Honorable Judge Timothy Dyk, members of the nomination committee, Ladies and Gentlemen:

It is my great honor to be elected recipient of the Inventor of the Year Award 2007 by your esteemed organization. I am even more pleased to accept it because this award recognizes excellence in, and quality of a body of work.

These are the core concepts that form the backbone of my life and my work, first as a chemistry major graduating summa cum laude from National Taiwan University, and then, as the first Asian woman enrolled in the Rockefeller University Ph.D. program in 1973.

Already regarded as an astute organic chemist, my interest was immunology, a field far from the rigor of the physical sciences, based on my understanding from a respected elder that "immunology is the secret weapon of medicine." My first exposure to immunology was at the opening graduate class when we discussed the potential of "synthetic antigen" wherein a small peptide loop was able to mimic immunologically a functional domain of the enzyme Lysozyme.

I intensely followed the literature in the field of "T and B lymphocyte interaction", the elements involved in the generation of immune responses and the structure features required of immunogens, the key ingredients in any vaccine. Based on our understanding of the fundamental principle of immunology, the amenability for incorporating many of the design features into a synthetic peptide immunogen, fully captured my attention.

I spent my first year as a graduate student in the laboratory of 1984 Nobel Laureate Dr. Bruce Merrifield. My goal was to master "Merrifield's solid phase peptide synthesis" as one of the tools to facilitate my future ability to design any peptide based immunogens for biomedical applications.

After mastering peptide synthesis technology, I searched the limited number of protein sequences and 3D structures available in 1975 for

creative designs for actual application. Realizing the time was not ripe for immunogen design capable of directing the immune responses for biomedical application, I joined a human immunology laboratory under the leadership of Professor Henry Kunkel, a pioneer in clinical immunology. This laboratory was also the cradle for structure elucidation of a very important molecule in the immune system, the "antibody," for which his first graduate student, Gerald Edelman received the 1972 Nobel Prize in medicine. It was a challenge to work in a medically oriented environment where the science in immunology was still at the very primitive "cellular" and descriptive levels. Nonetheless, I had the confidence of youth to examine findings and discussions with a rather different view and was intrigued by the opportunities presented.

With a determination to combine immunology and synthetic peptides in biomedical application, I set out on a course that has lasted nearly 30 years since my graduate student days. I did my best in exploring the surface antigens of the lymphocytes by molecularizing them at the biochemical level and confidently marking "molecules" on the surface of the blood cells initially by polyclonal and then by monoclonal antibodies.

Upon my graduation, this cumulative expertise brought me to the field of cancer biology as head of the molecular immunology laboratory at the Memorial Sloan Kettering Cancer Center in the early 80s under the leadership of Dr. Robert A. Good. Cytokines secreted by these immune cells were then added to the list of the functional molecules – more pearls for my exploration.

In the late 70s and early 80s, two areas of biotechnology emerged, the birth of hybridoma technology facilitated the development of an endless number of monoclonal antibodies and the advent in molecular biology allowed rapid cloning, sequencing and production of previously precious immune molecules. The field of immunology has been thoroughly molecularized over these past three decades.

Meanwhile, the molecular structures of pathogenic viruses causing devastating diseases such as AIDS, hepatitis, avian flu, and recently

SARS, to name a few, were being elucidated as soon as the specimens became available. The field of virology exploded as well.

With the advance in bioinformatics, the golden time for molecular design of synthetic peptide based antigens and immunogens for diagnosis, prevention and treatment of many devastating diseases had **at long last** arrived.

My scientific enthusiasm and entrepreneurial spirit carried my family and my UBI colleagues to venture into designing synthetic peptides for immunological applications of future clinical impact. We started United Biomedical Inc. [UBI] in 1985 with a very small initial capital for our venture.

During the past 20 years, we began to build up an arsenal of design tools employing synthetic peptides amenable for immunological applications. The process from discovery, to creation, to proof of efficacy is a very long and expensive one. Until one identifies useful molecular entities and chemical compositions, and then tests the prototype products by extensive functional screening, such explorative exercises are like a fishing expedition. Even venture capitalists would not put their valuable dollars into such a fishing expedition. Who then would shoulder the financial burden to allow a curious mind to mine/design the golden molecules in search for efficacy in any given application during this exploratory stage?

The commercialization of inventions employing the identification of antigenic viral peptides and development of blood screening antibody tests, such as AIDS and hepatitic C virus, provided UBI short term revenues to further support the commercialization of inventions that will lead to long term high impact vaccines and immunotherapeutic products.

I will highlight key points along this journey leading to the discovery of the “UBITh immunogen” and some applications of human and veterinary impact.

UBI **[slide 2]** has become internationally recognized as a leader in the development of site-specific peptide vaccines for immunotherapy and

immunization against infectious and chronic diseases and for veterinary applications.

UBI corporate headquarters is located on Long Island, New York **[slide 2.1 3]**. Additional operational divisions are UBI-Asia in Hsin-Chu, Taiwan [slide 2.2]and UBI-China in Shanghai [slide 2.3]. Together, the divisions of UBI strive for synergy **[slide 3]** and value. Aided by easy access to Information technology, our 350 employee international organization offers an efficient around-the-clock mode of operations

Our new classes of site-directed biologicals have been developed through application of our advanced core technologies **[slide 4]**.

