Woodrow Wilson International Center for Scholars
Division of United States Studies

Friends of CANCER RESEARCH

Confronting Cancer Now

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ABOUT FOCR

Friends is a nonprofit organization that raises awareness and provides public education about cancer research in order to accelerate the nation's progress toward prevention and treatment of cancer.

Founded in 1996 to mark the 25th anniversary of the National Cancer Act, *Friends* is a blend of strong voices within the cancer community. *Friends* engages and collaborates with leaders of cancer centers, patient advocacy groups, oncology professional societies, public and private corporations and representatives from the media and entertainment industry on its programs.

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PART 1

A New and Emerging Era of Cancer Research

DR. ANDREW VON ESCHENBACH

Keynote Address

I am here today not only as the Director of the National Cancer Institute but as a cancer survivor. It is therefore important to me, both personally and professionally, that we work together to seize the extraordinary opportunities that will allow us to change the face of cancer.

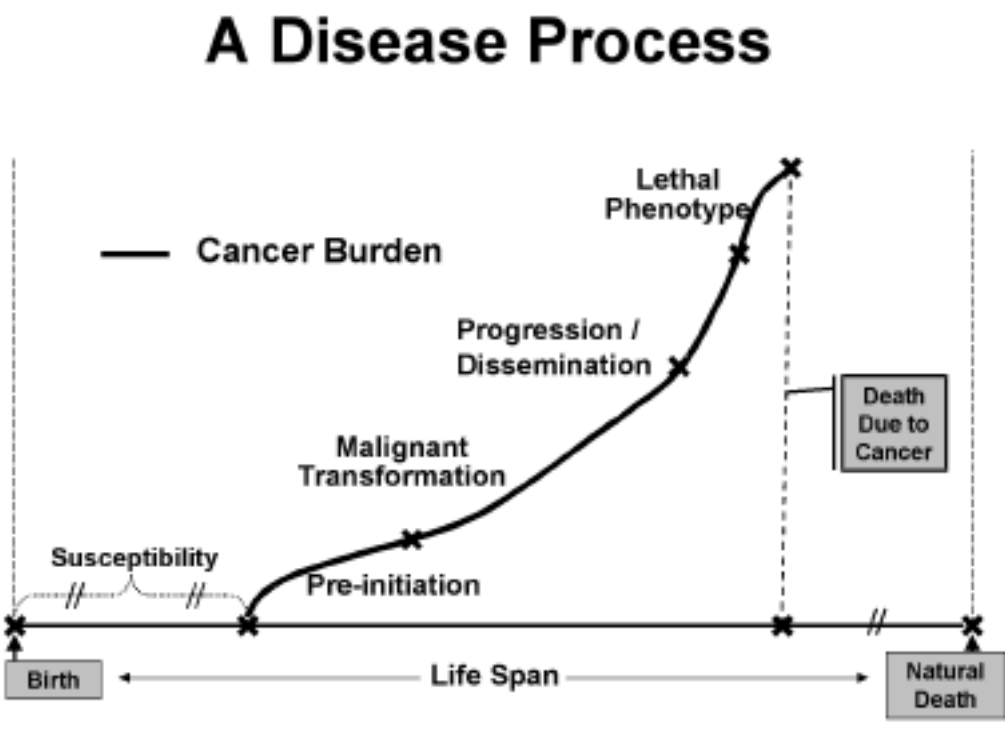
We are at a very special moment in which we can look at the pain and suffering that comes from cancer and see a new opportunity for the future—one that promises the elimination of cancer. That vision is the fulfillment of a promise that this country made in 1971 with the passage of the National Cancer Act.[1] As a nation, we agreed that we would make the conquest of cancer a national crusade. While the problem has proven far more complex and the issues far more difficult than we could have imagined then, that commitment nonetheless set the nation on a trajectory of progress that now finds us able to imagine eliminating the suffering and death that is due to cancer.

We have made progress over the past thirty years, though the journey has been frustrating. Back in 1971 there were only three million cancer survivors in this country. Today there are over nine-and-a-half million cancer survivors, and we expect that number to continue to rise. Nonetheless, one patient in this country dies every minute as a result of cancer. Although we have made progress, we must capitalize on our current opportunity to make even more.

The National Cancer Institute (NCI) has committed itself to continuing this trajectory of progress by setting a challenging goal for ourselves and for the entire research community. We seek to create a future in which no one in this country suffers and dies from cancer. Our aim is to accomplish that goal by the year 2015 and then to share our knowledge with the rest of the world.

This is a feasible goal because biomedical research has led us to a point where we are beginning to understand cancer as a disease *process*. We now understand, as we did not in 1971, that the process of cancer has multiple

FIGURE 1



mechanisms that are vulnerable to our intervention and, ultimately, our control. We now see that the trajectory for the future of cancer research is not linear but exponential. The progress we are making is exploding both in the increase in our understanding and in the tools available to further that understanding. The exponential expansion of scientific knowledge and enabling technologies has been extraordinary during the past five to ten years and will be even more so as we go forward in the next months and years, wedding genomics and proteomics and metabolomics to developments in nanotechnology, information technology and molecular imaging so that we can actually see the biology of cancer. We can think about our ability to conquer cancer in a fundamentally different way than we could just a few years ago. Only the "seek and destroy" paradigm was available in the 1970s when I began my career. Now, however, we can look at a future in which we can target and control cancer, preempting the cancer process on its way to becoming a lethal disease.

Susceptibility to cancer can begin as early as birth, depending on our genes and the environment with which we interact. (Figure 1) One out of every two men and one out of every three women in this country will experience a

malignant transformation in which a cancer cell will develop in the body and begin to grow. But before the cancer is formed, there is a pre-initiation phase that ultimately gives rise to the development of a tumor or a lump, whether it begins in a woman's breast or a man's prostate, that continues to progress locally and then metastasizes or spreads. At that point the cancer has achieved the lethal expression that creates the suffering we associate with the disease.

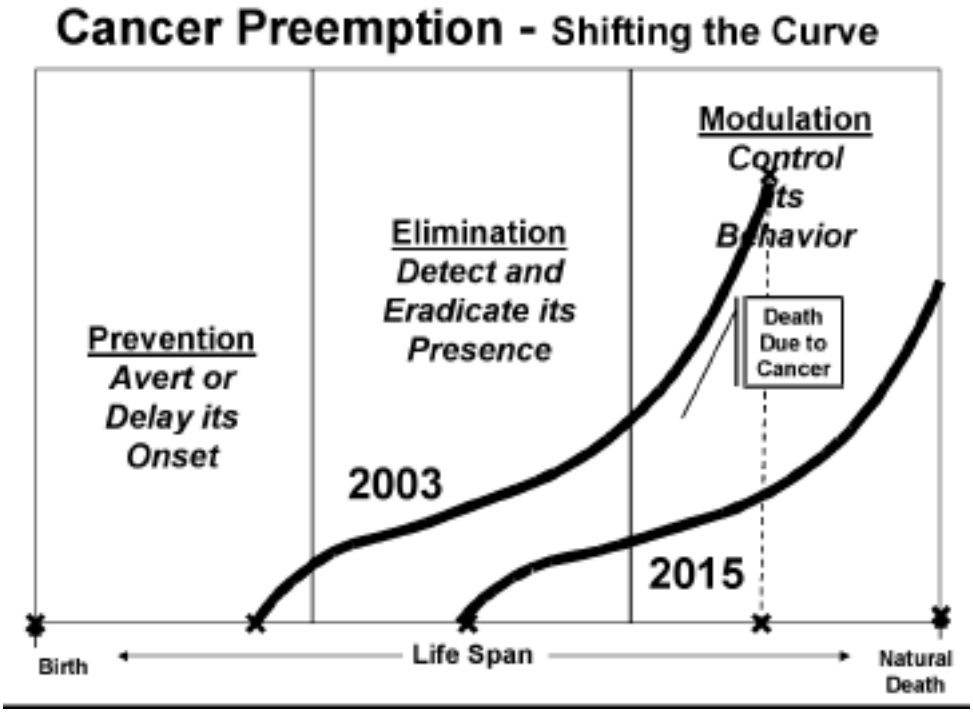
As our scientific knowledge has improved, we have observed this disease process across a period of time and come to recognize all of the associated steps that lead to premature death due to cancer. There is no magic bullet or single intervention that will enable us to disrupt the entire process, but there can and will be strategies that enable us to alter our susceptibility, based on our understanding of which genes make us susceptible to cancer and which other genes make us resistant, and on our knowledge of how those genetic particularities interact with our environment.

We now have multiple strategies to eliminate malignant transformation early in the course of the disease. We are in an era of proteomics and genomics in which we can detect cancers at the very earliest stages of development, at a stage where the weapons we have already developed enable us to cut short the disease process while the cancer is still localized and small. People do not die because they get cancer; if that were the case, I would be twice dead. People die because they develop cancer which then progresses in an uncontrolled manner. Even now when we begin to think about the end stages of cancer—where the process has become metastatic and disseminated—biomedical research and development are enabling us to develop interventions that can alter the behavior of cancer. Our opportunities are multifaceted and require adaptation for specific patients under specific circumstances.

At the National Cancer Institute our strategy is one of preemption and prevention. (Figure 2, next page) What we intend to do is enhance our ability to avert or delay the onset of cancer, shifting the curve for many patients so that they never get cancer at all. For others, we will change the shape of the curve by stopping or eliminating the progression of the disease so that, in some cases, patients with cancer will live out their natural lives rather than die from the disease. For those patients cancer will be a chronic disease, much like diabetes or high blood pressure, and as long as it is controlled we will not see the suffering and death currently associated with cancer.

We will continue to cultivate a portfolio of discovery, development and delivery through fundamental research. We do not yet know enough about cancer, but we are in the process of rapidly expanding our knowledge base and we must not allow the pace to slow.

FIGURE 2



At the same time, we must recognize that the process of discovery is necessary but not sufficient. In addition to deepening our understanding of cancer, we must be certain that those discoveries are translated into the development of new interventions designed for detection, diagnosis and prediction as well as treatment and prevention.

But even that is not sufficient. The new interventions must be applied so that the delivery of treatment will allow us to extract new knowledge and a new understanding of the biology of cancer in patients. This is not a disease of laboratory animals; it is a disease of human beings, and we must be certain that the discovery, development and delivery paradigm is integrated and coordinated so that we continue to learn about the disease.

The NCI is very proud to have a group of talented and dedicated individuals who are committed to furthering this integrative and collaborative effort. We have outlined some key strategic initiatives for the coming year that we believe to be necessary in order to complement the portfolio that already exists. We aim to foster programs that will help us more fully to understand the causes of cancer at the molecular and genetic levels. We will continue to drive the development of more interventions and apply those techniques through an enhanced integrated clinical trial system. In

the area of technology and technology platforms, we will in the coming year make a specific commitment to bioinformatics.

One of the major challenges facing us is the acceleration rate of the development of therapies and preventative agents; right now, the process is too slow, too laborious and too expensive. In order to enhance the speed of development, we need to continue to collaborate and cooperate with the various agencies within the federal government and, more importantly, with the larger research community. Later today Mark McClellan and I will announce an initiative that will bring the Food and Drug Administration (FDA) and the National Cancer Institute together in that effort.

Eliminating the suffering and death due to cancer does seem like a fantasy, a dream, but it can be a reality for tomorrow. Let me give you an example of the way dreams can become realities. Lance Armstrong was born in 1971. He is now a member of the President's Cancer Panel, which grew out of the National Cancer Act that was passed in that same year. I began my career in urologic oncology in the 1970s. If you had told me then that a young man with testicular cancer with metastasis to his lymph nodes, lungs and brain would be alive five years after diagnosis, I would have told you that was a dream. If you had told me that he would not only be alive but that he would be a five-time winner of the Tour de France, I would have told you that was a fantasy. But in fact Lance Armstrong was diagnosed in 1996 with testicular cancer with metastasis to his lymph nodes, lungs and brain, and yet all of us watched him cross the finish line and win the Tour de France for the fifth consecutive year in 2003. Fantasies can become dreams and can be converted into realities. It is the National Cancer Institute's commitment to convert the vision of a world in which no one suffers and dies from cancer into a reality and to do so by 2015.

DR. CHARLES M. BALCH

Those of you in the policy area should be proud that your investment through the years has paid significant dividends in our understanding of the science of oncology. That new science has created major improvements and potential improvements in the diagnosis, treatment and prevention of cancer. Several hundred new drugs and agents are currently being developed, along with sophisticated molecular tests that will enable us to determine which patients should receive the new agents. The new challenge, on which we must all work together, is the delineation of the process for clinical trials of cancer drugs and the subsequent FDA approval necessary to make them available across the country.

DR. NANCY DAVIDSON

I am a medical oncologist and scientist, and I direct the Breast Cancer Research Program at Johns Hopkins University, an academic medical center. I will discuss some of the challenges and barriers that we face during the process of taking a project from the laboratory to the clinic, using as an example our efforts to carry out a pilot trial of an innovative treatment for women with advanced breast cancer that involves a low-dose chemotherapy and a cancer cell vaccine.

We believe that the rationale for this trial is extremely strong. Our success in laboratory models has been reported in the medical literature. We have promising results with this kind of approach in clinical trials with other types of cancers, such as pancreatic cancer. In order to apply this approach to breast cancer, we need people, we need adequate resources, and of course we need regulatory approval. Let us look at each of these in the context of this clinical trial.

First, we need personnel. We need a physician-scientist to lead the trial, a research nurse who is an expert in data collection, a data coordinator, and regulatory specialists. The kind of physician-scientist who can lead this type of project is an endangered species. Leisha Emens, who is leading the trial, is an M.D. and a Ph.D. trained in medical oncology. That represents fifteen years of formal training, which means society must make a huge investment in order to get someone to the point of being able to carry this type of trial forward.

Second, we need resources, and here the greatest need is for funding. The trial will require a patchwork of funding from sources such as the National Institutes of Health, the Department of Defense Breast Cancer Program, the Maryland Cigarette Restitution Fund, various philanthropic organizations and of course our home institution, Johns Hopkins. The manufacture of the cancer cell vaccine in particular will require very specialized support.

Third, we need regulatory approval. The list of groups with which we have interacted to try and activate this trial includes the following:

- The Food and Drug Administration
- NIH, whose approval we need because it is a partner in funding
- The Department of Defense, another partner in funding
- The Recombinant DNA Advisory Committee
- The State of Maryland Institutional Review Board (IRB)

- The Johns Hopkins IRB, which protects patients who participate in clinical trials
- The Johns Hopkins Institutional Biosafety Committee, which is responsible for protecting the health of individuals who will help with the trial and individuals who live in the neighborhood of Johns Hopkins.

This is not a linear process; in fact, all of these entities interact and the discussion goes back and forth among them.

In short, in order for us to bring this trial forward we must have the right people; the right resources, defined very broadly; and an enormous amount of input from regulatory groups. The net result is that we have been working for two years to get this trial activated. We hope that it will be activated soon, but two years from laboratory to clinic is too long to wait for the trial of an idea as good as this one.[2]

DR. MEL SORENSEN

The following is a short discussion of the barriers and the challenges from the view of a large pharmaceutical company. I have been in the pharmaceutical industry for seven years and spent seven years at the National Cancer Institute before that. All the patients I saw at the National Cancer Institute were in Phase I trials; almost all of them are now dead. This is what spurs me every day to try and find new treatments for cancer patients.

