Opening Statement of Joan S. Brugge, Ph.D.
Chair of the Department of Cell Biology
Harvard Medical School

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First, let me thank Chairman Harkin, ranking member Specter, and members of the committee for this opportunity to report to you some remarkable advances that have occurred in biomedical research because of your strong support for NIH. I hope that I can convey as well my personal excitement for the incredible potential still to be realized in my own field of cancer research. Unfortunately, this enthusiasm is dampened by profound concerns that the four years of flat funding has compromised significantly our ability to fully realize this potential.

When I was a sophomore math major at Northwestern University, my sister was diagnosed with a malignant brain tumor. This event and her subsequent death redirected me towards a career in cancer research. Most of my career has been spent in universities and medical schools. However, for five years before I came to Harvard Medical School, I served as the Scientific Director of a biotechnology company focused on cancer and other diseases. My industry experience significantly shaped my understanding of issues critical to the translation of scientific discoveries into therapies for patients. It taught me among other things, that though the path to treatment can be arduous, today the path between basic discovery and successful drugsalso can be remarkably short.

The early 70's, when I entered cancer research, was a heady time in science. Many of us expected, based in part on the success of the polio vaccine and the Congressionally mandated War on Cancer, that we would soon have a cure for this horrible disease. However, it soon became evident that cancer, unlike polio, is not a single disease with a single cause. There are hundreds of different forms and, indeed, tumors from individual cancer patients carry unique sets of genetic changes. This unexpected complexity – unique to cancer –precluded rapid development of a single vaccine or simple cure.

Though we certainly underestimated the complexity of cancer, the Congressional investment in cancer research is now beginning to pay off. We have made enormous progress in understanding the cause of this disease and its molecular underpinnings. This fundamental information has led to revolutionary approaches to treatment, aimed specifically at the unique vulnerabilities of specific tumors; we now know how to target a tumor's genetic or molecular Achilles' heel. In addition, new imaging modalities and biomarkers provide the potential to identify tumors at early stages when treatments are most effective.

Today, I feel a new confidence that we are poised to make rapid progress in developing effective and less toxic treatments for the myriad different cancers. This confidence is based on initial evidence of success. We now have multiple examples of effective treatments that target the molecular alterations of specific subsets of tumors (such as Tarceva for a subset of lung tumors, Gleevec for chronic myelogenous leukemia, and Tykerb, approved just a week ago for treatment of certain breast cancers). These successes provide a blueprint for the development of treatments for many more types of cancer.

Cancer treatment in the future will involve a molecular diagnosis of each tumor, followed by customized therapies. Already this is being done for breast cancer, in which tumor tissues are

probed for several markers that predict which tumors will respond to specific drugs (like Tykerb, Herceptin, or estrogen antagonists) and which will not. The results are dramatic, adding years to the lives of many patients with the most aggressive forms of breast cancer, and sparing patients of treatments that offer no promise of efficacy. For the first time, we are seeing a decrease in deaths associated with cancer. The tip of the iceberg is visible, underneath lies the foundation for a rapid pace of breakthroughs in cancer detection and treatment based on the research investment in the past.

We cannot afford to stand still—the demographics are against us. There is an impending increase in cancer due to the baby boomers aging into their cancer-prone years, which has been referred to as an impending tsunami. You are all keenly aware of the ramifications for government of Medicare entitlements associated with this surge in cancer. But unlike a real tsunami, which comes unexpectedly with no time for preparation, we are well aware of this impending crisis. And We know that the Congressional investment in basic and cancer-focused research has positioned the cancer research community to make more rapid progress in translating basic discoveries into the diagnosis, treatment, and eventually, prevention of cancer. We owe it to the public to capitalize on these investments; failure to maintain the pace of advancement towards reducing the suffering of cancer is not an option the American people should support or will support. We are all in this together.

This brings me to my profound concerns regarding the state of NIH funding today. Four years of flat funding have had a devastating impact on the trajectory of cancer research. We are losing the momentum and the dedicated careers that were fueled by the previous federal investments. We are now damaging the research infrastructure, and this will certainly delay relief from the cancer burden.