The UBITh® platform technologies in functional antigenics proceed through a series of steps **[slide 5]**

1) **identify** functional antigenic sites on ligand and receptor proteins through molecular modeling and immunological process of site-directed serological validation,

2) **mimic** target sites as synthetic peptide immunogens through molecular design.

3) select peptide target sites by assays such as neutralization, inhibition of histamine release, inhibition of Fc receptor binding, dependent on the specific applcations for functional antigenicity.

4) **amplify** therapeutic immune responses to synthetic peptide immunogens with the key UBITh® technology for immune enhancement.

5) **Test** prototype vaccine in animal model for safety, tolerability, immunogenicity and efficacy.

All of our immunogens are the result of extensive experimentation. We have no simple universal method to impart any target site with optimal immunopotency. Rather, we have a set of useful tools and protocols for design, where each design element of a UBITh immunogen is selected and proven step-by-step by 1) peptide synthesis, 2) immunization, and 3) assays for functional antigenicity .

The UBITh T helper epitopes are a collection of promiscuous sites recognized by T helper cells [slide 6] that were directly derived from highly antigenic pathogens such as measles virus, or hepatitis B virus as shown in this list, or were adapted from these pathogens and designed to hold idealized T helper motifs **[slide 7]** as shown in this slide. Idealized sites include combinatorial UBITh sites having both invariable positions and variable positions. This can accommodate a T helper cell site to a wide range of MHC haplotypes, for broad responsiveness in genetically diverse populations. Our UBITh sites in combination cassettes with functional B cell targets have been effective in eliciting strong antibody responses against **foreign** pathogens and they have also overcome the barrier to achieving **anti-self** responses.

UBITh immunogens **[slide 8]** direct the antibody response almost entirely to the target peptide, i.e.the functional B cell epitopes, when compared to the conventional Toxoid-peptide conjugate. Another advantage, for ease of manufacturing and for quality control is that our UBITh peptide immunogens are chemically defined biologicals.

The UBITh® technology significantly amplifies the therapeutic immune responses to our vaccines and immunotherapeutics. The UBITh®-enhanced peptide immunogens are then formulated with our proprietary vaccine delivery systems into adjuvanted vaccine preparations for rapid responsiveness followed by long-term duration of immune response.

UBI vaccine development efforts [slide 9] are linked to top academic centers worldwide, and have received significant support and validation through grants and collaborations with the U.S. National Institutes of Health (NIH), Food and Drug Administration (FDA), Department of Defense (DOD), the World Health Organization (WHO), and the United States Department of Agriculture (USDA).

The UBI platform technologies have proven equally applicable to animal healthcare and animal husbandry. Our animal health programs focus on the health and productivity of farm animals. We have been developing a line of veterinary products in collaboration with national and international

institutes and organizations, including many listed on this slide. Our veterinary products are entering the market beginning with a swine FMD vaccine in China, the world's largest swine market, to provide an early revenue stream, ahead of our human immunotherapeutics and vaccines.

Our portfolio of veterinary products **includes**

1) FMD Diagnostics, developed in response to the FMD outbreak in Taiwan in 1997 [slide 10] and
2) UBITh FMD Vaccine **for swine, a product that does not require the use of biohazardous viral lysate, [slide 11]**

UBI immunotherapeutics and vaccines for human applications currently in preclinical and clinical development for the following diseases and infections include :

1) UBITh® AD Vaccine for Alzheimer's Disease, targets the amyloid-beta peptide. [slide 12]
2) UBITh® Allergy Vaccine, targets a specific site on IgE that interferes with the release of histamine. [slide 13]
3) UBITh® HIV-gp120 Preventative Vaccine, targets specific sites of the virus itself that interfere with its ability to bind to the CD4 molecule on the host cell [slide 14] and
4) UBITh® HIV-RC Therapeutic Vaccine for HIV infection, targets the HIV receptor on the CD4+ host cell – a member of a new class of HIV entry inhibitor interventions. In 2005, UBI was awarded a five year contract from the NIH to manufacture and development of the first therapeutic vaccine for HIV infection. [slide 15].

There are extensive efficacy and safety data in non-human primates for our UBITh® products for Alzheimer's Disease, Allergy and HIV infection and AIDS, to allow us to enter into human clinical trials.

In conclusion [slide 16], the UBI core technologies have led to the development of a pipeline of site-specific immunotherapeutics and vaccines for chronic and infectious diseases. The UBITh peptide immunogens are

chemically defined entities produced by controlled processes that provide a framework for the GMP-compliant manufacture, expedited entry into clinical trial and commercialization.

In closing [slide 17], I would like to once again thank you for this award, one that I accept as being made not only to me as an inventor, but to my dear UBI colleagues, international collaborators, my distinguished colleagues at Morgan & Finnegan, especially Maria Lin, and my family members who have all supported me wholeheartedly since the beginning of the venture and throughout this long path. They all have assisted me in my pursuit of this quest, not for the glory, but to create out of amino acids, the very sands of life, cost effective and highly efficacious treatment for diseases which ravage the human spirit and body. Thank you.