Prostate, breast, lung and colorectal cancers account for over 50 percent of cancer cases. The fatality rates in the SEER (Surveillance, Epidemiology, and End Results) data for 2003 indicate that a great deal of work remains to be done, even though huge progress has been made in diagnosing and treating some tumors such as breast cancer. (Figure 1, next page)

There are an additional million cases of non-invasive skin cancer. One in four of us will die from cancer unless we achieve the research successes and treatment goals currently being sought by the NCI and other researchers.

In the United States, the five-year survival rate is about 62 percent for all cancers and there are nine million cancer survivors. The cost of cancer to the economy is huge, and the financial expense is of course in addition to the personal pain and suffering that the disease produces. Finally, as Figure 2 illustrates, cancer treatment, compared to cancer prevention, is only the tip of the iceberg.

FIGURE 1

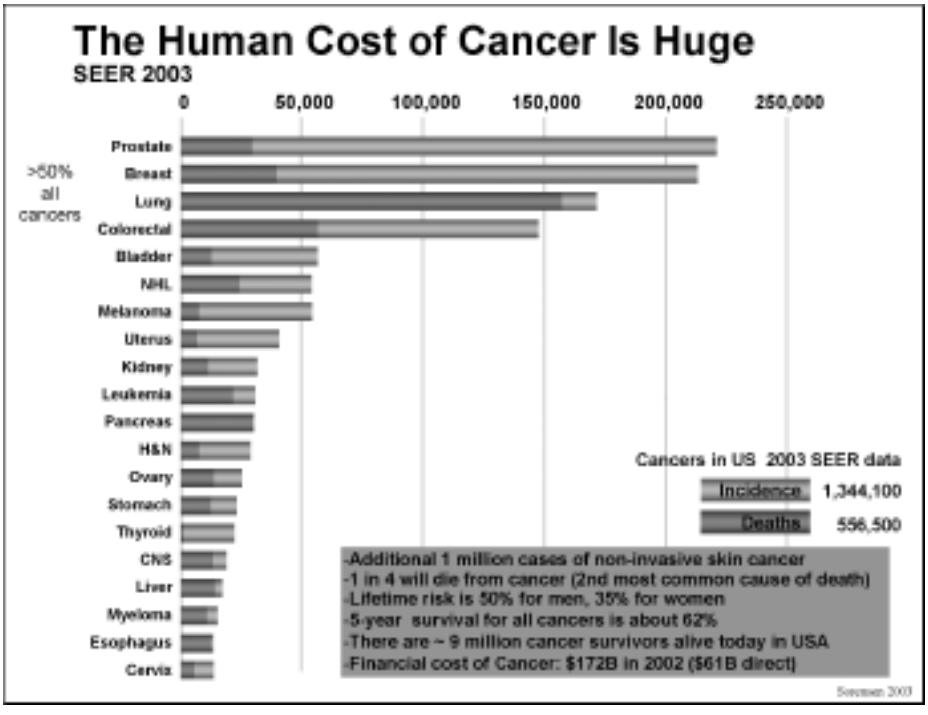


FIGURE 2

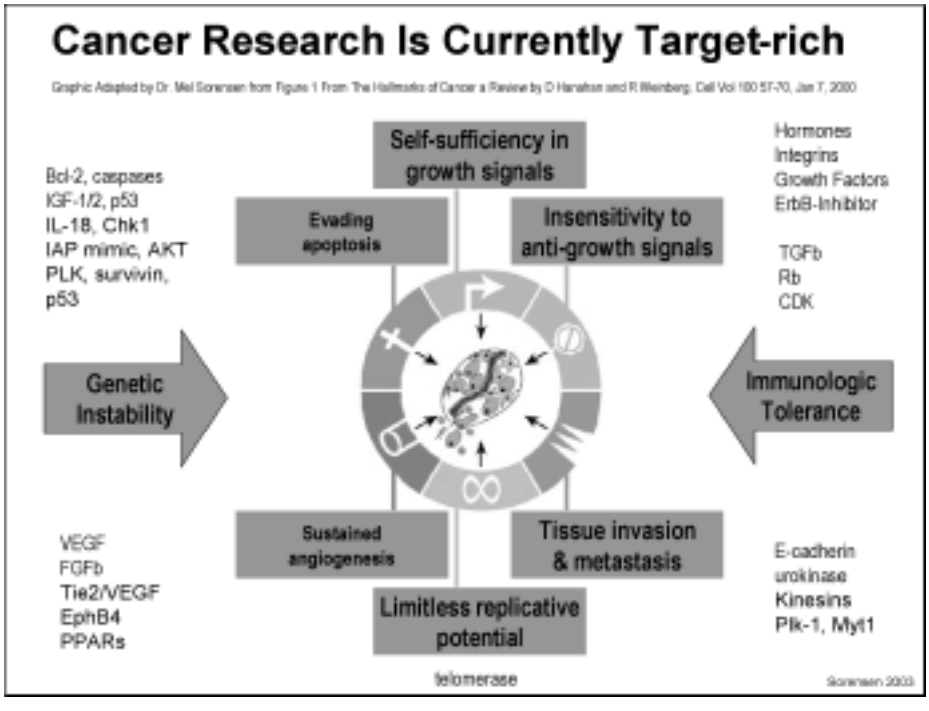
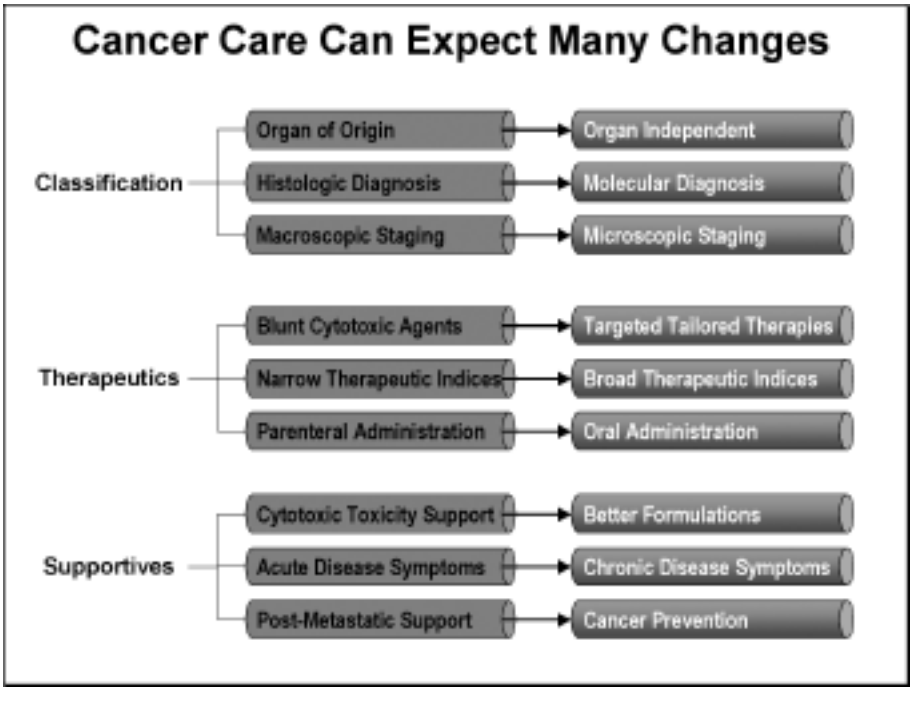


Figure 2 is a diagram originally published in 2000 by Drs. Douglas Hanahan and Robert Weinberg. I have added the factors of genetic instability and immunologic tolerance. The diagram indicates that during the last ten or fifteen years we have been able to identify the mechanisms of cancer in great detail. That is extremely encouraging and justifies a sense of optimism that we are on the cusp of a curve of great improvements, assuming that we continue to deliver new treatments at the same speed. We can therefore hope for and expect many changes in cancer care.

The pharmaceutical industry survives by encouraging people to invest in very long-term endeavors. While the mission of a politician, who has to answer to voters, may be to make the world better and safer, our mission is to make new medicines for cancer patients so they can live longer and healthier lives. But we also have to answer to our shareholders—and that includes everybody who has a pension and who decides to put money into companies that are willing to perform risky and expensive cancer research.

FIGURE 3



Cancer care is changing. We are moving from a characterization of tumors by organ of origin to an organ-independent diagnosis, from an histologic diagnosis to a molecular diagnosis, and from macroscopic staging (with a CAT scan) to microscopic staging (e.g., a PET scan). We are shift-

ing cancer medicines from blunt cytotoxic agents to targeted tailored therapies; in some cases, to individual patient-specific therapies. (Figure 3) We are moving from drugs that are highly toxic and have narrow therapeutic indices to medicines with broader therapeutic indices, meaning that the drugs are more tolerable. We are also going from intravenous or parenteral administration to oral administration. We are witnessing a shift from supportive care to better formulations, treating chronic disease symptoms and getting into cancer prevention.

Drug development must also change in order to keep pace with these scientific advances. (Figure 4) We must move from a single cytotoxic agent that shrinks a tumor to looking at pathways that we will have to inhibit in parallel in order to obtain any benefit. We also have to shift from looking at cytoreductive response endpoints to seeking cytostatic endpoints in which the tumor does not shrink but also does not grow.

All of this presents challenges, one of which is that developing medicines is an extremely risky endeavor. The analysis in Figure 5, adapted from work by Henry Grobowski and his colleagues at Duke University, shows that only three out of ten marketed drugs actually produce revenues that match or exceed the average costs of research and development (R&D).

FIGURE 4

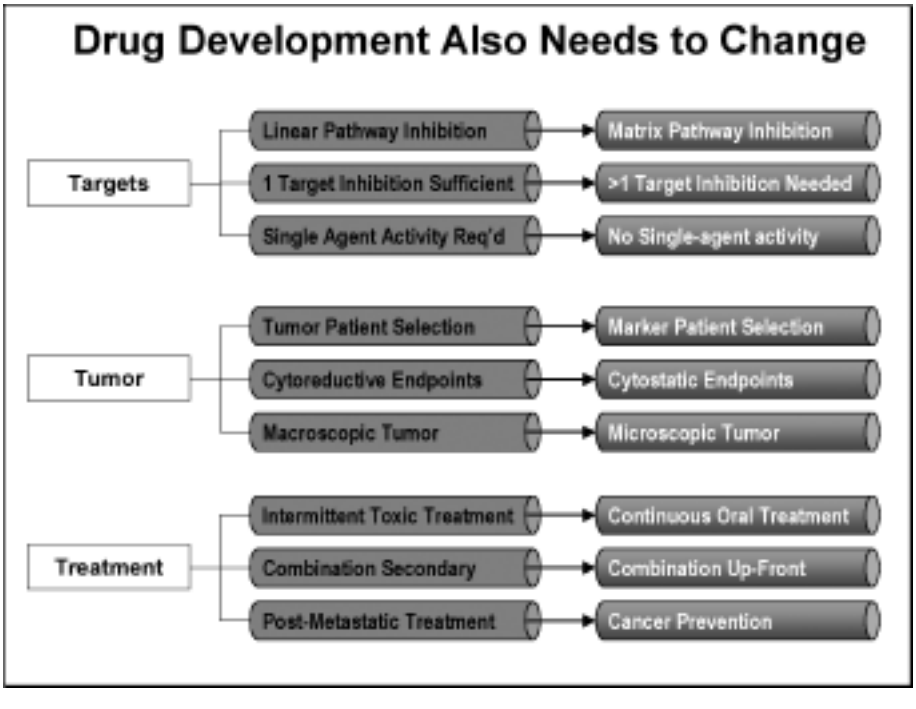


FIGURE 5

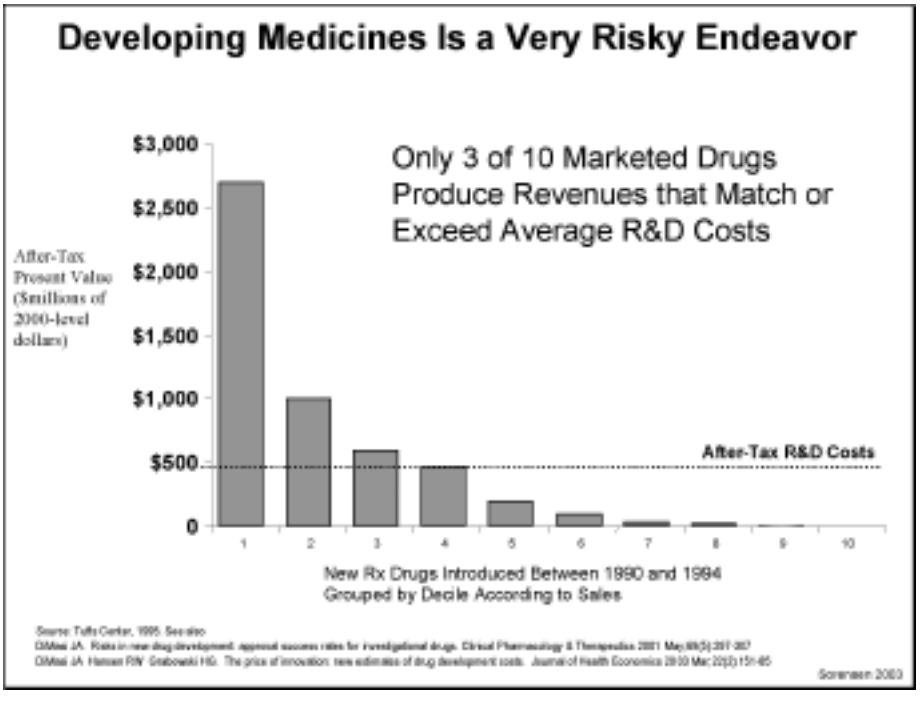
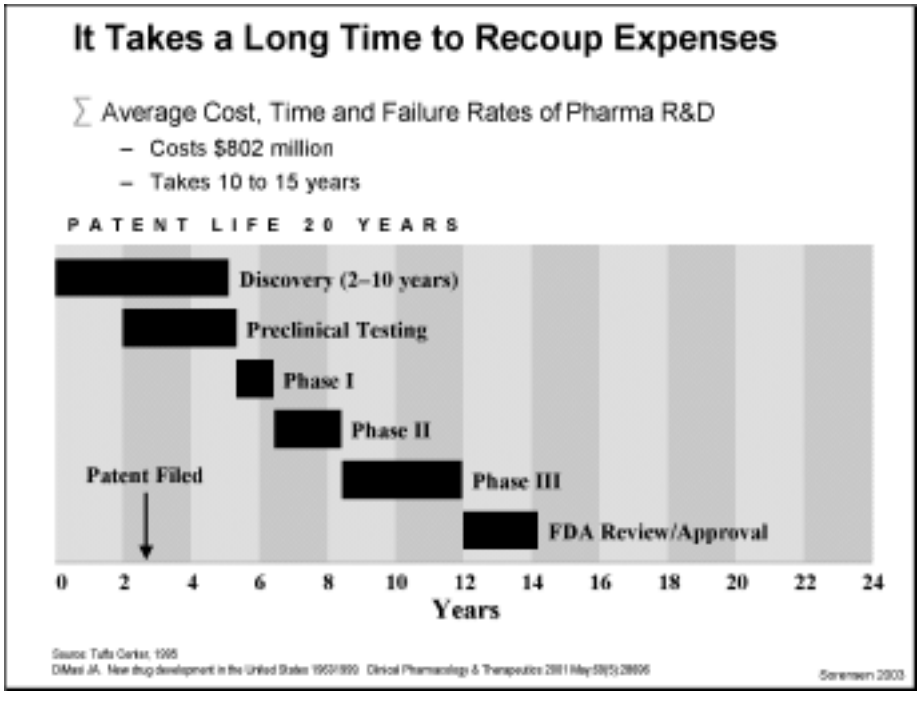


FIGURE 6



As Figure 6 indicates, it takes a very long time to recoup expenses. The numbers might be different for subsets of drugs for the treatment of cancer but Grobowski et al. calculated the average cost of expenses recouped at $802 million. The process takes ten to fifteen years and only one in 5,000 molecules will result in a drug.

