Thank you Dr. Martin for that kind introduction and a special thanks to our board members, family, and friends who have traveled here from so many far off places. We certainly appreciate your taking the time out of your busy schedules to join us.

When I was asked by the Dean and the Council for Harvard Medicine to deliver tonight’s keynote address, you can imagine my reaction.

After getting over the initial shock, I was finally able to ask myself two fundamental questions…the first, “why me?” and close on the heels of that one, was “why now?” It does seem like a bit of a reach. I have a feeling that a number of you, in tonight’s very prominent audience, might also be asking yourselves the same question. But sorry, it’s too late. The program was already printed. So I thought I would share with you how I grappled with those 2 questions that somehow links Harvard and the Jeffrey Modell Foundation.

It all started in 1975. Our son Jeffrey suffered from a somewhat mysterious disorder called Primary Immunodeficiency, an umbrella term for a condition that includes more than 140 genetic defects. Taken together, the disease affects as many as one million children and young adults in the United States and ten million worldwide. We asked Jeffrey’s doctors in NY to reach out to the greatest experts anywhere in the world on this disease, and most especially on the specific B cell complexities that affected Jeffrey. We offered to go anywhere at anytime to help unravel the puzzle of what was wrong with our son. The answers were always the same.

“You must try to reach Dr. Fred Rosen, Professor of Pediatrics at the Harvard Medical School and Chief of Immunology at the Boston’s Children’s Hospital. He is the expert.”

Dr. Rosen took our call. And in a short time he offered the definitive diagnosis of Jeffrey’s condition…Hypogammaglobulinemia. He started Jeffrey on a new protocol, which he helped to develop, called intravenous immunoglobulins, or IVIG. Over the years, he monitored
Jeffrey's condition and gave him a real quality of life. He also gave us confidence to share a normal life with our son.

Eventually, Jeffrey lost his long fought battle with this disease at the age of 15, but his short life was improved, enhanced and enriched by Dr. Fred Rosen and his team at Harvard.

About a year later, we established the Jeffrey Modell Foundation. We soon began to hear from families across the nation and around the world who were going through some of the same things we had experienced. It was at a time when there was very little research on these diseases. There was virtually no funding. There were few treatments. There were no cures. There was little hope. We set out on an uncertain course, but Vicki and I were passionately committed to changing that landscape by building greater awareness of Primary Immunodeficiencies.

Dr. Rosen moved on to lead Harvard’s Center for Blood Research as its President, and Vicki joined his board. Dr. Raif Geha succeeded Dr. Rosen as Chief of Immunology at Boston’s Children’s Hospital and both Dr. Rosen and Dr. Geha championed our Medical Advisory Board. They developed the 10 Warning Signs of PI which is widely utilized in at least 25 countries and available in 19 languages all around the world. Harvard framed the Foundation’s mission by developing programs of basic and clinical research, physician education, patient support and public awareness. Those early days marked the beginnings of a close working partnership between JMF and Harvard.

Dr. Rosen made it clear that with our precious and limited funds, we must be committed to one overriding principal… put simply “pursue excellence wherever and whenever you find it.” We came to know that it could be found right here at Harvard. What we didn’t know, is that we would be so graciously welcomed to the Harvard Medical School, the Boston Children's Hospital, and Harvard’s CBR Institute for Biomedical Research. This working collaboration flourished for over 30 years and the culmination of this rich partnership was reached just about a year ago.

Vicki and I were invited to meet with Dr. Rosen, Fred Alt, and senior leadership at the Harvard Medical School. They presented to us their vision for a unique, freestanding Immunology Center to be centrally located right here on the Harvard Medical School Campus. It would bring increased attention to the rapidly expanding field of Immunology, and position its importance in our understanding of a variety of diseases. It would focus not only on Primary Immunodeficiencies, but would also foster emerging biomedical opportunities in vaccines, cancer
therapies, stem cell research, bone marrow and organ transplantation, and gene therapy. They envisioned an active and vigorous center for immunologists, graduate faculty, and students working in immunology from across the Harvard Medical School campus, its affiliates and the entire scientific community.

