THE CANCER LETTER INTERACTIVE

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Von Eschenbach Presents His "2015 Goal" As Logical Progression Of Cancer Program

NCI Director Andrew von Eschenbach said science has the tools to "eliminate the suffering and death from cancer" by 2015.

"This is...not a pipe dream," von Eschenbach said in an interview May 12 with ***The Cancer Letter*** *editors Kirsten Boyd Goldberg and Paul Goldberg. "It is a natural extrapolation of the progress that has been made."*

In the interview, von Eschenbach described cancer as a "systems problem" that can be addressed through better coordination of resources. One such effort is the Institute's nascent collaboration with FDA, aimed at streamlining development of cancer therapies, he said.

Von Eschenbach said "proof of principle" has been established for several strategies for preventing and treating cancer. "I don't have to prove to you that chemoprevention is, in fact, a viable strategy," he said. "That has already been done.

"What I have to do is get more of them."

CL: You were scheduled to give a talk at the American Association for Cancer Research meeting last month. The meeting

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In Brief:

City of Hope Selects Pharmacia Executive Michael Friedman As President And CEO

MICHAEL FRIEDMAN, former Pharmacia senior vice president, FDA acting commissioner, and NCI associate director, was named president and CEO of City of Hope. He replaces **Gil Schwartzberg**, who has retired.

"Dr. Friedman's expertise in research and development, coupled with his distinguished career in regulation and public policy, are of enormous benefit to the scientific vision and strategic plan of City of Hope," said **Jack Suzar**, board chairman. "His formidable accomplishments in both the private and public sector will further City of Hope's leadership role in developing innovative therapies for serious diseases, including cancer and diabetes, in addition to numerous immunological and genetic disorders."

Friedman spent nearly a decade at the University of California at San Francisco Medical Center, serving as an associate professor of medicine and eventually becoming interim director of the Cancer Research

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NCI, FDA Form Task Force To Improve Drug Development

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was cancelled. What were you going to talk about?

VON ESCHENBACH: That was really unfortunate, because I was really looking forward to that being a way to flesh out and really provide a lot more detail to the challenge goal of 2015. That is going to still actually occur, because, you know, we rescheduled the meeting.

The unfortunate thing, though, was that I would have loved to have done that at the AACR when it was originally scheduled, and then that would have set the stage very nicely for this presentation that is coming up just in a couple of weeks, which is the joint presentation at [the American Society of Clinical Oncology annual meeting] between [FDA Commissioner] Mark McClellan and myself.

Mark was confirmed at 10 o'clock on a Thursday night by the Senate, and that next morning, Friday morning, at nine o'clock, we had our first meeting. Mark and I have been working, collaborating, and discussing how we could effectively bring the two institutions together. We formed a joint task force that actually had its first meeting a week ago.

We are looking at opportunities where we can work together, because I was really looking at structuring our effort in the context of a portfolio that contained the three D's as they are referred to now—discovery, development, and delivery.

The idea being that we wanted to rapidly and continuously accelerate the engine of discovery, but then based on that knowledge, translate it rapidly into the development of interventions that could then be delivered to patients who are in need, in the context of a clinical research construct that gave us the opportunity, even in the application of these new interventions, the development of new knowledge about the biology of cancer and the disease's process.

So, that really is a circular process in many respects, and part of that ability to really accelerate discovery, development, and delivery calls into play the need for collaboration and cooperation, and so FDA is a critically important partner, because if we can work effectively together in the discovery, in the development, and the approval process, then both of those organizations really, I think, have an opportunity to meet their mission.

One of the things that we want to share is a very strong commitment to put the patient at the center of everything that we do. We have our roles and our responsibilities. The role and responsibility of the Cancer Institute is research. We have to be responsible for developing the knowledge and understanding of cancer. FDA has a responsibility for the safety and the demonstration of efficacy as part of the regulatory process. But in both cases, those missions have a purpose, and the purpose is to improve people's lives.

CL: What specifically would you be doing with FDA?

VON ESCHENBACH: We want to look at two things. We want to look at, first of all, are there programs where we could develop initiatives that would bring the two institutions together to work collaboratively? And, are there processes that are under way in the institutions that could address that, and that would make it more efficient, and more effective. There are a lot of things going on at the grass-roots level, with different people, and for example in NCI's Cancer Therapy Evaluation Program working with people at the FDA.

In the intramural program, we have had [NCI's] Lance Liotta working with [FDA's] Emanuel Petricoin in terms of the proteomics initiative and developing markers for cancer, or signatures for cancer detection.

So, there have been a lot of things that have been going on, but what we are looking at are ways

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that we can kind of help facilitate those interactions. The task force is looking in the areas where we can begin to try to work collaboratively, for example, in bioinformatics.

CL: How about endpoints?

VON ESCHENBACH: Endpoints is another area in which we are going to be focusing and working together in terms of defining—we are looking at a title or a new label that we consider to be endpoints of clinical benefit, a euphemism for what people refer to as surrogate endpoints.

The point being that there is a lot of work that has to be done in terms of how that gets integrated into the validation process on our end, and how it gets integrated into the approval process on their end. But we both recognize that as we look down the road at the new paradigm, that we are looking at outcomes that are not going to be dependent upon survival, and may not even be dependent upon the demonstration of objective response to the tumor, but are going to be dependent upon our ability to demonstrate the module to the pathway, or we have affected a marker of gene expression, or a kinase expression, or whatever.

CL: This is being done between FDA and ASCO right now. Is this going to be different, or is it going to be the same process?

VON ESCHENBACH: We are trying to do this in a way that it is all integrated. The ASCO effort, the NCI effort, the FDA effort—these all are going to be coordinated and integrated in a way—the National Dialogue on Cancer effort.