While you have seen the statistics regarding grant awards presented by Dr. Zerhouni and others at NIH and are aware of the inflationary erosion of our buying power, the mere numbers mask the profound effects on the research community. I would like to give you an appreciation for what these numbers mean to the cancer research community, which is emblematic of the whole research enterprise. While the eventual success rate of grants is 20%, this number reflects success of either the first, second, or third submission of a grant. The success rate of the first submissions is now about half of this; thus the vast majority of scientists are subjected to a lapse in funding and the negative consequences of this. Not only can a lapse in funding force labs to cut back, let staff go, and redirect efforts to finding alternative funding and resubmission, it creates an environment of insecurity and anxiety that is anathema to the conduct of creative, innovative exploration. Recovery after a 6-12 month funding gap requires retrenching and retraining of new staff. Many leads will never be followed up. Loss of continuity is one of the most serious problems for a scientist. For new investigators, repeated failure to launch their research program is also demoralizing, and discourages taking original and risky paths.

Researchers at all levels are affected —those beginning their careers and senior investigators with long and sustained track records of major discoveries. For example, multiple colleagues at Harvard Medical School who are leaders in their field with outstanding accomplishments, are suffering lapses in funding or losing grants that received priority scores in the 10-20

percentile range. Peer review is too imprecise to distinguish differences in the quality of the grants in this tight range.

Secondly, in order for the success rate of grants to hit the mandated target number of grants, NIH has resorted to cutting grant size dramatically—at NCI, 24-29% (2006). Aggravating this situation are reductions in buying power due to inflation and the 30 percent increase in mandated stipends for graduate students and postdoctoral fellows over the past seven years (an increase that we applaud). Lab directors are faced with carrying their labs at funding levels equivalent to those 7-10 year years ago, at a time when there is a significant increase in cost of the new technologies required for state-of-the-art research. As a result, almost every grant is severely under-funded for achieving the approved goals, and scientists are starving for resources.

The frustration and anxiety of lab directors is not going unnoticed by trainees, and many young scientists are looking for other venues to exercise their talents, ones where their long training investment will not be jeopardized by this lottery in NIH grant review. This has major implications for the science of tomorrow, since we will not be able to fill in the gaps of this lost generation.

I would like to reiterate the long-term implications of the current research budget shortfall on the economy. Cancer incidence for those 65 and older is 10 times greater than for those under 65, and the death rate is 16 times higher. By 2030, 20% of the U.S. population will be over age 65 compared with 12% in 2004. The cost consequences of this tsunami of baby boomers hitting their cancer-prone years could devastate our economy.

A one percent decrease in cancer mortality is reported to be worth $500 billion to our economy according to an NCI report. Getting these potential new therapies I have outlined to patients will take a significant new investment in translational and clinical research, the cost of which can dwarf the cost of basic research. But without the most promising basic discoveries, we will not be able to improve early stage therapies and more and more translational and clinical endeavors will result in dead ends. We can't be shortsighted.
We recognize the challenges each member of Congress faces in balancing worthy priorities, but I can assure you that from a scientific perspective there is justification for fully supporting basic, translational, and clinical pursuits. Basic science now more than ever fuels the success of effective disease diagnosis, treatment, and prevention in the future.

Through the foresight of the members of this committee and others, the public has generously provided a start toward eradicating one of the scourges of human health. We are in fact in a better place to detect, treat, and potentially, prevent cancer. But just as new therapies based on our cellular and molecular understanding are emerging from our labs, the opportunity to expand them to other types of cancer, to build on them, and to provide for a future of more discoveries has idled. We can't retreat now that the infrastructure is in place and we are mobilized to launch a full force attack on a disease that we now understand. For the sake of the American people, please find a political route to keep progress against cancer at a sustainable pace. The research findings are clear. There is a path to major advances in cancer

detection, diagnosis, therapy, and prevention. Help us get those advances to the public and fulfill the promises of the best in scientific research.

Thank you for your time,