The Immunology Center would welcome investigators from many different overlapping disciplines including Cell Biology, Genetics, and Biochemistry. It would provide new space for teaching, seminars, meeting rooms, an auditorium, and a reception area - encouraging interaction, shared ideas, inspiration and scientific collaboration. It would be home to the Robert A. Good Library, a fitting tribute to a beloved and gifted scientist whom we lost 2 years ago. Bob Good was considered one of the greatest immunologists of the last half-century. His thousands of publications and awards would be archived, creating a library that would graphically bring to life the history of Immunology for young scientists.

Needless to say, we were very impressed with Harvard’s vision. The Foundation and Harvard reached the same conclusion…Immunology had indeed emerged as the key to treatment, prevention, and care of a host of deadly and debilitating diseases, and so we offered our help to advance this project.

Tonight I can report to you that the dream of an immunology center at Harvard is to become a reality. This new building will be named:

The Jeffrey Modell Immunology Center at Harvard Medical School

What a proud moment for Vicki and myself, and how meaningful it is to share this honor with all of you, who can fully understand the importance of this initiative. Thank you all and thank you Harvard for this tremendous honor.

So, the answer to the first question is perhaps best understood in the context of a long history of collaboration that began with Dr. Fred Rosen examining a five year old boy in 1975, culminating in the Jeffrey Modell Immunology Center which will become a reality this coming year.

When I tried to address the second question…“why now?”…I began to think about this very moment in our understanding of science, discovery, genetics, and immunology. If you step back
and take a broad overview of these complex disciplines, I think you will agree that we are
embarking upon an era that will produce spectacular achievements and unprecedented
accomplishments in the near future. It brings to mind another period of extraordinary genius
and output that flourished in classical music at the end of the 18\textsuperscript{th} and beginning of the 19\textsuperscript{th}
century. Over a very short period of time we had Franz Joseph Haydn who wrote over 100
symphonies.

We had Mozart, whose entire life spanned only 35 years, but in those years he wrote over 600
compositions, which he began writing when he was 4. We had Beethoven and Schubert.
Schubert lived for only 31 years but in 1 year alone, he wrote more than 150 compositions. They
came to him so quickly that he had to write them down on napkins in cafes. It’s hard to believe
that Haydn, Mozart, Beethoven and Schubert all lived in Vienna at the same time. And shortly
thereafter, we had Mendelssohn, considered a genius at the age of 16, Chopin whose great works
were produced before he was 19, Franz Liszt, Robert Schumann, Hector Berlioz, Richard
Wagner, Johannes Brahms and more.

These artists expressed their genius in unimaginable ways, far beyond our ability to understand
their world. There is no way to account for this enormous outburst of inspirational expression in
such a short time. It is, quite simply, overwhelming, unimaginable, and miraculous.

I think the case can be made that this is our time of spectacular discovery and genius. For us, it
is in the field of science and medicine, but it is equally miraculous and unimaginable. This time
it is not in Vienna. I would argue that it is right here in Boston.

Having mapped the entire human genome just a few years ago, investigators can now approach
their understanding of diseases on 3 separate levels. First, \textit{Molecular Medicine}...medicine on the
cellular level, giving us greater precision in identifying the genotype to treat the phenotype.
Second, \textit{Genetic Medicine}...medicine on the DNA level that allows physicians to offer patients
more precise prediction. And finally, \textit{Genomic Medicine}...the promise of treatment drawing
upon the mapped human genome, by combining molecular and genetic research into medical
practice.