While the cost of research and development for pharmaceuticals has risen from $2 billion in 1980 to $30 billion in 2000, the number of new drug approvals has not gone up proportionally. After seeing these charts, how many people would move their pension funds from other investments into the pharmaceutical industry?

FIGURE 7

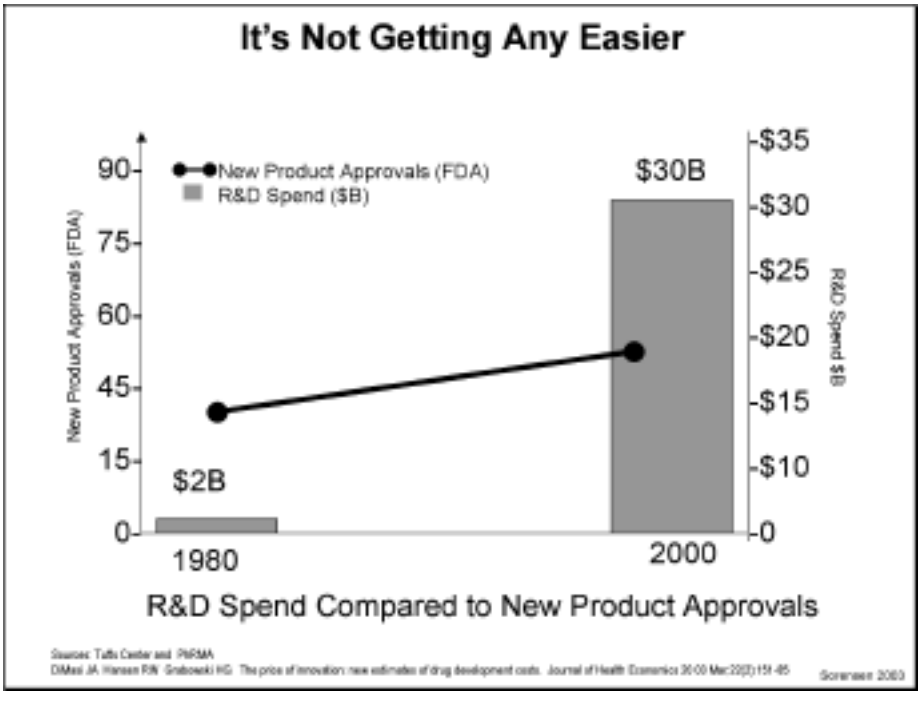


Figure 7 does contain hope, however, because it shows how much industry money has been put into the discovery side of research. As there is frequently a significant lag in the stages of discovery, development and delivery of compounds, Figure 7 indicates that the effort has been made and there are many encouraging signs that it will translate into valuable new medicines. There are industry concerns that make it difficult to prioritize cancer over cardiovascular disease or other diseases in making decisions about where invest. The incidence and lethality of cancer do not translate into prevalence. Cardiovascular disease affects 62 million

Americans; mental illness affects 50 million. Cancer is not a single disease. There are hundreds of distinct disease settings, stages and pathologies, and the number is only likely to increase as new targets and markers are discovered. We could have 5,000 types of cancers as we are better able to define these targets!

Cancer therapeutics are highly segmented and involve surgery, radiotherapy, chemotherapy, immunotherapy, biologics, and so on. Cancer investigational agents even compete with each other. The Dana-Farber organization has said this year that there are 395 new agents in development for cancer, as compared with only 123 for cardiovascular disease and 18 for stroke.

One of the key hurdles to overcome, if we are to have the greatest possible impact on furthering support for cancer research, is to find predictive surrogates akin to cholesterol for cardiovascular disease. There may now be a move to find better markers. The purpose would be to reduce the time to develop drugs, and of course the key factor in this area is increasing the speed and reducing the risk involved in finding new medicines.

As we look forward to possible solutions, we find many ways of encouraging more cancer research:

1. Reduce the burdens on participation in clinical trials. Only five percent of cancer patients now enroll in clinical trials.
2. Encourage closer regulatory collaboration to get the regulators ahead of the cancer research curve.
3. Think outside the pathologic categories and learn to see cancers, such as breast cancer, as several diseases.
4. Be open to approvals of combinations of investigational agents, and to regulatory recognition of standard as well as approved therapies.
5. Pursue more creative accelerated approval approaches, such as exploratory surrogates, Special Protocol Assessments and fast-track designation. Some of these solutions are already being utilized.
6. Become better informed about the unintended consequences of one's actions—regulatory, political, and so on. A difficult and uncertain regulatory path can delay or derail many interesting scientific explorations.

JUDGE RALPH M. BURNETT

The problem I want to address is the recruitment of patients for clinical trials, which directly affects the rapidity of cancer research. Cancer research can be viewed as a table with four legs. One leg is funding; the

second, public and private collaboration between industry and research; and the third, the FDA, which is now doing a magnificent job of bringing more research to faster review. The fourth leg is accrual of patients into clinical trials. It is the most elastic of the components in this equation and the tighter it is pulled, the faster the trials go; the more patients who are involved, the faster and quicker and more efficient the trials are. These are key to bringing translational research to the bedside quickly.

The accrual of patients has been and remains an enormous problem. Traditionally the patient seeks out his or her oncologist for advice as to what clinical trials to pursue, but most oncologists' knowledge of specifics about trials is limited. Information about clinical trials is available on the Internet, but it is extremely sparse and usually consists only of the name of the clinical trial, the inclusions, the exclusions, and the names of the medicine and of the person or institution to contact.

In short, the potential patient population suffers from a serious lack of knowledge and, like other wise consumers, when cancer patients know nothing about what they are buying, they don't buy. They need knowledge, and there has been an unfortunate lack of knowledge about crossover provisions and about what has happened in the past. There are prior statistical empirical studies which could be provided to patients but are not now made available. Patients who have undergone clinical trials can volunteer to discuss their participation with potential clinical trial enrollees. This would in no way violate ethics or the 1996 Health Insurance Portability and Accountability Act (HIPAA)[3] or other laws.

A great effort must be made to increase elasticity so that more patients are enrolled. That would shorten Dr. von Eschenbach's projection considerably, by perhaps as much as two to five years, but it will require an effort that has not yet been made. There is a challenge in the tension between what physicians loyal to the scientific method want and the more rapidly available knowledge that we advocates want.

An additional challenge is the gap between the information available to those with the affluence and education necessary to find out about clinical trials and those without such resources. Those who have the skills resolve the problem by doing what I call reverse engineering. They don't use http://www.clinicaltrials.gov at first, although they eventually arrive at that site. They find out which organizations, which foundations, and which nonprofits are involved in research and where they are meeting, and then they either obtain direct access to the meetings or access the groups through CDs or the Internet to find out what is hot in the field. When I want the best information about potential treatments I go not to my doc-

tor but to my best stock investment Internet site. I use the information generated by pharmaceutical companies and stockbrokers and then eventually I make my way to http://www.clinicaltrials.gov. It is only, however, perhaps one percent of one percent of the entire population that has the ability to do that. This is an unfair system that needs to be changed as soon as possible.

QUESTION AND ANSWER SESSION

QUESTION: The biggest problem is getting new information to physicians in small to medium-sized communities. Even specialists, for example, really do not know the difference between genetic signatures and the tumor aggression associated with radiation-induced and sporadic papillary thyroid cancer—the differences between a radiation-induced thyroid tumor and a sporadic thyroid tumor.

DR. VON ESCHENBACH: The very important issue that you have identified is that there is not one kind of cancer. Cancer is a family of diseases and there are significant differences even among thyroid or breast or prostate cancers. The National Cancer Institute is funding research in Chernobyl, looking at the effects of radiation and beginning to try to sort out those differences. We need to look at tumors at their genetic level and again in terms of the kinds of proteins that they produce, and we must determine and influence how they might behave in different people. We must then work with the pharmaceutical and biotechnology industries to develop the unique and specific interventions for a particular tumor in a particular person. Clinical trials give us access to tissue in tumors from patients and enable us to create bio-repositories where we can look at tissue from different patients with different diseases and do exact profiling. We are aggressively and actively funding such research.

QUESTION: Dr. Davidson, you talked about the two-year process for developing this clinical trial. Is there any way to collaborate with pharmaceutical companies and other entities to shorten this process without compromising safety? Is there anything that advocates can do to help with the process?

DR. DAVIDSON: Two years and counting certainly is too long. We might be able to address some of the issues involved. One is the chain of regulatory agencies with which we have to work. Surely there is a way that we can speed that process along and still protect all the stakeholders—the patients who are going to participate and the individuals who will be involved in their care.

We must also develop an approach and a product that will interest a large pharmaceutical group. We must get to the point where a larger drug company will want to take this on. It would be nice to shorten that process and get a go or no-go decision.

DR. VON ESCHENBACH: There is no single solution for the problem of shortening the time line, and we must attack it in a variety of ways. Commissioner McClellan and I will describe today one particular way we plan to do that by analyzing how we share information.

Patients and survivors are important in this effort. We need to move beyond our current idea of a clinical trial, which is that we give you a drug, get a response, and the trial is over. We need to follow patients long after the endpoint of the clinical trial so that we can look for toxicity and for side effects that may not show up for a long period of time. We need the patient to be an active participant in this process and commit himself or herself to the follow-up process and to sharing information. We ended the trial of Letrozole, a drug that prevents breast cancer recurrences in women who have finished Tamoxifen, earlier than expected, because we discovered it had a very definite benefit in stopping recurrences. But we need to continue to monitor those patients to watch for late-term side effects.

DR. SORENSEN: In the pharmaceutical industry, we would probably abandon any protocol at any site where approval took two years to get the trial open. Our target would be to open a trial in three or at most six months. It is a huge endeavor that requires the collaboration of a great many people. I think the only solutions to these obstacles are systems solutions. A centralized IRB is not common in oncology. Nancy, I was quite shocked to hear about the number of committees you had to go through at Hopkins. That is frightening for a company like GlaxoSmithKline that knows it cannot wait that long to get a study done. Among the things that can be done are informational improvements and agreements between different fiefdoms within academia. It is intolerable to wait two years for a good idea to be tested.

JUDGE BURNETT: Advocates will continue to knock on doors and tell people that they want things done. That is important because it adds urgency to the issue. Advocates can ask for more parallelism: trial aspects that can be performed not sequentially but in parallel. Industry does that now.

DR. BALCH: Part of the equation is the HIPAA regulations that involve the IRBs in the process of obtaining informed consent and protecting the privacy of individuals. What impact do these regulations have on the pace of accrual to clinical trials?

DR. DAVIDSON: The impact is huge. In the example I discussed, we not only had the trial to treat the patients but we had to have a separate trial approved by the IRB so that we could follow the patients over the long term in order to get the sort of toxicity information Dr. von Eschenbach mentioned. That is another enormous regulatory burden. The HIPAA has a positive effect on the important job of patient protection but it certainly has made it difficult to move our research forward in an efficient way. It has, for example, hamstrung our ability to use archived pathology specimens that have been in the banks for several decades and that might be appropriate for tissue-based research. A great deal of bureaucratic maneuvering is now necessary before we can access that kind of very valuable specimen.

QUESTION: I'd like to ask about some of the silos in academia that prevent cooperation and acceleration of some of the research data, particularly in regard to the NIH's Clinical Research Center program. There are tremendous opportunities for doing Phase I clinical trials but little opportunity for funding them and little help in getting through the IRBs and red tape. Do you have ideas or are you interacting with the Clinical Research Center program to try to accelerate some of these clinical Phase I ideas?

DR. VON ESCHENBACH: We do need to find ways to work across the various barriers. One of our strategic initiatives this year entails looking at the entire clinical trials system. The NIH is also examining ways to reengineer clinical research so that we can meet the opportunities and the challenges and provide the absolute best state-of-the-art care for patients while protecting them from undue risk. We are asking what kind of information technology systems will enable us not only to gather data about the efficacy of the drug but to continue monitoring its safety, while addressing the standards that the HIPAA has established for protecting patients and their confidentiality.

This is a systems problem, not a matter of a single intervention. We will be looking at trial design. You mentioned Phase I, where there are trials to determine what, if any, side effects occur at what dosage. One of our highest priorities for the coming year is to determine how we can accelerate Phase I to the point where we are in Phase III and Phase IV trials, in which we provide the intervention to large populations.

DR. BALCH: Dr. Davidson, how do you overcome such silos in a large and complex organization such as Johns Hopkins?

DR. DAVIDSON: I don't know that I have any special solutions. Cancer researchers are very dedicated, very interested in moving these innovative

ideas forward and testing them, and we have learned to get around some of the silos. We hope they will come down, but in the meantime we are learning to work within them.

DR. VON ESCHENBACH: One of the ways to get people to work outside the silos is to give them the tools. We are unfolding an initiative called the cancer Biomedical Informatics Grid, or caBIG (http://caBIG.nci.nih.gov). We are creating a common information technology platform, similar to the nation's electrical grid, that researchers can access. All of our comprehensives and NCI-designated cancer centers around the country will then be able to communicate with each other rapidly and effectively, which is one way to eliminate some of the barriers you describe.

DR. BALCH: Dr. Sorensen, what kinds of barriers are there in the pharmaceutical industry regarding new agents that may have similar mechanisms but that are being developed by different companies or that might need to be used in combination?

DR. SORENSEN: The problem of silos exists not only between companies but also within companies. Any very large organization has such obstacles; it takes very efficient management and very good information systems to keep them to a minimum. In academia, the silos are often made worse by the workload of the oncologists. You could get all the relevant committees to give you approval in a single day if they all met on that day. Now, however, they are all spread out, with their members having to spend perhaps half of their time on patient care. One of the biggest problems is getting people in the same room at the same time to make what is actually a very straightforward decision.

In industry we have the same problem, with many people doing many different things and not communicating well with each other. Our lab scientists are going one way, while we on the clinical trial side go another. It is important that we interact continuously. It is really a matter of information systems. I think industry does it better. We have fewer silos because a company that has to meet a bottom line has a lower tolerance for them, while an academic center or the NCI finds them much easier to tolerate. Venues such as this, however, are very helpful at breaking them down.

DR. BALCH: There are a number of forums in the advocacy community, such as the Cancer Leadership Council, the National Dialogue on Cancer, and the Alliance for Childhood Cancers, which are coming together and becoming an important force for conveying information and informing the public about clinical trials. Judge Burnett, would you like to add anything about the silo effects from the perspective of the advocacy community?

JUDGE BURNETT: The tension and the rivalry between various support groups and research foundations within a particular subset of disease has been too great over the years. This is a problem that needs to be resolved. I know this from my own years as chairman of the National Prostate Cancer Coalition, experiencing fights with my friends at Us Too and Man to Man and a few other organizations. We are currently trying to resolve that problem, furthering collaboration to ensure that we make more progress.

QUESTION: Are there any initiatives for partnering with third-party payers or insurance carriers to support accrual to clinical trials and improved payments for clinical trials?

