Commission on Economic Competitiveness and the Commerce Committee Robert J. Alpern, MD; Dean, Yale School of Medicine February 3, 2017

Speaker Aresimowicz, Majority Leader Ritter, Representative Tong, Senator Hartley, Senator Franz, Representative Simmons, Mr. McGee, and Members of the Commission on Economic Competitiveness and the Commerce Committee, thank you for the opportunity to present to you our plans for a Connecticut Program in Precision Medicine.

Why do some people die young, while others live to an old age? Why do some patients respond to a treatment while others do not? Why do some patients tolerate a drug well while others suffer harmful side effects?

The difference lies in a multitude of factors that define who and what we are.

- First and foremost, is our genome, the genes we inherit from our parents.
- Then there are the modifications that occur to us throughout our lives.

Precision Medicine is the use of a patient's genomic information, environment, and lifestyle to assess a person's risks for disease and to develop more effective and targeted treatment plans and therapies. Precision medicine takes advantage of your genetic information to improve the precision by which your health is maintained and diseases are treated.

When you hear that a treatment worked in 70% of patients, what is the difference between the 70% who responded and the 30% who did not. The most likely difference lies in the patient's genome, the sequence of their DNA. Today we have to treat all 100 patients so that 70 can be successfully treated. Someday, we will sequence the DNA of the patients prior to treatment and know who will respond and who will not respond. Then, we would not treat the non-responders and we would have a 100% response rate in those treated. This is Precision Medicine.

Today, Precision Medicine has some applications, while for many conditions it remains a dream, but it is a dream that will soon be realized. The first challenge was to be able to sequence the DNA of a patient. When I started in research, one would spend an entire day sequencing 100-200 bases. Given that the human genome contains 3 billion bases, sequencing of the entire genome was viewed as impossible. Then the NIH initiated the Human Genome Project. Over 10 years, at a cost of \$3-5 billion, the first human genome was sequenced in 2000. The most important accomplishment of this project was not the sequence per se, but the development of the technologies to rapidly sequence large amounts of DNA. Since that time, DNA sequencing has become steadily faster and cheaper at a rate that has been steeper than that of microchip technology. With the latest instruments, we can sequence a human genome in days for under \$1,000.

Then we have to ask the question, why Yale? Why Connecticut? All across the country, medical schools and hospitals are talking about Precision Medicine. Yale School of Medicine formed the first Department of Genetics in the country in 1972. Since that time, faculty have identified the genes that cause patients to have a wide array of diseases, including hypertension, strokes, polycystic kidney disease, macular degeneration, dyslexia, metabolic syndrome and many other disorders.

In 2010, we formed the Yale Center for Genome Analysis (YCGA) with an investment of \$10 million in DNA sequencing instruments. Since that time, we have replaced our sequencers a number of times to purchase faster machines, and we are about to now purchase new Illumina NovaSeq machines, the fastest machines that can now sequence the entire human genome in a few days. Yale developed the technique of Exome sequencing, was named by the NIH as a Center for Mendelian Genetic Diseases, and now is second in the country in the number of newborn clinical DNA sequences it has performed. Although my focus today is on precision medicine, I would point out that the same DNA sequencing technology is used to analyze the microbiome, about which you will hear later in the session. This sequencing could all be performed in Connecticut at the Yale Center for Genome Analysis.

We have had discussions with the University of Connecticut and Jackson Labs, and believe that the three institutions are well situated to make Connecticut a leader in genomic medicine. Patients followed at Yale and the University of Connecticut would have their DNA sequenced at the Yale Center for Genome Analysis, and then the patients would be followed at both institutions, correlating clinical outcomes with genome sequence. Information would be analyzed at all three institutions in a multitude of collaborative projects. All patient at Yale are presently on the Epic electronic medical record. In April 2018, the University of Connecticut will be on Epic, permitting easy sharing of deidentified patient data.

In 2016, the NIH awarded Yale School of Medicine \$366 million in grants. We are confident that through this Connecticut Personalized Medicine Consortium, grants would increase significantly to Yale, the University of Connecticut and Jackson Labs. If we are successful in establishing ourselves as a leader, companies would then move to or start up in Connecticut. Both NIH dollars and new companies would lead to many high paying jobs.