Think of it! Today, from a single drop of blood, scientists can read our DNA, and look for which
genes are present or missing, intact or broken, making specific diagnoses of disorders that only a
short time ago were unheard of, uncertain, or misunderstood. From that, they have been able to begin to decipher the consequences for a patient’s life, health, and even longevity. And then move on to predictive, preventative, and personalized treatment, shaped and tailored to each patient’s DNA…using massive information at our fingertips to materially impact on patient outcome. It has been characterized by some as Information Based Medicine…the right medication, for the right person, at the right time.

Add to this, the excitement of joining together Micro Array Technology with the laboratory. It is mind boggling. This amazing technology allows us to routinely include millions of DNA probes on a single glass chip the size of a dime.

Just a few months ago, our Foundation entered a 3 way partnership with the National Human Genome Research Institute at the NIH, and Affymetrix, the company that invented and developed the Gene Chip Technology. Vicki and I had a chance to visit with Affymetrix at their California Headquarters, and let me tell you what we saw. We were introduced to a gene chip scanner that generated a computerized array of letters and numbers representing a cluster of genes.

The technicians then scrolled through thousands of markers to find a genetic mutation – the piece of DNA that is scrambled. Using their specialized “cutting edge” technology, they could then unscramble the data, positively identify the defect, and pinpoint its exact location. They could also show us its absence…which was described to us as a “no call” on a particular chromosome…a piece of DNA missing, resulting in a partial deletion of a gene. Amazing new technology, new science, new medicine. And for us, this was something very real, very exciting, and very personal.

Until recently, infants afflicted with Severe Combined Immunodeficiency, “SCID, or “Bubble Boy Disease”, died within the first year of life. It was certain! Today, we can perform newborn screening of diseases such as SCID, with 99% accuracy by screening the DNA in the laboratory. When you add the new microarray technology, we can confirm the findings of that screen and any new mutations within the context of these genes, and then go after the other 1% with the gene chip scanner to reach a definitive diagnosis. With that information in hand, we have a real chance to effectively treat the disease. Here’s how:
Immunity restoring bone marrow transplants for many of these defects now have a better than 90% cure rate. Cure…not a gradual or subtle improvement, which in itself would be a great achievement, but a cure for a child with a fatal disease who can now live a long, healthy, and productive life. Vicki and I have been blessed to have spent time with several of these children who have had transplants, and are living a perfectly normal, happy and healthy life. And beyond these spectacular outcomes, there is clear and overwhelming evidence that it is cost effective to pursue the paradigm of laboratory screening, microarray technology, treatment, and cure.

Listen to what Dr. Richard O'Reilly, Chairmen of Pediatrics and Chief of Transplantation at Memorial Sloan/Kettering in New York said recently in the Wall Street Journal [Quote] “If we catch it early, curing a baby with SCID today is a trivial exercise in medicine costing less than $10,000. However, for babies given transplants, after developing severe infections, the success rate falls to 60%, as these babies often require long and repeat hospitalizations with total bills as high as $1 million.”

So here we are, now able to screen for a life threatening disease with at least 99% accuracy, treat with a 90% cure rate, and offer a cost effective paradigm. It goes on. Scientists have reached critical new understandings of innate and adaptive immunity. These insights are now giving us clues to disease as never before. The excitement centers on the recently discovered existence and crucial role of human proteins called Toll-Like Receptors. The proteins act as molecular sentinels recognizing the presence of a bacteria or virus and rousing the rest of the immune system to respond. Pharmaceutical companies are now developing drugs that activate those sentinels, essentially fooling the body to thinking it’s been affected without actually exposing it to real pathogens. Thus, we are beginning to be able to stimulate the immune system in order to help fight cancer, hepatitis, immunological disorders, and many other diseases.

And what about treatments? Today the Plasma Protein and Biotherapeutics Industry has responded to immunodeficient patients with newer, safer, purer, higher quality immunoglobulins that are effective and have dramatically improved the patients quality of life. And these treatments can be administered either through intravenous infusions on subcutaneous delivery that is expected to be approved by FDA in the next few weeks, giving patients even
greater comfort and wider choice. And, we are just beginning to realize the long awaited promise of gene therapy. Much of the research is being done here at Harvard.