DR. VON ESCHENBACH: Mark Clanton, the NCI Deputy Director for Cancer Care and Delivery Systems, has a masters degree in public health. He is a pediatrician, and he is also first national vice president of the national board of the American Cancer Society. The most important part of his background, however, is that he learned about Blue Cross and Blue Shield while practicing in Texas. He is helping us develop exactly the kind of partnerships and collaborations that you mention. We have to find ways to take the benefits of discovery and development and give people access to them.

We all share the same bottom line, which is that we must eliminate the suffering and deaths due to cancer. That will require a systems approach. We have to learn a lot more about delivery, particularly from the people who are coping with, responsible for, and paying for that delivery.

DR. BALCH: Will Medicare pay for the standard care costs of patients on clinical trials?

DR. VON ESCHENBACH: Yes.

DR. DAVIDSON: Maryland requires that all patients in the state be eligible for this sort of coverage through their third-party payers.

DR. VON ESCHENBACH: California is another such state. There are state laws that require private insurers to pay for the standard care costs of patients who contribute to clinical trials and there is good evidence that the cost of the care of patients who enroll in those clinical trials does not go up. In fact, the cost remains the same but the quality and consistency of care and the contribution to knowledge increases.

JUDGE BURNETT: That is a good example of the type of collaboration I was talking about earlier. Most states with statutes that govern payment for clinical trials by private insurers have enacted them because of the good lobbying work of organizations like Us Too and Man to Man and various breast cancer organizations. Other states need to be brought to that level of care standard.

QUESTION: What impact will flat funding have at the NCI, the NIH and the cancer centers?

DR. VON ESCHENBACH: We are going to face the challenge of redeploying our resources so as to take advantage of the opportunities before us. We must find ways to leverage those dollars by finding partners and collaborators that can cost-share in the strategic investments we must make.

Another very important deputy at the NCI is Dr. Anna Barker, Deputy Director for Strategic Scientific Initiatives, among whose areas of responsibility is the examination of our discovery-to-development transition, whether in the biotechnology industry or the device industry. She is analyzing how we can more effectively accelerate the transition and suggesting the kind of public/private partnerships we need to create to make that rapid acceleration possible.

DR. BALCH: Dr. Davidson, perhaps you can comment on what difference the investment of accelerated funding in the last few years has made in the research community and what dangers there might be in flat funding.

DR. DAVIDSON: Johns Hopkins has invested extensively. We have new facilities that reflect our state-of-the-art science and we have recruited some of those physician-scientists I mentioned—the people in whom we as a society have invested an enormous amount. Without additional funding, however, we are not going to be able to make use of their good ideas and their brainpower. That makes me fearful about the future of our field.

QUESTION: My question is directed primarily to Drs. von Eschenbach and Sorensen. Approximately 35 to 40 children are diagnosed with cancer every day—the equivalent of one or two classrooms. Cancer is the number one medical killer of children and the age-adjusted incidence of cancer actually peaks at the young years: approximately 15 to 20 of those 35 – 40 children will die.

Only about 50 percent of the children who are diagnosed with cancer are enrolled in clinical trials. When there are agents available they are subscribed almost immediately. Clearly, there are more patients who could enroll in trials than there are agents available. In the last decade or so, however, about 50 new products have been approved for adult cancer therapy but there has been only one approved for children. What do you see as the barriers there?

DR. VON ESCHENBACH: One aspect of your question concerns the way we integrate the scientific discoveries we are making across the spectrum of tumors, whether they are adult tumors or pediatric tumors. From the mechanistic point of view, many of these tumors may share a common denominator, so we can begin to see them not in the categories of pedi-

atric or adult but in the category of mechanism. One of the major challenges in pediatric cancer is of course brain tumors, and one strategy is to apply to pediatric diseases the lessons we learn from adult disease.

The other thing that you point out is the issue of life span. We have to pay much more attention to survivorship issues, especially among pediatric oncology patients, because many of them are experiencing long-term side effects such as cognitive dysfunction and learning disorders as a result of the successful elimination of their cancers.

Our portfolio, again, is meant to be balanced. We need to learn more about the biology of pediatric cancers and to develop even more effective interventions, which requires capitalizing on our growing understanding of cancer's mechanisms. At the same time, we need to develop the long-term ability to monitor and impact the quality of survivorship. I spoke of eliminating both suffering and death; both are important.

DR. SORENSEN: The safety hurdle is higher in pediatric trials, which probably leads us to go first into the adult population, particularly the population with advanced disease. That may create a problem with some medicines with new mechanisms of action, as they may work in different populations or only in the early stages.

We have a great deal to learn from the pediatric world. You mentioned that 50 percent of children are in clinical trials; I think it's 50–60 percent of all children with cancer. Why is it only 5 percent in adults? My guess is that it has something to do with the highly segmented organization of pediatric oncology in the United States. I would strongly recommend further intensive study of this discrepancy. In addition, there is now only one major cooperative group, Children's Oncology Group, for pediatrics, but there are many for adult cancer patients.

Finally, a word about the attitude of the pharmaceutical industry toward pediatric trials. We want to get drugs approved as quickly as possible—we must, in order to stay in the business of research and development. We have several pediatric oncology programs right now with several different agents. One in particular probably will work only in either a very limited pediatric population or a very limited adult population, so it is an economically unfavorable situation, but we are working on it nonetheless.

DR. BALCH: Judge Burnett, you made an important point about patients and their families having access to information about their cancer and about where they can go to get into clinical trials. From your perspective, where are the barriers? What do you recommend that patients or their families or the public do to gain access to information about their cancer or about how they can participate in clinical trials?

JUDGE BURNETT: The best source of information about where to find clinical trials continues to be your physician. There is now more collaboration between physicians from the Specialized Program of Research Excellence (SPORE), through meetings run by various nonprofit foundations such as CaP Cure, and more sharing of information about clinical trials. Nevertheless, the barriers remain great, and the knowledge remains limited.

Today, there are more ongoing clinical trials with more treatments than ever in the history of this disease. When I was diagnosed in 1996 there were 20 prostate cancer clinical trials; that number is now approaching 200. Every patient knows that there is the possibility for help somewhere in those clinical trials and there is tremendous frustration from not being able to obtain the necessary information. The expectations are huge, and the industry simply is not meeting them.

I spoke earlier about going to a clinical trial site on the Web. There is literally nothing there. All you get is the name of the disease, the name of the product, the inclusions, the exclusions, and a phone number. When you call it, you are invited to go see a physician who gives you the same limited information and says, "Take it or leave it." I went through such a process with a woman who had ovarian cancer and who said, "No, I'm not putting up with this, I'm leaving." She could have benefited from that trial. There has to be a major overhaul so that we can get the information to the patients.

DR. BALCH: Dr. von Eschenbach, what do you recommend to the public and to patients for access to information about clinical trials in cancer?

DR. VON ESCHENBACH: There is a variety of points of access. There is http://www.cancer.gov and 1-800-4-CANCER for information from the National Cancer Institute. The American Society of Clinical Oncology (ASCO) has a very active program. ASCO has been at the forefront of the effort to help us understand the different perspectives on cancer and cancer trials. Patients are not the means to an end in a clinical trial, and we must always conduct those clinical trials in a way that protects the patients' interest. When the American people understand and recognize that bond of trust, as well as the fact that there is an entirely new and hopeful paradigm in oncology, they will change not only what they think about cancer but what they feel about cancer. I believe that when we reach both their minds and their hearts about the future of oncology, their willingness to participate in clinical trials will increase dramatically.

DR. BALCH: I'll just mention that ASCO has a very extensive website at http://www.peoplelivingwithcancer.org which has sections about clinical trials and links to other groups with clinical trials information such as TrialCheck (http://www.trialcheck.org).

NOTES

1. National Cancer Act of 1971 (P.L. 92–218).
2. The trial discussed by Dr. Davidson was approved after the conference and the first patient was enrolled in early 2004, under the care of lead investigator Dr. Leisha Emens. As of March 2004, the patient was receiving vaccine alone and doing well, and other patients were moving through the enrollment process.
3. Health Insurance Portability and Accountability Act of 1996 (P.L. 104–191).

PART II

Joint Announcement by the Food and Drug Administration and the National Cancer Institute

DR. ANDREW VON ESCHENBACH

We have spoken about our tremendous progress in understanding cancer and in our ability to translate that knowledge into the development of effective interventions. Our delivery of the interventions to patients, so that we improve their lives and eliminate the suffering and death due to diseases like cancer, is equally critical.

Collaboration is key to that effort. There has been a long-standing partnership between the Food and Drug Administration and the National Cancer Institute and the National Institutes of Health. Almost immediately after his confirmation as director of the Food and Drug Administration, Mark McClellan and I agreed that we would work together to further enhance and intensify the close working relationship between the NCI and the FDA. To that end, we created a joint task force that began in May 2003 to identify ways to streamline our discovery and approval of such interventions. Our joint task force has been addressing issues such as training in joint appointment programs, bioinformatics platforms, the use of markers of clinical benefit and the ways in which we can improve our procedures.

Today we want to share with you two of those initiatives and report on some of the progress we have made.

We have begun a bioinformatics initiative in which the NCI and the FDA will jointly create critical trial management software and informatics platforms that will link cancer researchers to the FDA so as to share data and reduce the time it takes for new drugs to be reviewed and approved for clinical trials. This new information platform will become an integral part of the NCI's cancer Bioinformatics Grid, or caBIG, which is being developed to integrate and coordinate all of our NCI-designated cancer centers across the country. By creating a common bioinformatics platform to share data among our academic cancer centers, and then integrating and coordinating that platform with the FDA, we will facilitate the rapid acceleration of discovery and approval of interventions that will be applied for the benefit of patients.

DR. MARK MCCLELLAN

As Dr. von Eschenbach reported, we are moving rapidly toward a more effective modern technology-based information system for collecting and analyzing data from clinical trials. This is a significant improvement over the paper submissions of applications to the FDA that were the norm not so long ago. The use of electronic data enables us to review more rapidly, integrate information from different kinds of studies more effectively, and learn more at a lower cost and in less time about which treatments are most effective. This is an important step and a key element in our new collaboration with the NCI.

My hope is that this model can be applied more widely in developing medical technologies. There is no better place to start than cancer care, in large part because of the work that the NCI has done to implement a system for cancer bioinformatics platforms that we can use as a model for other areas of disease treatment development.

As Dr. von Eschenbach mentioned, there is a second element to today's announcement: a new joint fellowship program that will be cosponsored by the NCI and the FDA. The goal of this fellowship program is to make training opportunities available for NCI researchers at the FDA, in order to give them greater familiarity with the practical questions and issues that must be addressed in assessing the safety and effectiveness of new treatments. As a result of this effort, the NCI staff will become more familiar with our part in the process for developing new cancer treatments.

As with so much of our collaboration with the NCI, this will be a two-way street. The interaction allows us to learn more about the cutting edge technologies and ideas that are being developed in the laboratory and that are being tested in clinical trials, so that we can improve the process for demonstrating that new treatments are safe and effective. The result is that the entire process will be better informed and more up-to-date, enhancing our ability to deliver safe and effective treatments to cancer patients.

QUESTION AND ANSWER SESSION

QUESTION: Can you give us an idea of how this agreement might work to reduce the time of the new drug approval process? Will it be months or years?

DR. MCCLELLAN: Potentially, at least months. This is a large effort that we hope will make the entire process of submission to the FDA and the entire clinical testing process electronic. Electronic data holds the potential

for making studies less expensive by obviating the need for paper records to be transcribed once when they go to a product developer and then again when they are sent to the FDA.

It also will help us learn more about entire categories of cancer treatments across different kinds of studies. Right now, there are many studies of similar kinds of treatment with similar mechanisms of action but, as the data from each of these studies are not stored and developed in the same way, it is very difficult to identify patterns. When it comes to steps like using new genomic information to identify potential toxicities in certain kinds of patients or identifying trends of differences and effects in particular subgroups of patients—minority patients, elderly patients and the like—we have to use too much guess work because these data systems are not in an electronic form that enables us to pull the findings together. This electronic system will make the process more efficient and less costly. It will enhance our ability to identify the treatments that are safe and effective in particular kinds of patients.

DR. VON ESCHENBACH: Our commitment is not simply to an initiative but to a relationship in which we will not only initiate projects like the information platform and the training program, but one in which we will constantly monitor and improve those processes so as to shorten the time line. As Commissioner McClellan indicated, we expect to make immediate incremental gains but we will not stop there. We expect, for example, that a joint training program will begin to develop a cadre of individuals who can be a resource for the entire community.

PART III

The Food and Drug Administration and Drug Development

DR. MARK MCCLELLAN

Keynote Address

The FDA and the NCI are working together on electronic submissions of investigational new drug applications to the FDA, in order to help us move further down the road to an electronic system for clinical trials information. This is important for doctors and drug developers, but it is most important for patients. We are making sure that we use the best modern technologies to learn as much as possible about the risks and benefits of new treatments, to make clinical trials more accessible, to get them done faster, and to make the information they generate more widely available and more useful as we continue our quest to identify the treatments that are most effective in individual patients.

Enabling the development of safe and effective new medical technologies is a fundamental part of the FDA's core mission, which is to protect and advance the health of the public. Today, that mission involves some unprecedented challenges, principal among which is our responsibility for ensuring the safety and effectiveness of increasingly sophisticated products. As people involved in cancer care know extremely well, the products available today are far better, more numerous, and more complex than they were just a decade ago.

The opportunities for improving patient care have increased. So, however, have the potential problems in delivering that care that result from the growing complexity, medical interactions, and higher survival rates, which in turn lead to patients who are living with more and more chronic conditions. We believe there is more that we can do to respond to these challenges and that developing better information systems, as we are doing through this collaboration with the NCI, is a very important step.

Much is being done in the fight against cancer, but there is of course even more that needs to be done. Cancer continues to devastate too many lives. This year we expect to diagnose more than 1.2 million new cases in the United States and experience well over 500,000 cancer deaths. If cur-

rent trends continue, this country can expect a doubling of the number of people diagnosed with cancer by 2050.

I don't think it needs to be this way. I think there are reasons for us to be optimistic that we can achieve a different, healthier future. Thanks to the dedication of scientists and patients and advocates, we are translating new biological insights into cancer care in a way that has begun to make a real difference in the lives of patients. Today the NCI reports that in the last ten years there has been an average annual decline in cancer mortality of more than one percent. That means that someone diagnosed with cancer in 2003 has a 60 percent chance of being alive in five years, compared with only a 40 percent chance in the 1940s.

At the FDA, we are working with the NCI to achieve this goal of reducing the burden and harm caused by cancer. The breakthroughs in genomics and proteomics and other fields of molecular biology have dramatically extended our understanding of what is required to turn a normal cell into a cancer cell. This holds potentially important insights for individualized and effective treatments for the many different types of cancer. There are now about 400 cancer drugs under development and, as there are more genomic investigational new drug applications (INDs) being filed with the FDA than ever before, it appears that progress toward highly targeted drugs may increase significantly in the years ahead. INDs are filed when a product begins clinical testing, to ensure that the methods being used and the ethical oversight are appropriate. The electronic submission steps that Dr. von Eschenbach and I announced are so important because we are currently seeing so many more applications. We want the process of clinical testing to be as smooth and as low-cost as possible while providing appropriate protection for patients and appropriate study design.

