifications to be called a "pediatric oncologist" but it is the patients, families and my dedicated colleagues who teach me every day what it means to care for children with cancer and how much more we need to do.

- <u>Increased Awareness of Pediatric Cancer is important</u> because cancer is a leading cause of death from disease in children within the US. No child is a number but I will share a few statistics for your consideration. **Approximately 1 in 285 children in the U.S. will be diagnosed with cancer before their 20th birthday.** Today survival rates are better than ever, 80% of children with cancer are cured, however, every child deserves curative therapy and we must reduce the short and long-term side effects of treatment. Currently in the US, 1/640 young adults between the ages of 20 and 39 is a survivor of a childhood malignancy. Unfortunately, two thirds of survivors of childhood cancer have at least one chronic medical condition and one quarter of the children who are cured of cancer face a severe or life threatening late effect of the curative treatments. Some side effects become life-long problems like infertility, growth delays, learning problems, and even secondary cancers later in life. We need safer, more specific and effective treatments so more children are cured with fewer side effects during and after treatment.

We have made significant progress in treating childhood cancer. Just last week, Adam a new PhD student at the University of Pennsylvania came to my lab to ask if he could do his PhD work with me to find new treatments for childhood cancer. He had an impressive resume having worked at some large pharmaceutical companies as an undergraduate and now in the biochemistry PhD program at Penn. He had great insight into childhood cancer and its current treatments. When I asked why he chose biochemistry and drug development in childhood cancer. He said because he had leukemia as a child and had recently lookup the therapies he had received. He said he was fascinated by how those "old drugs" work and in the new therapies for cancer. He felt fortunate to be a survivor and wanted to give back. He and the childhood cancer survivors here today are passionate about this cause and the need to cure cancer with less toxic therapies. They are the next generation of cancer researchers and advocates.

- <u>Cancer is a spectrum of diseases that are increasingly categorized by genetic changes in the cancer cells.</u> This has significant implications for developing new treatments for children with cancer.

  Cancers that occur commonly in adults, such as breast, prostate, lung or colon carcinoma, have many consistent genetic changes that can be targeted by drugs. For example, for adults with lung cancer that has a specific change in a gene called ALK, a pill called crizotinib has improved the life expectancy for these adults from 4 months to more than 7 years after being diagnosed with this specific type of lung cancer. However, childhood cancers are biologically different from most cancers in adults. When I think about genetic changes in childhood cancer I consider 3 groups 1) Same cancer; 2) same genetic change but different chancer or 3) cancer that occur only in children that have unique a genetic change. Each poses a different challenge to new therapies.

  1) Same cancer: Hodgkin lymphoma is essentially the same in adults and young adults who are afflicted. In this case, both can benefit from the same drug if the drug dosing is safe in children. A recent success is the FDA approval of immune checkpoint inhibitors for children and adults with relapsed Hodgkin's lymphoma. Efforts are now underway to do clinical

trials in both young adults and older adults to bring the most effective new therapies to all patients sooner.

2) Sometimes the molecular change that occur in a cancer in adults is the same genetic change that occurs in a childhood cancer, even if the cancers are very different. An example is cancers that have a genetic change in a gene called NTRK. In adults, NTRK fusions occur in rarely (<5%) adults with common cancers including some types of colon cancer and occurs in more than 90% of infants with a rare sarcoma and in some children with brain tumors. In the past year in a major success in drug development for children, two drugs that target NTRK have been FDA approved in both children and adults. I led the clinical research team that brought one of these drugs, entrectinib, to children at CHOP and other children's hospitals and FDA approval. It has been truly remarkable to see the cancer in an infant rapidly shrink after taking an oral medicine with very few side effects. NTRK inhibitors have redefined success in drug development for childhood cancer, however we know that the types of genetic changes that create these "oncofusion proteins" that are drivers of the malignant cell are uncommon.

As an example of how extraordinary NTRK inhibitor therapy, I care for a 4 year old who was born with a very aggressive cancer on his foot. He nearly died in the delivery room from bleeding from the tumor. He was treated with conventional chemotherapy but the tumor continued to grow despite the harsh chemotherapy. He had a partial amputation of his foot at age 2 and then the cancer spread to his lungs. His cancer was found to have an NTRK fusion and he was started on an NTRK inhibitor. Within 6 months, his cancer is gone. He is happy and runs around clinic with a prosthetic foot. Now that NTRK inhibitors are FDA approved we have a clinical trial to help us understand how best to use these drugs to avoid chemotherapy and radical resections in these young children and monitor for long term side effects.

3) Most children have cancers that fall into the third category: cancers with genetic changes specific for the rare childhood cancer. A major challenge in drug development for childhood cancer is discovering, developing and testing drugs in clinical trials that are pediatric –cancer specific targets. One success in this category is dinutuximab, a drug that targets a glycoprotein on the surface of neuroblastoma cells which was FDA approved for children with high risk

neuroblastoma based on improvement in survival of children who received this drug. But we need more drugs and clinical trials for children with brain tumors, sarcomas, and relapsed leukemias.

- Support for access to new drugs and clinical trials must be expanded. The pediatric oncology community has worked together for more than 70 years of clinical trials to increase overall survival for children with cancer. NTRK inhibitors, dinutuximb are recent successes. We need more successes. On average each year, the FDA has approved 10 new drugs for testing in adults, a small number were tested in children, and four were recently approved for use in children with cancer. As the number of new drugs increases we must continue to work together to perform the laboratory experiments and systematically collect information our patients to treat more children with new drugs that work while decreasing the number of children who are exposed in ineffective therapies. We must begin now to explore mechanism of resistance to new drugs and understand the potential late effects of new therapies.

  As cancer therapy becomes more specific, we must work together in Pennsylvania, nationally and internationally to make sure that the most promising new therapies are evaluated safely and efficiently in children and that drugs that are specific for childhood cancer are developed.

As a pediatric oncologist, each day I see my young patients combat the despair of cancer with the hope inherent in being a child. My message today is one of hope. I have seen the progress first hand, but we need to do more. We often say, hope is vitally important, but hope is not a plan. We need funding for basic and clinical research for pediatric cancer to allow us to make discoveries and find new treatments to permit our children to enjoy living and grow without cancer or the devastating side effects of treatment.

Again, I would like to thank you Mr. Chairman, Senator Martin, and members of the Committee for this opportunity to testify and share my experiences. I look forward to answering any questions you may have.