There are already successes curing Immunodeficient children in France, England, Italy and Switzerland covering a wide variety of genetic defects.

We have met with many of these families in these countries and have had an opportunity to embrace their perfectly healthy children. For us it was emotional, overwhelming, unimaginable, and miraculous.

Finally, all of us are aware of the enormous potential of embryonic stem cell research. Stem cells give us the potential for regeneration of tissues, and the prospects to cure a wide range of diseases are virtually unlimited.

The science and new discoveries in stem cell research will move forward relentlessly, regardless of anyone’s political agenda.

I think it is fair to say that medicine is not what scientists expected it to be. The road it has taken was not even constructed when today’s physicians were trained. Routine assumptions are now creating unforeseen conclusions. New medicine. It is here. It is real. It is now.

Two eras, the beginning of the 19\textsuperscript{th} and 21\textsuperscript{st} centuries...separated by 200 years...classical music and scientific discovery...seemingly unrelated disciplines but intimately intertwined and connected by unprecedented accomplishments that profoundly define the period.

All of us here tonight support research, because we know that science and discovery leads to validation and eventually improves clinical outcomes. New discoveries will have impact on the lives of our parents, our children and grandchildren, our brothers, sisters and those yet to be born. Every family will be affected. There is great excitement. There is great hope. There are great challenges. And, there are also great opportunities.

As we enter the most explosive period of scientific discovery ever, each of you individually can impact on advancing science to improve lives. How does one do this?
In my view, there are 3 very practical initiatives well within our control; first, we need an unwavering commitment to research...basic and clinical... from the mouse model through translational research to clinical trials and finally to the bedside. We all know that research is narrowly targeted, but so often, discovery erupts entirely by accident...emerging through serendipity.

Invariably, that unexpected discovery will lead to disease prevention and treatment. Second, we should encourage and support the new technology that can target disease, improve diagnosis, help develop new protocols and personalize treatment. This amazing new tool can be brought to the bedside, and we should encourage its integration in healthcare. Finally, we should commit our support to the most advanced academic medical centers in the world such as the Harvard Medical School, and its affiliates. Here we have access to a community of the best and the brightest, committed to alleviating human suffering caused by disease. Just like Dr. Rosen said to Vicki and myself 30 years ago, “pursue excellence wherever and whenever you find it.”

Make no mistake about it, that excellence resides right here at Harvard, and the time is now.

Tomorrow we will have a chance to learn first hand about some of the fascinating developments taking place right here on this campus. We will learn about revolutionizing the prevention and treatment of disease worldwide, the latest in cancer immunology focusing on ways to stop disease before it begins, and updates from the Harvard Stem Cell Institute.

We have an incredible opportunity to be part of an historic period of discovery, that surely has never been seen before and may never be repeated again. Nothing else in our busy lives can be as gratifying as participating in this journey. When you fund a great institution such as Harvard Medical School, there is no question that it is an act of pure generosity, but it is also an investment in high quality.

If you truly believe in the work of an institution like Harvard, its medical school, its affiliates, a specific department, a division, an investigator, a physician, or a professor, add to that support your commitment and your connection to their work. Advocate for their research. Tell your friends and family and colleagues about their “cutting edge” advances. You may be surprised to know that even members of the U.S. Congress want to know more about these new
scientific developments. After all, it is they that appropriate funds for research at our National Institutes of Health.

This is our moment and we should seize it. We can advance science, accelerate technology, and propel discoveries affecting a wide range of diseases. Now is our time to produce the greatest symphony of all, inspired by new technology, expressed by brilliant investigators, and harmonized by our collective support.

Discovery will flourish, and this elegant symphony will provide hope, enrich lives, create dreams, and together we will rejoice in the most exciting period of scientific discovery ever. Let us go forward. Thank you for joining us tonight on this wonderful occasion celebrating the Council for Harvard Medicine.