If these increases in the applications for INDs are any indication, the drugs that are likely to result in successful FDA applications are going to be more targeted and less toxic than ever before. While there are many promising new features of these treatments in development, however, they generally have not yet been proven to be safe and effective. The process of going from a good idea in the lab to a safe, effective and reliable treatment in patients is long and difficult. Part of the problem is that the process for developing drugs has become more costly and uncertain. By some estimates, it has doubled in cost over the last ten years without becoming any more predictable. Fewer than one in two of the drugs that enter Phase III testing, the last step before an application comes to the FDA, actually results in an application.[1]

It should therefore be no surprise that while we have seen some improvements in cancer care, we have not yet seen dramatic breakthroughs, and yet the cost of treating cancer continues to rise. The NIH estimates that the overall cost of cancer was about $157 billion in 2001, which is larger than the gross domestic product of all but a few nations on earth. According to the consulting firm of McKinsey & Company, the cancer bill worldwide could triple by 2010, but the most important cost that cancer patients face is the immeasurable suffering associated with this debilitating and often fatal disease. For medical progress to continue, especially in an era of greater concern than ever about the cost of health care, we need to find better, less expensive, and more predictable ways to develop new treatments, reduce costs and improve access to better care.

We at the FDA cannot do this alone, but we in government do have an important supporting role to play in helping patients obtain the best and most effective care possible. We need to create a healthful environment for medical care: one that encourages and facilitates continued progress in medical treatment and in which doctors and patients have the best scientific information possible and are supported in using it effectively as they make individual patient-care decisions.

In order to make sure that our regulatory processes are as efficient and up-to-date as possible as we address some of these challenges, the FDA announced a major new medical technology development initiative earlier this year. Over the next few months we will be talking about taking further steps to improve the process of bringing new medical products through the entire development sequence, improving and speeding the critical path that all new products must follow in order to turn sound science into good medicine. That involves working closely with the NCI.

One question, for example, is whether we could be using different endpoints such as biomarkers in clinical trials to prove that new treatments are safe and effective. Richard Pazdur, the director of the FDA's Division of Oncology Drug Products, has suggested that a delay in the progression of cancer may be a more useful clinical endpoint than survival benefit in some cancer trials, and that in some cases this may allow us to learn more about a drug benefit sooner. Another question is whether there are alternative clinical trial designs that could help us learn about the benefits and safety of new drugs faster than we do now with conventional trial design methods.

There is not enough work being done to answer such practical applied questions so we, in collaboration with the NCI, the American Society of Clinical Oncologists (ASCO) and other expert organizations in cancer

care, have begun addressing these problems. The FDA is currently holding a meeting on the review and development of better evidence and endpoints for colon cancer treatment. We will publish new guidelines for demonstrating the safety and effectiveness of colon cancer drugs in clinical trials, based on expert input from the NCI and product developers.

All of these efforts in the areas of colon cancer and other cancers will focus on obtaining the best and latest science to guide our thinking in deciding whether products are safe and effective.

Information technology systems like the ones announced today will play a critical role in speeding up the development and lowering the cost of new drug discoveries. They will also provide some additional opportunities to promote safety even in those cancer patients with serious illnesses, who too often suffer substantial side effects and complications from treatment.

As our mission at the FDA becomes more challenging, it is important for us to make use of such information systems. The complexity of medicine is increasing and the opportunities for drug interaction and other problems pose new risks. We can have an extremely effective system for monitoring the ways in which new drugs are used to spot potential side effects more quickly and for providing appropriate warnings to doctors and patients, but we must do a better job of learning about new drugs without having to start a large and expensive clinical trial from scratch every time a new question arises about a drug's safety or effectiveness.

There has been a growing recognition by the government that information technology can play a critical role in achieving these goals, as Secretary of Health and Human Services Tommy Thompson's E-Health initiatives indicate.[2] There is a similar growing recognition throughout our healthcare systems, and we see more physicians and hospitals and healthcare organizations becoming paperless. There has not, however, been sufficient recognition of what this means for the areas of greatest concern to the FDA's mission: assuring the safety and effectiveness of medical products. We can do this by developing and filing information from clinical trials with the FDA electronically, or utilizing electronic prescribing systems to get the right prescription to the right patient at a lower cost, or using new technological systems for real-time monitoring of real-world practices for signals that treatments either may be causing potentially serious side effects or may be having important patient benefits that do not appear until after they have been approved. All of this can have a fundamental impact on helping us to fulfill our mission more effectively.

The Medicare legislation pending before Congress is also relevant to this issue.[3] We need improvements in the safety and quality of healthcare

delivery, not just in making drug coverage more readily available and drug prices lower, but in creating better and faster systems for monitoring the risks and benefits of new medical products and communicating that information more effectively to healthcare practitioners and patients.

That is why the system that we will implement in partnership with the NCI is an important step in creating a far better information technology infrastructure. It will enable us to review applications faster and, hopefully, get treatments out to patients more quickly, more predictably and at a lower cost. This is part of the larger effort, the Cancer Biomedical Informatics Grid, that Dr. von Eschenbach mentioned earlier.

In order to make the best use of the information generated during clinical trials, we must also get the information into electronic form so that it can easily be queried, evaluated and archived. The NCI is being especially helpful as we move toward this electronic system. Thanks to its leadership, the universe of cancer doctors and the NCI's cancer cooperative groups are already among the most technologically proficient healthcare practitioners in the country. Bottlenecks in clinical trials can occur because of delays in transmitting information from the bedside to drug developers and then to the FDA, but in many cases, doctors working in the NCI's groups are now entering this information electronically. Their experience demonstrates that electronic systems shorten and improve the process of making information available to us and to the FDA reviewers.

This will enable some significant cost reductions. For example, instead of researchers having to go through patient medical files to piece together fragments of information scribbled on paper records every time new questions arise about a new treatment, they will be able to access the information electronically and answer queries in a matter of minutes on the basis of a larger volume of patient data.

Finally, we believe that the NCI can be extremely helpful to us even after the approval decisions based on these electronic studies are completed, when we still have the critical responsibility of monitoring the drugs for any important safety problems that may emerge and for more evidence about effectiveness. Many new cancer drugs are approved under accelerated programs based on their effects on a surrogate marker such as the ability to shrink a tumor. It is therefore important that we continue to test these drugs after they are approved in order to confirm that benefits observed in the clinical development process actually translate into meaningful gains in comfort and life expectancy for patients.

Dr. von Eschenbach and I referred to joint fellowships that will be cosponsored by the NCI and the FDA. This information-sharing at the

level of expert scientists at the FDA and at the NCI will be in addition to the development of better data systems and will also help us work together more effectively to make sure the latest and best science guides all of our efforts to promote the development of safe and effective treatments.

I would also like to mention the important role that people can play through the daily decisions that have an effect on their health. The ability to cure disease is only part of what makes modern medicine so remarkable, but we now know that it may not be the most important part and that disease prevention is even more significant in reducing costs and improving lives. It is better for us to focus more on keeping people from getting sick at all. While some scientists have been making headlines with dramatic improvements in surgical interventions and new breakthrough treatments for people with cancer at advanced stages, others have been working to prevent these diseases from occurring or from progressing in the first place. There is good scientific evidence that our everyday lifestyle decisions can reduce our chances of developing cancer and many other chronic diseases. This includes not only decisions about whether or not to smoke and whether or not to exercise but, importantly, decisions about our diet.

Research shows, for example, that diets rich in fresh fruits and vegetables can actually cut the risks of developing some forms of cancer as well as a number of other chronic illnesses. We are partnering with the NCI and other healthcare groups to develop a system that will give consumers accurate and up-to-date science-based information about the smart diet choices and other steps that they can take to reduce their risks of developing cancer. This is an important complement to our work on improving medical treatments. As genomic information improves, we must not only create incentives for patients to understand how important their daily decisions are to the risk of cancer; we must also create incentives for food producers to innovate in developing foods that both taste good and help people reduce the chance of developing certain diseases. The combination of these efforts—the medical product innovations side, the encouragement of consumers to become better informed consumers about their daily choices, the encouragement of more innovation in food production to help people lead better lives—can all converge in a truly effective integrated system for preventing cancers from developing and progressing.

There are still more things that we can do to get the best care possible for Americans who have cancer or who are at risk of developing cancer. We need to focus special efforts on the increasing number of people who are facing medical costs beyond their means. We need to create a healthful

environment for providing high quality care. But I am encouraged by the stage we have reached, thanks to these collaborative efforts with the NCI and to other new FDA initiatives.

I practiced internal medicine for a number of years and have seen too many people die from cancer. The story of cancer today still has too many tragic losses. I believe, however, that the stubborn efforts of scientists, product developers, and leaders of government and non-governmental organizations will make a difference and that together we will develop real changes in cancer treatment and prevention.

DR. BALCH: Dr. McClellan, as a member of the cancer community and as a representative of ASCO's more than 15,000 oncologists across America, I want to salute you and Dr. von Eschenbach for the formal collaborations that you have announced today and for the many informal collaborations that exist as well. It is reassuring to know that these two vitally important executive branch agencies are working together. It gives those of us in the cancer community real hope that these advances will be made in an accelerated, cost effective and, most importantly, safe fashion. How can those of us in the cancer advocacy groups assembled here best support you in your efforts?

DR. MCCLELLAN: I appreciate what you are doing already. We would be grateful for your continued input through the many public forums at the FDA, to make sure we have standards for demonstrating the safety and effectiveness and reliability of new cancer treatments. As I mentioned, in the weeks ahead we will have additional announcements about where we see critical gaps in the process of turning good ideas into safe and effective treatments. As the NIH has recognized in its clinical roadmap, there is a huge drop-off between ideas that seem to show promise in the lab or in animals or in *in vitro* studies or, increasingly, in encyclical studies, and getting those treatments to human patients in an effective way. There are additional gaps as we move from early stage clinical testing to confirming the safety and effectiveness of the treatments and then on to the stage of demonstrating reliable manufacturing and taking other practical steps to assure the effective use of products. These are often not the kinds of high-level questions that win people Nobel Prizes but they are the problems that have to be solved in order to get treatments to patients in a cost effective way. We and the NCI will be talking more about what we can do to help identify and address problems in the critical path from good research ideas to safe and effective treatments. We look forward to continuing to collaborate with all of you in the effort to pave this path for the development of new cancer treatments.

DR. SUSAN DESMOND-HELLMANN

I would like to emphasize both the sense of urgency that a cancer drug developer who works in collaboration with the FDA needs to feel as we continue our quest to make new products available to patients and my optimism about our future in cancer, due to the level of innovation taking place today.

As a recent cover of *Time* magazine indicated, 2003 is the 50th anniversary of the discovery of DNA.[4] It is remarkable to think about what is being done today as a result of this and subsequent discoveries. This year also marks the 27th anniversary of Genentech, the first biotech company founded on the basis of another innovation: recombinant DNA technology.

Something else that is happening in the year 2003 is our continued tapping into new mechanisms for understanding the way that cancer cells divide, spread and attack human beings. In 1971, Judah Folkman published a theory about an angiogenic switch, a potential key mechanism that allowed a small tumor of one to two millimeters to grow and to spread.[5] Many of us, on hearing about this hypothesis, were fascinated by the idea that perhaps we could starve a tumor to death—perhaps we could turn off a basic biologic mechanism.

In 1989, Dr. Napoleone Ferrara and others cloned an expressed VEGF (vascular endothelial growth factor) and for the first time gave us a potential target.[6] We sought to control the angiogenic switch so that it became a disadvantage rather than an advantage for cancer cells. In May 2003, a study showed for the first time that Avastin, an anti-VEGF anti-angiogenic drug, could extend survival.[7] There is a substantial difference in median survival of patients when an anti-angiogenic is added to standard chemotherapy in a rigorous well-controlled randomized trial. When I was in practice in oncology, treating patients with 5-fluorouracil, a drug that had been available for 25 years, we could expect patients to live with metastatic colon cancer for about ten to 12 months. Recently, new chemotherapy discoveries have extended that to about 15 months. We are now seeking to extend that survival further, to 20 months.

These are the kinds of steps that we take in clinical research and the kinds of incremental gains that we make. One might well argue that we have to do better than keep people alive for a few months longer, and I would certainly agree, but moving from ten to 12 months to what is now approaching two years is a big step forward. We treat patients earlier in their disease today, with the goal of making that tumor disappear permanently.

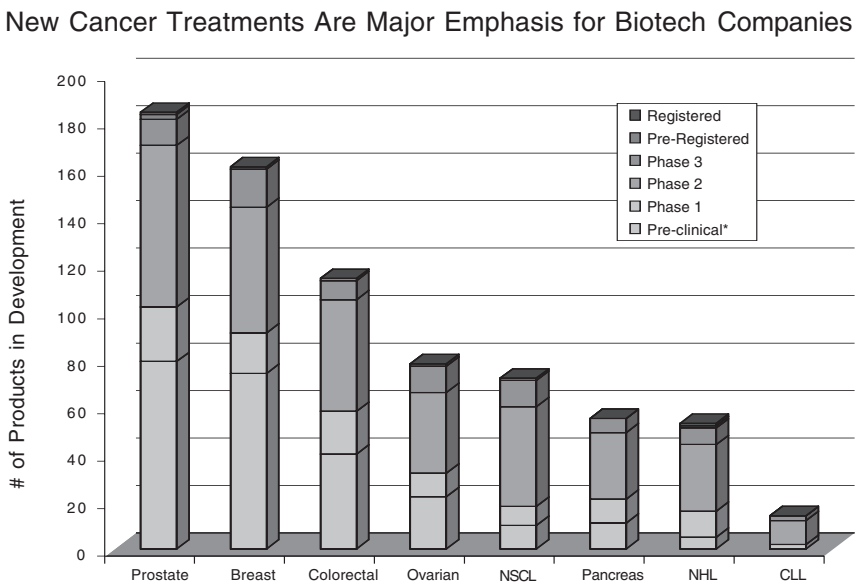
So what is exciting in biotechnology today? Genomics has been mentioned several times. Our ability to identify novel disease-specific antigens using

micro-array analysis and other new technologies is greater than it has ever been. There are biology-based discoveries in many areas. For example, there are what we call the HER2neu family receptors, which are used as new targets for molecular-based therapies for breast cancer and other major cancers. I mentioned angiogenesis inhibitors and other means of inducing apoptosis (cell death). Can we use the new biology to trick the cancer cell into committing suicide? We have used antibodies in biotechnology as a tool with which to accelerate our ability to construct molecules that resemble the native antibodies present in all humans and to aim them at these new tumor antigens.

This list is not all-inclusive but it gives some sense of the pace of new targeted therapy development today. In 1997 Rituxin, a monoclonal antibody for the treatment of lymphoma, became the first monoclonal antibody ever approved in the United States as a targeted therapy for cancer. Since then the pace of development has increased dramatically. We are now seeing not only monoclonal antibodies like Rituxin and Herceptin, but also monoclonal antibodies that are linked either to a toxin, like Mylotarg, or to radiotherapy, like Zevalin. We are also seeing drugs like Gleevec or IRESSA, targeted therapies that are made using small molecule technology and, more recently, Velcade, one of the first new therapies for multiple myeloma in many years.

Figure 1 shows the new cancer treatments that are under study by biotechnology companies today. The value of patient advocacy is clear

FIGURE 1

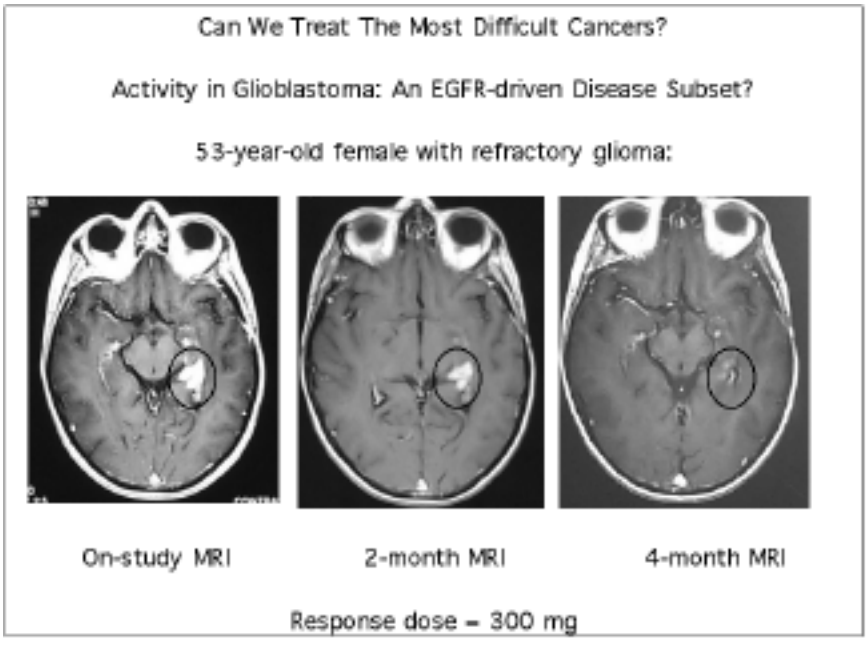


from looking at the prostate cancer number. Until recently, prostate cancer was a seriously understudied condition, but both prostate and breast cancer research have benefited significantly from patients pushing for new therapies for these very common forms of cancer. In fact, all forms of malignancy are now important topics of study for biotechnology companies.

We have made great inroads in treating many cancers. Today we can cure testicular cancer and leukemias. Can we start to treat the most difficult cancers, such as pancreatic or brain cancer? That is one challenge. Another is diagnosing the disease and selecting treatment based on the molecular signature of a specific tumor rather than the body part or the organ involved. Yet another challenge is making cancer a chronic disease and treating it with maintenance therapy. We were never able to use the term "maintenance therapy" in oncology before, as it was ridiculous to think that a patient could be maintained on the kinds of toxic therapy we used in the past. There is also the challenge of combining targeted therapies to improve patient benefit.

The case of brain cancer presents an example of the way we attempt to treat the most difficult cancers with a targeted therapy. We know that the most common genetic abnormality in brain cancer is Epidermal Growth Factor Receptor (EGFR) mutations. Figure 2 shows a patient treated with

FIGURE 2



Tarceva, a new EGFR blocker. The white area with the circle around it is the tumor, which is disappearing after four months of treatment. This treatment reflects a novel way of thinking about treating brain cancer by taking advantage of the new genetic knowledge and of targeted therapy.

As science creates new strategies, we face yet other challenges. Will we have patient numbers adequate for all the necessary trials? Can we overcome the barriers to participation? Will privacy legislation make tissue acquisition impossible? Can we balance the very important protections for patients with the need for numerous studies on tumor tissue? Will the regulatory process be transparent, efficient and predictable?

Patients, caregivers and drug developers are absolutely critical in enabling us to make new drugs. Will we find surrogates we can trust for patient benefit? Tumor shrinkage has disappointed us as a surrogate; perhaps stalling the time during which the tumor recurs can be an important surrogate for patient benefit. Will the early promise of combination therapy be fulfilled? Will we treat patients with combination therapy that does not include chemotherapy?

There is one final measure of success to our ability to answer all of these questions: patients who are living despite cancer.

DR. GERARD KENNEALEY

From the point of view of the large pharmaceutical companies such as AstraZeneca, GlaxoSmithKline and Genentech, there are pluses and minuses associated with dealing with the Food and Drug Administration in the twenty-first century.

There is an excellent relationship between the pharmaceutical industry and the Division of Oncology Drug Products at the FDA headed by Dr. Richard Pazdur. The interaction has always been collegial. The review cycle in the last few years has been extremely rapid. While we do not always agree with the suggestions or indeed the demands that come from the Oncology Division, we know that they are based on a sound scientific basis.

When I joined AstraZeneca's predecessor company in 1987, my first task was to submit a drug for the treatment of advanced prostrate cancer. It took 27 months for that drug to be approved. Drugs such as Gleevec, which represents a significant advance in the treatment of cancer, can now be approved in as little as eleven weeks. Most of the compounds submitted to the FDA today are approved in less than one year. That is a significant change for which the Oncology Division deserves full credit.

There is also a rapid response in the so-called fast track setting where the FDA contracts with a pharmaceutical company and constructs a collegial working relationship designed to get the drug to market as rapidly as possible. We saw this with our compound IRESSA and, as mentioned, Novartis experienced this with Gleevec.

The drug for advanced prostate cancer that took two years to be approved back in 1987 had already been approved in Europe. Now the reverse is the case. Drugs such as IRESSA are not yet approved in Europe.[8] Faslodex, a drug for women with advanced breast cancer that we have been marketing in the United States for a year probably will not be approved by the European Union until the first quarter of 2004.[9] As that indicates, while the situation is still not perfect, the Oncology Division has made significant improvements in its procedures over the past few years.

At the same time, however, there are some minuses. There is no single place to go for submission of drugs for cancer. While the Oncology Division processes most submissions, it does not deal with all of them; unfortunately, this leads to inconsistency and very different approaches in the way various FDA entities act in approving drugs and in industry interactions with various parts of the FDA. The director of one of the other divisions of the FDA has stated publicly that his division will not respond to e-mails from sponsors of drugs for the treatment of cancer patients. This is not the way the Oncology Division works and not the way that we want the FDA to work with respect to drugs for cancer.

The size and cost of trials are now major issues. The FDA recently asked us to conduct a post-marketing trial in patients with advanced lung cancer. These patients, unfortunately, have a survival rate of less than one year. It would require 1,000 patients for us to obtain the appropriate information in this trial. We are in the process of getting estimates from clinical research organizations that help pharmaceutical companies run trials, and so far we have received estimates of an average of $17,000 per patient (the estimate is higher in centers like Johns Hopkins and Duke and lower in places such as Eastern Europe, South America and the Pacific Rim). That means the cost of this trial is going to be $17 million. It is a very expensive way of developing drugs and getting answers. AstraZeneca is also attempting to demonstrate that one of our drugs is effective in the first-line therapy for women with advanced breast cancer. The size of the trial that may be necessary for that demonstration is in the thousands, but the largest global trial that has been undertaken to date is with fewer than 800 patients. This is a significant hurdle. The pharmaceutical industry, the FDA and others need to work together to find the appropriate endpoints for clinical trials.

Judging by time to progression is an improvement over the survival rate and may be a more valid endpoint for patients. We must also consider surrogate endpoints.

There are real incentives for doing trials in cancer prevention as well as in cancer treatment. The proof that the drugs work has been demonstrated in many areas. We have known since 1896 that hormonal therapy is of some benefit to women who have breast cancer, and there is also a potential role for more recently discovered agents that aim at a very few targets or even a single target and are much less toxic to patients. That may well make a difference to someone who is predisposed to cancer, if not to a patient with far advanced disease.

I have alluded to the disincentives, including time and cost. Prevention trials take even longer, as in the case of the trial that would involve 1,000 patients and cost $17 million. The recent trial for prevention of breast cancer involved 13,000 patients and the one currently underway involves 22,000; the prevention trial in prostate cancer includes well over 10,000. Another big issue for the pharmaceutical companies in dealing with prevention trials is patent protection. Each trial can take so long to complete that by the time it is done, assuming that it proves successful, the drug is off patent. The analogy is not to someone who starts a small business that fails; that, we would agree, is the entrepreneur's problem. But imagine that the business succeeds and someone else walks away with the profits. That would be akin to what happens to pharmaceutical companies when they invest in a prevention trial that comes to fruition only after patent protection has lapsed. It is a major disincentive for the initiation of such trials, and presents a problem that requires legislative action guided by scientific and regulatory expertise. It is a problem that cannot be ignored if we are to bring the full promise of molecular medicine to people we hope to keep from becoming cancer patients.

DR. H. KIM LYERLY

I would like to highlight the role of cancer centers and their potential value in the effort to treat and conquer cancer. The National Cancer Institute-designated cancer centers are a product of the 1971 National Cancer Act[10] and are comprised of coordinated interdisciplinary programs at American academic and research institutions. Figure 1 shows the university-based cancer centers that not only deliver cancer care but also have schools of engineering, applied physics, public policy, law and so forth. This broad array of expertise within the same institution gives the cancer

FIGURE 1

FY03 Total NCI Grant Awards and Numbers of Patients Discharged for Top 10 Cancer Centers

	Cancer Center	Grant Funding (in millions)	Patient Discharges
1	University of Texas MD Anderson Cancer Center	$98.3	
2	Fred Hutchinson/University of Washington Cancer Consortium	$81.0	866
3	Johns Hopkins University	$80.3	1712
4	University of Pennsylvania	$71.8	1614
5	Dana-Farber Institute and associated hospitals	$68.3	237
6	University of California - San Francisco	$64.4	746
7	Memorial Sloan-Kettering Cancer Center	$59.7	
8	Duke University	$59.6	3082
9	University of Michigan	$57.0	1578
10	Mayo Clinic	$48.1	
	Total of Top 10 Cancer Centers	**$688.5**	

centers the potential to break down barriers—barriers that could prevent a chemist from talking to a physician who is treating patients with breast cancer or an engineer from interacting with a neuro-oncologist who is challenged with delivering a drug to the central nervous system—and creating innovative solutions to problems and translating concepts into new therapies for cancer patients. The top ten cancer centers in the United States have received $688.5 million in grant awards from the NCI, which represents a significant portion of the overall NCI budget. An example of the pivotal role played by the cancer centers over the past decade is the current highly innovative and focused approach to translating ideas into patient care. These programs are known as the Specialized Programs of Research Excellence.

Today, there are significant opportunities in cancer research and care, but there are also critical issues in cancer drug development that must be addressed.

The level of uncertainty in drug development presents the pharmaceutical industry with a high level of risk. Fifty percent of trials that are in Phase III, representing the culmination of an $800 million investment, will not result in drug approval. That is an expensive lottery ticket: $800 million with no return. Another problem results, paradoxically, from an important advance. We are beginning to appreciate the genetic signatures of cancers, recognizing that instead of a cancer of the breast or the lung or the colon, these genetic signatures represent highly specific patterns of, e.g., thyroid cancer that is spontaneous or radiation-induced. The specificity of these genetic signatures means that the market for a specific drug is increasingly fragmented. We are moving toward very individualized drugs and treatments rather than a "one drug cures all" approach. A drug that treats

Americans with obesity, for example, has an enormous market, while a drug that targets a highly specific genetic alteration in a breast cancer patient may appeal to a market that is so small that the recovery of the investment may be inadequate. We must think about solutions to this problem.

Cancer centers play a role in drug development for two major reasons, the first and major of which is that they are dedicated to improving the lives of our cancer patients and their families. The second reason is that cancer centers want to work in concert with the pharmaceutical industry to determine not only whether a specific drug works, but also to determine whether the pathway being targeted is a valid pathway to attack. The Avastin trial led by Duke University investigator Dr. Herbert Hurwitz, for example, proves that blocking angiogenesis prolongs life for colon cancer patients. In that scenario we have therefore relied on the combination of the academic/research world and the pharmaceutical companies' entrepreneurship to find improved and less expensive strategies for blocking blood vessels. The approval of a product that blocks blood vessel growth leads not only to a single product, which is itself exciting, but also to an opportunity to improve the pipeline so as to develop better products targeting that pathway. This combination is critical and is the reason cancer centers and cancer physicians around the country are so linked to the pharmaceutical industry, acting together to balance patient care and the advancement of new therapeutics.

We have already discussed the potential for surrogate markers to shorten the time needed for drug development. There is another way to improve approval of new therapeutics. It typically requires seven to ten years to show improvement in breast cancer patients, treated in an adjuvant setting, who are defined clinically as having a reasonably good prognosis. A study carried out by Duke University using genetic profiling, however, demonstrated that some genetic markers tend to indicate a very poor prognosis for breast cancer patients.[11] We have the potential to take patients with that poor prognosis profile, treat them, and accelerate proof that the agent has had an effect on them. Shortening this process allows physicians to optimize the thousands of potential compounds that could be effective treatment for individual patients. By identifying patients who have highly-defined outcomes or by developing surrogate markers, we can eliminate the long process of clinical development of new drugs. In fact, we can shorten the time needed to develop a new drug from perhaps ten to twelve years to five to seven years.

Cancer centers are rising to the challenge and are taking an aggressive approach to establishing partnerships with the NCI, industry, patients and

patient advocacy groups. We have a collaborative effort in biomarker development, for example, with Drs. Lance Liotta of the NCI and Emanuel F. Petricoin of the FDA**.** We are attempting to develop companion studies within all of our clinical research enterprises to improve and validate biomarkers, and to develop formats in which these dialogues can occur.

I am very pleased with the support we have received from Dr. von Eschenbach to develop forums for discussions with the FDA and the NCI as well as among cancer centers, in order to develop strategies to improve and accelerate the approval process for new drugs. We have common goals: to accelerate the approval of a single drug, and to prove at the same time that a pathway being blocked is the target for multiple new drugs and multiple new strategies.

CHARLENE GADDY WALLACE

My name is Charlene Gaddy Wallace. I live in Southeast Washington, D.C. I am married with four children and I am both a student and an administrative assistant at The Catholic University of America. I am also a breast cancer survivor who participated in a Phase III clinical trial at Howard University Hospital in 2001.

That year, I was diagnosed with carcinoma of the left breast. I went to Greater Southeast Washington Hospital for a lumpectomy. My doctor first told me to think positively and then said that I needed a mastectomy. Deciding to take his advice and think positively, I became proactive. In my mind cancer was abstract. I knew nothing about it. It was foreign to me but losing a breast was vivid. I soon realized that I now needed more people in my life than I could ever have imagined.

After consulting with several people, I was drawn to Howard University Hospital. I started developing my team of doctors, one of whom was the oncologist who introduced me to the Taxol Phase III clinical trial. My parents and friends were quite apprehensive about my participation in a clinical trial: African Americans can sometimes be skeptical about medical treatment because of bad experiences, such as the Tuskegee syphilis case and the Willowbrook hepatitis experiments.[12] I knew nothing about what it would mean for me to participate in a clinical trial: Would I have rights? Would it really benefit me, or were the doctors just experimenting?

Fortunately, I was able to find other people who had been involved in clinical trials, which alleviated some of my fear. I asked myself, "Do you want to live? Are you willing to take the chance? Are you willing to be in the

front lines of cancer research, working with the doctors who are constantly seeking to improve the treatment of cancer and the quality of life of cancer patients?" And I thought that yes, with four children I had better be willing to take the chance; with the thought of leaving my husband behind to raise those four children, I had better be willing to take the chance; with all the things I wanted to do in life, I had better be willing to take the chance.

That is why I later became a patient advocate. I speak constantly with patients, urging them to take an active role in their treatment. "What are your doctors talking about?" I ask them. "Have you asked them about any other treatment or clinical trials? Maybe there are other options. Ask those questions. Be involved! Be encouraged that it is possible that one day cancer will be no more." I know that will not happen overnight, and some people will lose their battle with cancer—but the chance of my surviving, of others surviving, is worth fighting for.

NOTES

1. Phase III clinical trials are large trials of a treatment or drug that has been shown in Phases I and II to be efficacious with tolerable side effects. After successful conclusion of Phase III clinical trials, the drug will receive formal FDA approval and can be marketed.
2. Secretary Thompson's E-Health Initiatives have included, e.g., the facilitation of information-sharing by government agencies working in the field of health research (http://chid.nih.gov) and the advertisement of health-related information for individuals (http://www.healthfinder.gov).
3. The Medicare Prescription Drug, Improvement and Modernization Act of 2003, P.L. 108–173, was signed into law on December 8, 2003.
4. "Solving the Mysteries of DNA," *Time*, February 17, 2003.
5. Folkman, Judah, "Tumor Angiogenesis: Therapeutic Implications." *New England Journal of Medicine.* November 18, 1971, 285 (21): 1182–1186.
6. D.W. Leung, G. Cachianes, W.J. Kuang, D.V. Goeddel, N. Ferrara, "Vascular endothelial growth factor is a secreted angiogenic mitogen." *Science.* December 8, 1989, 246 (4935): 1306–1309.
7. National Cancer Institute, "Bevacizumab (Avastin) Improves Survival in Metastatic Colorectal Cancer," June 10, 2003, http://www.cancer.gov/clinicaltrials/results/bevacizumab-and-colorectal-cancer0601.
8. As of late March 2004, IRESSA had not yet received marketing approval from the Committee for Proprietary Medicinal Products, the scientific advisory body to the European Commission. *Pharma New Bulletin*, "Iressa widely used in Europe without marketing authorization," March 24, 2004, http://www.pharmamarketing.se/PharmaNews2.asp?Id=4289.
9. Faslodex received marketing approval from the European Union in March 2004. AstraZeneca International, "Marketing Approval Granted for Faslodex

(Fulvestrant) in European Union," March 12, 2004, http://www.astrazeneca.com/pressrelease/1506.aspx.

10. National Cancer Act of 1971 (P.L. 92–218).

11. Huang, E. et al., "Gene expression predictors of breast cancer outcomes." *Lancet*. May 10, 2003, 361 (9369): 1590–1596.

12. Between 1932 and 1972, the Public Health Service enrolled 399 African-American sharecroppers in Macon County, Alabama, in a program that they were told would treat them for syphilis. Rather than receiving treatment, however, they were used to study the effects of a lack of treatment of the disease. They went untreated even after the discovery of penicillin and its adoption for treatment of syphilis throughout the United States. In 1997, President Bill Clinton issued a formal national apology for the study.

The Willowbrook State School, a New York State institution for "mentally defective persons," deliberately infected children with the hepatitis virus between 1963 and 1966 so that doctors could study the disease and experiment with possible treatment. Parents seeking to enroll their children at Willowbrook discovered that admission would be denied unless they consented to having the children infected with the disease.

PART IV

The View from Capitol Hill

SENATOR EDWARD M. KENNEDY

I have been a foot soldier in the army battling cancer since before I entered the United States Senate. In 1961 I traveled through my state of Massachusetts with Sydney Farber, one of the earliest pioneers of research on cancer whose impact was so great that one of today's great cancer centers, the Dana-Farber Cancer Center in Boston, bears his name. I remember coming to Washington after we had traveled all over Massachusetts, developing support from local communities and finding that the response was overwhelming. We had, and continue to have, an enormously active citizenry in my state, one that is intimately tied to the research community and to various clinics and hospitals in Boston.

Then I came to the United States Senate and the first bill I had the opportunity to help pass as Chairman of the Health Subcommittee of the Senate Committee on Labor and Public Welfare was the 1971 National Cancer Act that Dr. von Eshenbach mentioned. It was based on the recommendation of an early 1970s bipartisan panel and was an extremely controversial proposal. We wanted to establish an independent government research group to focus on cancer research but encountered a good deal of reluctance, to the point that the *New York Times* editorialized three times against having an institute independent of the War on Cancer at the National Institutes of Health (NIH). The concern was that the creation of a new institute would result in a different management system, budgeting system and focus. The National Cancer Institute was eventually developed nonetheless, and Dr. Benno Schmidt made an extraordinary contribution in developing an advisory group that intersected with the Cancer Institute.[1]

Five weeks after we passed the Cancer Act, I found out that my son Teddy had osteosarcoma in his leg and that, based on the treatment available at the time, his chances of survival were only about 15–18 percent. We were fortunate to get him enrolled in an NIH trial in Boston, where he had a positive reaction to the treatment. His leg was amputated and he underwent treatment for a three-day period every three weeks over the course of

two years, but he survived. Today he is fit and strong and lives a very full life. He is the proud father of two wonderful children and he has raced in the handicapped skier's race, going seventy miles an hour downhill on one ski. His survival serves to remind us all of the importance of research, because without that trial treatment, he would not be with us today. His story reminds us that there is no family immune to this devastation.

There is obviously a great deal that can be done at the national level to fund this kind of research. The bipartisan support for funding that has developed in recent years is both extraordinary and crucial at a time when the possibilities of the life sciences seem virtually unlimited. The potential breakthroughs that we have been hoping and praying for are closer than ever before. The efforts of organizations such as Friends of Cancer Research are crucial to our continued efforts and to getting information about the latest treatments and trials out to cancer victims.

We have also seen funding for cancer research slow down at a time when there is great promise in research efforts. The idea that we are going to increase the NIH budget by only 2.5 percent means that numerous promising and hopeful projects will have to be sidelined. That is unacceptable, given our national commitment to ending suffering due to cancer. We have invested resources in this research; we have assembled experts and clinical trial volunteers; we have created opportunities for breakthroughs. Now is not the time to equivocate: finding a cure for this disease is a national priority. It is a priority for American families in towns and communities across this country. They want these programs fully funded, and American families are entitled to have their priorities reflected in the federal budget.

One of the things that concerns me about the changes in Medicare has to do with reimbursement for oncological care. That can make an enormous difference in the availability of treatment for cancer patients. Reduction of oncologists' reimbursements is something that we have to be very careful about and I hope that all those who have been working on this reduction will continue their best efforts.

There is still much to be done in the field, as can be seen with respect to the breathtaking progress we have made in children's cancer care. There has been some progress with breast cancer and lung cancer, colorectal cancer and prostate cancer, but we need to focus on the areas where progress has been slower and find ways to develop information to maximize the opportunities for further progress.

Senator Warren Magnuson was once asked what the greatest headline in the world would be. His reply: "Cancer Conquered."

SENATOR TED STEVENS

Cancer research is a subject that is very close to my heart. I watched my grandfather, my father and my brother die of pancreatic cancer. I remember the day twelve years ago when I was diagnosed with prostate cancer, and so I know firsthand how the disease changes your life. Much has happened to cancer research and cancer treatment since then.

As you know, Congress has doubled the NIH budget in the last few years. In doing so, we have tried to provide the cancer research community with desperately needed resources. The additional funds have enabled NIH to continue its quest to determine the causes of cancers and develop targeted therapies to halt their progress or, preferably, to achieve a cure for all cancers. The support of patient advocacy groups and cancer research advocates is equally essential in moving our efforts forward.

There are five areas in which changes or improvements are possible as part of our strategy in the fight against cancer.

First, new treatments and technologies that benefit cancer patients must not face unnecessary hurdles. One example, Positron Emission Tomography or PET technology, springs to mind. I have long been an advocate of PET. This imaging technology, developed by my good friend Dr. Michael E. Phelps at the University of California – Los Angeles, revolutionized our ability to diagnose almost all types of cancer. Yet even though PET was invented in the early 1970s and has been ready for use in clinical practice for at least a decade and is widely used in Europe, I and several other members of the Senate have spent years trying to obtain Medicare coverage of PET scans for seniors. While significant progress has been made with the Centers for Medicare and Medicaid Services, the agency that oversees Medicare, we have not yet achieved Medicare approval for physicians who wish to order a PET scan in the same way that they can now order a CAT scan or an MRI. The Medicare coverage process must be changed now to benefit patients who need these new therapies and technologies.

Second, the NIH director needs broader authority to fund cross-institute research. I believe that type of collaboration will enable multi-disciplinary research efforts that could help us determine the molecular bases of all cancers and develop new target therapies to treat them. Large-scale collaborative projects involving multiple institutions also need encouragement. Today, the NIH director has little ability to do this; instead, research funding authority is split among the NIH's 27 institutes and centers, which unwisely guard their institutional territory. One collaborative effort that might be successful is the blending of nanotechnology and molecular

imaging. By bringing the science of nanotechnology to bear on systems biology and using molecular imaging, we might be able to decode the molecular basis of many varieties of cancer, which could possibly be cured by molecular therapies.

Unfortunately funding for this type of collaboration is unlikely under the current system of peer review at the NCI or at NIH. The recommendation, in the July, 2003 Report of the Institute of Medicine, that the NIH director be given expanded resources and authority to bring together multiple disciplines, should be followed.[2]

Third, we must increase funding for other federal agencies such as the National Science Foundation and the Department of Energy, which support research that assists in the fight against cancer. The Human Genome Project began not at NIH but at the Department of Energy. Much of the technology used by researchers funded by the NCI was developed by the National Science Foundation, the Department of Energy, NASA or the Department of Defense. NIH does not fund this kind of research but without it, medical researchers funded by NIH would not have the tools they need to conduct their current research efforts.

Fourth, Medicare and private insurers should be encouraged to pay for clinical trials of new therapies. Private and public insurers now provide little coverage for clinical trials. The trials are very expensive and currently can be funded only by large pharmaceutical companies. Small, innovative biotech companies and other researchers who develop promising new treatments are sometimes unable to bring those treatments to patients because they lack the resources for clinical trials.

Finally, we must educate the Congress and the public. Each year the Appropriations Committee faces tough decisions about allocating funds among our many obligations and worthwhile programs. I urge you to work to educate the Congress and the public at large about the beneficial results of investment in medical research. A substantial return on our investment will make it easier to persuade the Congress to sustain or increase the level of investment in medical research. I hope you will help us make those successes more visible.

SENATOR ARLEN SPECTER

In the last few years, we have made tremendous strides on funding. The budget of the National Cancer Institute is now up to $4.7 billion, and funding for the National Institutes of Health is a very high priority in the Congress. We increased NIH funding during 1995–1996 when Senator

Hatfield was chairman and have done so since Senator Stevens took over in 1997, so we have now doubled NIH funding. Logically, we should now seek to triple the funding, but we are finding that very difficult.

The front page of the November 12, 2003 *Washington Post* reported that discretionary federal spending has risen by 13%.[3] That will make it harder than ever to get more funding for NIH, as most of the increase has gone to the Department of Homeland Security. We had a difficult time this year when we sought to get an extra $1.5 billion for NIH, which was in excess of budget allocation and so required 60 votes. The debate in the Senate was hot and heavy. I offered the amendment in collaboration with the chairman of the committee. You would think that when the chairman of the committee and the chairman of the subcommittee are behind an amendment, it would have a very good chance of passing. I thought we were going to get the 60 votes until Senator Frist [William Frist, the Senate Majority leader and a heart surgeon] joined the debate on the other side. Senator Nickels [Don Nickels, a member of the Budget Committee] was also on the other side. The final vote was 52 senators in favor of increasing the funding by an extra $1.5 billion. If you look at the *Congressional Record* you can identify the 48 senators who did not vote for the increase in funding, and I would suggest that it might be a good idea to make your wishes known to them.

This year, as I indicated, we hoped to increase NIH funding by a figure between $1 billion and $2.5 billion. Then we senators went into conference committee with the House, whose members were aiming for only a $600 million increase. Tough negotiations followed. Senator Stevens has managed in the last several days to come up with $1.2 billion more than they originally were willing to budget, and I am pleased to tell you we are going to be back at the $1 billion level. I am not at all pleased to tell you that even that is subject to challenge, because the House is not happy with adding the additional funds. It is quite an exercise to work with 535 fiefdoms. There are 535 different ideas. As Secretary of State George Schultz once said, "Nothing is ever settled in Washington." So we are still struggling with funding for cancer research, and we will continue to do so.

We are also struggling with the enormously important issue of stem cells. It will require a national campaign to change the policy of the federal government on using NIH money to fund stem cell research. In Spring 2001, before we were preoccupied with al Qaeda and Iraq, we were able to muster 76 senators in favor of changing NIH policy to support stem cell research. When that became known, the president, realizing that his veto could be overridden, made the August 9, 2001 statement in which he

agreed to have 63 existing stem cell lines used for research.[4] Unfortunately, they have proved to be inadequate.

When stem cells became part of the national discourse in November 1998, the Labor, Health and Human Services, and Education Subcommittee of the Appropriations Committee held 14 hearings to develop the record about the opportunities for stem cell research. At the moment, however, we are stymied. Recently, the President's Council on Bioethics declared that some of the stem cell lines were not appropriate for research because they have mass feeders.[5] That is true; we need more untainted stem cell lines. The potential for the medical use of stem cells in treating diseases such as Parkinson's, Alzheimer's, heart disease and cancer is enormous, which makes it scandalous that we are not using the full scope of our medical research on stem cells to combat those maladies. It is estimated that 128 million Americans are directly or indirectly affected by these diseases. That could be a very potent political force.

QUESTION AND ANSWER SESSION

QUESTION: Will opportunities to develop public/private partnerships receive support from Congress? We have been trying to create cross-sector opportunities for collaborative research projects. While advocacy groups can be a formidable force, there are other entities with other interests. Industry, for example, needs to know that its investments are protected before it will participate actively and collaboratively in public/private research investigations. What visions do you have? What opportunities do you see for making these kinds of collaborations in cancer real?

DR. VON ESCHENBACH: We have been very concerned about the ability to create partnerships. We can drive the engine of discovery but we must translate that into the development of interventions. PET scanning is an example.

PET scanning and more improved isotopes enable us actually to see the biology of cancer in real time. We must develop the collaborative public/private partnerships that will enable us to expand that technology. We are looking, for example, at what occurred in the semi-conductor industry as it collaborated around Semitec and enabled the producers of that technology to come together with the discovery science. We are actively discussing such models with industry.

SENATOR STEVENS: That is one of the most complex areas we have dealt with. Senator [Joseph] Biden and I started the concept of challenge grants for improving national parks. We ought to examine how we can put

these engines together and have them run at the same time towards the same destination. The difficulty is that we have private investment in research and we have public investment in research and we lack the ability to coordinate them well. The key to doing so is to protect private rights, because once you become a partner with the government you lose your rights to your patents unless you have a good basic underlying law. I believe we should work for a basic law that permits the formation of public/private collaborations. Such efforts could include the great foundations of this country as well as state governments. Lee Hood of the Institute for Systems Biology in Seattle is trying that now and deserves support.

QUESTION: We have passed many state laws that require insurers to reimburse patients enrolled in clinical trials. Those laws, however, apply only to plans that are not part of the ERISA (Employee Retirement Income Security Act) community, which now includes 76% of Americans.[6] We certainly need to have the federal government look again at the issue of reimbursement for clinical trials. The question is, how can the patient advocacy community unite with you in your desire to move the nation into a voluntary system of payment for clinical trials enrollment?

SENATOR STEVENS: That takes us into the antitrust field. We will have to find some way to get the Department of Justice on board so that participating groups will not be liable for antitrust violations. We might be able to do so if we design a plan that will allow for small and medium entities to participate. The government currently requires large pharmaceutical companies to pay for that research. I doubt that we can get Congress to reimburse them for what are gigantic expenditures, but we ought to find a way both to give them better credit for doing it and to increase the tax incentives for the small and medium entities. We must also redefine the scope of those clinical trials so that they are much more meaningful and we will not have to waste too much money getting them started and getting approval of the product they want to test. The problem is that we have never gotten all the possible participants together and asked them what they would need if they are to participate. We ought to ask the people who design the requirements for clinical trials to see if we can make them less expensive.

QUESTION: Senator Specter, you and your colleagues work tirelessly to increase the funding of the NIH. Where are we falling short? What can we do better, and what will make us more effective in helping our major supporters?

SENATOR SPECTER: Identify the senators who did not vote for the extra $1.5 billion for NIH. Have them contacted by voters from within their

states. Identify the people in the House of Representatives who have not supported NIH and who wanted to allocate an inadequate $600 million.

You also ought to push stem cell research, where our current policy is scandalous. Those are the two current big items: funding, and stem cell research.

SENATOR STEVENS: Find ways to parade the successes of these investments. We are not doing enough to convince the taxpayers, who should be telling their senators that doubling NIH research funds has been meaningful. We need more people telling the stories of what has happened as a result of this process. Senator Connie Mack began the process of doubling NIH funds, which he did because of his personal history.[7] There are millions of American families with the same kinds of experiences. They need to know that the research has brought results and that further research will increase the positive results we have had so far.

NOTES

1. Dr. Benno Schmidt chaired the National Panel of Consultants on the Conquest of Cancer established by the Senate in 1970 (S Res 376, April 27, 1970) to study and recommend federal action in the field of cancer research. The panel recommended establishment of an independent cancer agency to coordinate a national crusade against cancer. *See* S Rept 91–1402, report of the Senate Committee on Labor and Public Welfare, released Dec. 4, 1970.

2. National Institute of Medicine of the National Academies, *The Role of Academic Health Centers in the 21st Century* (July 17, 2003), http://www.iom.edu/report.asp?id=13728.

3. Jonathan Weisman, "Government Outgrows Cap Set by President: Discretionary Spending Up 12.5% in Fiscal '03," *The Washington Post*, November 12, 2003.

4. "Remarks by the President on Stem Cell Research," August 9, 2001, http://www.whitehouse.gov/news/releases/2001/08/20010809-2.html.

5. The President's Council on Bioethics, *Stem Cells: Moving Research from the Bench Toward the Bedside: The Role of Nongovernmental Activity* (September 4, 2003), http://www.bioethics.gov/transcripts/sep03/session4.html.

6. The Employee Retirement Income Security Act of 1974, P.L. 93–406, is a federal law that sets minimum standards for most voluntarily established pension and health plans in private industry to provide protection for individuals in these plans.

7. In 1997 Connie Mack, a cancer survivor, was still a member of the U.S. Senate. He and Senator Dianne Feinstein introduced and secured unanimous passage of a Sense of the Senate resolution establishing the goal of doubling funding for the National Institutes of Health over a period of five years. Within three fiscal years, NIH grew from $12.7 billion in fiscal 1997 to $23.2 billion in fiscal 2002.

Glossary

ADJUVANT – a substance added to a drug to aid its action, specifically to increase immune response.

ANGIOGENESIS – the process in which a tissue develops new blood vessels. Crucial for sustaining tumor growth as it allows oxygen and nutrients to feed the tumor.

ANGIOGENETIC SWITCH – mechanism by which cancer cells induce healthy tissues to produce new blood vessels, thus facilitating metastasis.

ANTIBODY – a specialized protein produced by certain white blood cells in response to the presence of an antigen, thus creating immunity to the antigen.

ANTIGEN – a protein that is capable of inducing a specific immune response and of reacting with the products of the response. A substance that causes the immune system to make a specific immune response.

APOPTOSIS – a form of natural cell death in which a sequence of events leads to the elimination of cells without releasing harmful substances into the surrounding area.

BIOLOGICS – agents such as vaccines that provide immunity from diseases or harmful biotic stresses.

BIOMARKER – a specific biochemical in the body that signals a changed physiological state due to disease.

BIOINFORMATICS – the use of computers in solving problems in the life sciences through the creation of extensive electronic databases on, e.g., genomes and protein sequences.

CAT SCAN – Computerized Axial Tomography. A radiographic technique that uses a computer to assimilate multiple X-ray images to reveal many soft tissue structures not shown by conventional radiography, using the same dosage of radiation as conventional X-ray machines, but with about 100 times more clarity.

CYTO – prefix for cell. Cytotoxic – cells of the immune system that inhibit or help to terminate an immune response; cytoreductive – reduction of the number of cells in a malignancy; cytostatic – an agent that suppresses cell growth and multiplication.

DNA – desoxyribonucleic acid, one of the two types of nucleic acids found in all cells.

GENOMICS – the study of all of the elements in the chromosomes of an organism, with the goal of enhancing understanding of the molecular mechanisms of cancer to improve the prevention, early detection, diagnosis, and treatment of cancer.

GLIOBLASTOMA – a type of tumor that forms from glial (supportive) tissue in the brain; highly malignant and grows very quickly.

HER2neu FAMILY RECEPTORS – sites or structures in a cell that combine with a specific anticancer drug from Genentech called Herceptin, a monoclonal antibody, which binds with those structures and prevents them from functioning. Used in some breast cancer treatments.

HISTOLOGY – the study of cells and tissue on the microscopic level.

INFORMATICS – research in applied computer science.

IN VITRO – pertaining to a biological reaction taking place in an artificial environment, literally "in glass," as in a test tube.

LYMPHOMA – cancer that begins in the lymph tissues.

METABOLOMICS – the measurement of thousands of metabolic products in a single sample to get a full picture of the physical and chemical processes of cells, as a baseline against which to measure changes with time or treatment.

METASTASIS – the transfer of disease from one organ or body part to another organ or part not directly connected with it.

MICRO-ARRAY ANALYSIS – a sophisticated computer method for measuring differences in genes after treatment.

MOLECULAR IMAGING – the formation of computer images of molecules produced by means of radiation.

MONOCLONAL ANTIBODY – an antibody derived from a single clonal line of cells, used as drugs to fight cancer (see HER2neu above).

MRI – Magnetic Resonance Imaging. A special imaging technique used to image the soft tissues of the body; used for detecting some cancers or for following their progress.

NANOTECHNOLOGY – techniques that measure precise molecular features less than 100 nanometers (a billionth of a meter) in size which enable scientists to detect cancer at its earliest stages, deliver anti-cancer drugs specifically to malignant cells, and determine whether the drugs are killing malignant cells.

ONCOLOGY – the branch of medicine that deals with tumors, including study of their development, diagnosis, treatment, and prevention.

OSTEOCARCOMA – cancer that arises from the cells which produce bone.

PAPILLA – a small nipplelike projection occurring on tissues or organs.

PET SCAN – Positron Emission Tomography. A highly specialized research imaging technique. Very sensitive in picking up active tumor tissue but rarely used in clinical settings because the radioactive substances used are so short-lived and the equipment is so expensive.

PHENOTYPE – the observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences.

PROTEOMICS – the separation, identification, and characterizations of the complete set of proteins present in the various cells of an organism.

RECOMBINANT DNA – artificially created DNA that combines DNA from two or more sources in a single molecule.

SILOS – intellectual barriers to information sharing that exist between and within research and academic centers, government agencies, and private industry.

SURROGATE MARKER – a laboratory measurement of biological activity within the body that indirectly indicates the effect of treatment.

Speaker Biographies

CHARLES M. BALCH, M.D., Professor of Surgery and Oncology at Johns Hopkins University, is Executive Vice President and CEO of the American Society of Clinical Oncology. He was formerly President and CEO of the City of Hope National Medical Center. Dr. Balch has also held numerous positions at the M.D. Anderson Cancer Center, including Executive Vice President for Health Affairs. He received his medical degree from Columbia University; his postgraduate training included a surgical internship at Duke University, a surgical residency at the University of Alabama–Birmingham, and an immunology fellowship at Scripps University. Dr. Balch has served in a leadership role for numerous professional organizations and has published over 500 articles.

RALPH BURNETT has been an Associate Judge of the District Court of Maryland since 1993. Currently the SPORE (Specialized Programs of Research Excellence) Prostate Cancer Representative for Johns Hopkins University School of Medicine, Judge Burnett has served as the Chairman of the National Prostate Cancer Coalition. He founded Cindy's Fund to support early cancer screening in and around Garrett County, Maryland. He received his B.A. from Dickinson College and his law degree from the University of Baltimore, and has served as both a State's Attorney and on the Board of Governors for the Maryland State Bar Association.

NANCY DAVIDSON, M.D., is Professor of Oncology and Breast Cancer Research Chair in Oncology at the Johns Hopkins University School of Medicine. A member of numerous editorial boards, she is the recipient of professional honors including the American Cancer Society Research Award—Maryland Division (1998), the American Cancer Society Clinical Oncology Cancer Development Award (1988–1991), the Susan Komen Foundation Award (1987–1988), and the Brinker International Award for Breast Cancer (1999). Dr. Davidson received her medical degree from the Harvard Medical School in 1979. Her postgraduate training in internal medicine included an internship at the University of Pennsylvania, a residency at Johns Hopkins, and a fellowship at the National Cancer Institute.

SUSAN DESMOND-HELLMANN, M.D., M.P.H, the Chief Medical Officer and an Executive Vice President at Genentech, is also Adjunct Associate Professor in Epidemiology and Biostatistics at the University of California–San Francisco. She was previously the associate director of clinical cancer research at Bristol-Myers Squibb Pharmaceutical Research Institute and the Project Team Leader for Taxol, and is the recipient of numerous honors and awards for her work in Oncology and AIDS research. Dr. Hellmann holds bachelor and medical degrees from the University of Nevada–Reno and a master's degree in epidemiology and biostatistics from the University of California–Berkeley School of Public Health. She is board-certified in Internal Medicine and Medical Oncology.

GERARD THOMAS KENNEALEY, M.D., is AstraZeneca's director of Global Products for Faslodex, a new hormonal agent used in the treatment of women with advanced breast cancer. Dr. Kennealey formerly directed the multi-functional team that inaugurated the Expanded Access Program for IRESSA. He is board-certified in Internal Medicine and Medical Oncology. Prior to joining the pharmaceutical industry and AstraZeneca sixteen years ago, Dr. Kennealey was a practicing physician specializing in oncology in Connecticut as well as a Fellow in Medical Oncology at Yale University School of Medicine, where he conducted his internship and residency in medicine. He has long been an active volunteer in the cancer community.

SENATOR EDWARD M. KENNEDY has represented Massachusetts in the United States Senate since 1962 and is now the Senate's second most senior member. He is currently the senior member of the Health, Education, Labor and Pensions Committee and serves as well on the Judiciary Committee, where he is the senior Democrat on the Immigration Subcommittee, and on the Armed Services Committee, where he is the senior Democrat on the Seapower Subcommittee. He is also a member of the Congressional Joint Economic Committee. Following his service in the Army, Senator Kennedy graduated from Harvard University and the University of Virginia Law School. He was an Assistant District Attorney for Suffolk County before his election to the Senate.

H. KIM LYERLY, M.D., Professor of Surgery, Associate Professor of Pathology and Assistant Professor of Immunology at Duke University Medical Center, is also director of the Duke Comprehensive Cancer Center. He was part of the team of investigators that first reported the use

of AZT for the treatment of HIV infection. Dr. Lyerly also pioneered the clinical testing of gene therapies for numerous forms of cancer. A member of numerous professional societies, he serves on the editorial boards of 12 professional journals. After completing his medical degree at the University of California–Los Angeles, Dr. Lyerly completed postgraduate training in Surgery and Research at Duke University Medical Center.

MARK MCCLELLAN, M.D., was the Commissioner of the Food and Drug Administration at the time of the conference. He is a former member of the President's Council of Economic Advisers, where he advised on domestic economic issues. He also has served as an Associate Professor of Economics and of Medicine at Stanford University, Director of the Stanford Program on Health Outcomes Research, and as a Visiting Scholar at the American Enterprise Institute. Dr. McClellan holds an M.D. from the Harvard-MIT Division of Health Sciences and Technology and a Ph.D. in Economics from MIT, and has twice received the Arrow Award for Outstanding Research in Health Economics. He is currently Administrator of the Centers for Medicare and Medicaid Services.

MEL SORENSEN, M.D., is the Vice President of Oncology-MSI, Clinical Development & Medical Affairs, at GlaxoSmithKline. He is a participant in several collaborative cancer research initiatives, partnering with the NCI, the NIH Foundation, patient advocacy groups and Friends of Cancer Research. Dr. Sorensen received his Medical Degree from University College in Dublin, Ireland, completed an Internal Medicine Residency in St. Louis, Missouri, and did a fellowship in Medical Oncology at the Mayo Clinic. His broad experience in oncology includes approximately seven years each in full-time patient care, federal academic clinical development (NCI's Cancer Therapy Evaluation Program) and pharmaceutical drug development (Bayer and GlaxoSmithKline).

SENATOR ARLEN SPECTER has represented the citizens of Pennsylvania in the United States Senate for 23 years. He sits on the Appropriations Committee and is Chairman of its Labor, Health and Human Services and Education Subcommittee. Senator Specter is Chairman of the Veterans Committee, is two seats away from chairing the Appropriations Committee, and is in line to become Chairman of the Judiciary Committee by the end of the 108th Congress. A graduate of the University of Pennsylvania and an editor of the *Yale Law School Journal*, he was the first Republican elected to public office in Philadelphia in more

than a decade when, at age 35, he became its District Attorney. He also served on the staff of the Warren Commission before his election to the Senate.

SENATOR TED STEVENS, the Senate's fifth most senior member, has represented the citizens of Alaska in the United States Senate for 34 years. As Senate President Pro Tempore, he is currently third in the line of succession for the Presidency. Senator Stevens is Chairman of the Appropriations Committee and the Defense Appropriations Subcommittee and serves on numerous other committees and subcommittees. Following service in the Air Force during World War II, Senator Stevens graduated from the University of California–Los Angeles and Harvard Law School. Before being elected to the Senate he was a U.S. Attorney, a Solicitor of the Interior Department, and a member of the Alaska House of Representatives.

ANDREW C. VON ESCHENBACH, M.D., is Director of the National Cancer Institute. A urological surgeon, he directed the Genitourinary Cancer Center and the Prostate Cancer Research Program at the University of Texas M.D. Anderson Cancer Center in Houston, where he was also Executive Vice President and Chief Academic Officer. Dr. von Eschenbach received his medical degree from Georgetown University Medical Center and then completed residencies in general surgery and urology at Pennsylvania Hospital in Philadelphia as well as a fellowship in urological oncology at the M.D. Anderson Cancer Center. He also served as a Lieutenant Commander in the U.S. Navy Medical Corps. Dr. von Eschenbach has published more than 200 articles, books, and chapters.

CHARLENE GADDY WALLACE is an administrative assistant in the office of admissions at the Catholic University of America, where she is also a student. In 2001, Ms. Wallace was diagnosed with breast cancer. She had a lumpectomy, a mastectomy and reconstructive surgery; went through a standard round of chemotherapy; and entered and completed the Taxol Phase III clinical trial at Howard University. She currently serves as a patient advocate for cancer patients at Howard University.

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