CL: How does the National Dialogue on Cancer fit in?

VON ESCHENBACH: Well, their Research Task Force has been looking at ways of streamlining the development of drugs based on genomics or proteomics, and issues that they have been looking at have to do with surrogate endpoints, and they have also been looking at ways of creating infrastructure, like a national tissue resource repository.

So, again, what you see, and I think what has been the real hallmark of this, is that there are a lot of groups who are working at various parts and pieces, and what really is, I think, our opportunity, is to help provide more integration and coordination among those pieces.

I think that is part of the NCI's leadership role, is to help serve as an integrating force.

CL: Would the FDA be involved in the NCI "State-of-the-Science" meetings and dealings with the European Organization for Research and Treatment of Cancer?

VON ESCHENBACH: Well, I don't have that kind of detail or that specificity for you at this point in time. The task force has had its first meeting, and we had a series of conversations. I have gone down to the FDA and presented to their Executive Committee in terms of what I am hoping to accomplish and achieve. So, we are in the process of looking for the answers to the specific questions you have raised, exactly how this will play out. I think that's a work in progress. The real important thing is that, in addition to there being a lot of effort at what you might call the grass-roots level, now, at the very top, as far as the Commissioner and the Director, you have a cohesive message of the fact that we want to cooperative and collaborate, and we are going to drive that agenda, and out of that should flow opportunities.

CL: What about endpoints for prevention? Is that an issue or is that also something that needs to be looked at?

VON ESCHENBACH: Prevention is another one of the areas that the task force looked at, and the prevention part of it has two pieces. One, prevention from the point of view of needing to look at, for example, things like diet.

CL: I was thinking of chemoprevention.

VON ESCHENBACH: Chemoprevention is the other piece, yes. That is on the agenda. The task force has identified various people who are kind of invested in those particular parts and pieces.

One of the things that I think the ASCO meeting will do is, when we have the joint presentation, immediately following that, I think we will be able to provide you with a lot more specificity in terms of the areas that have been identified, and here are the people who are going to be involved in some of the discussions, and these are the directions that these things are moving in, and I will be able to provide that.

CL: The overall goal is to streamline and speed up drug development and approval?

VON ESCHENBACH: Yes. I think what our vision is, is that if we can kind of partner effectively and synergize the strength and power that we have on the front end of the process, where we are responsible for driving the discovery, and the understanding, and do that in a way that is in concert with what they have to be responsible for, in terms of the approval process, that gives us an opportunity, I think, to streamline and find ways to accelerate, and

bring the pharmaceutical and biotechnology, the academic sector, into this in an effective way, so that we are all working from the same page of the book.

We don't want a process that goes on up here, and then when it goes down to the FDA, you find out that, well, you have got roadblocks or barriers that if you had only known up here, you could have steered it in a slightly different direction. We want to make it as fluid a process as possible to go from the very fundamental level of discovery, to the point where we really have an intervention that's being delivered to patients, and that intervention is safe, and that intervention, most importantly, is effective.

The worst thing that we can do, we both agree, is to provide things for people that are ineffective and that don't work. But we have got to find a way to address that, without it being a process that goes on for decades. I mean, that just is not acceptable.

CL: Do you want to talk about 2015?

VON ESCHENBACH: Yes. 2015—let me just back up and say that one of the things that we have not had a chance to talk about after our first interview, was how things have evolved over the first year (**The Cancer Letter**, Vol. 28 No. 13, March 29, 2002). When I came in, I began a process of really beginning to look beyond the Bypass budget, so to speak, or a year-to-year operation, and really began to look at a much longer-range strategic planning process.

What was apparent to me at that time as we discussed in the first interview, was the incredible amount of progress that had been made, and the incredible amount of success that had been achieved by virtue of what had gone on before—before my arrival here, and over the period of time that we have had this tremendous explosion in biomedical research, and since 1971, the tremendous progress that occurred by virtue of the National Cancer Act.

So, here we were in having this incredible opportunity that I described in the context of a strategic inflection. What we need to do is to look at that progress from the point of view of, number one, focusing on it, or focusing it, rather.

I use the tag line that this was "progress with a purpose," and the purpose, of course, was really for us to be able to alleviate the human suffering and death that is associated with cancer.

I mean, affecting people's lives is the purpose for this progress. So, first and foremost, I really wanted to call that focus into a very clear dimension, and put the patient at the center of everything that we were doing, and then, create a portfolio that drove towards serving that patient, and that portfolio made it clear when you looked at the continuum of discovery, development, and delivery, that everybody had an important part to play in that. That it was as much an important role for the basic scientist, for the population scientist, for the clinical scientist, that everyone had an important part. What we were really doing was not only accelerating the individual pieces, but looking for the integration. The concept that we required that individual excellence, but to win we had to really play as a team. We had to integrate. If one step back and looked at that progress, and looked at the trajectory that we were on, you began to realize that the trajectory is really not linear. It is really exponential. It's truly expanding at an explosive rate. Not only is our intellectual understanding of cancer as a disease process expanding at an exponential rate, it is being supported—that growth is being supported by, one, a significant investment in financial capital, and there has been significant development of intellectual capital. Third, is that that whole thing is being nurtured and supported by an equal expediential growth in enabling technologies. Now, you just step back and realize what is possible today, just because of the tools that we have available to us in informatics, in computational technologies, and you name it, robotics—I mean, pick one.

CL: Some scientists have expressed a lot of skepticism about your saying that you are going to eliminate suffering and death from cancer by 2015.

VON ESCHENBACH: Right. And they should. I welcome the skepticism. I welcome the opportunity to engage in that conversation, in terms of, so why do I think that this is, in fact, achievable? I won't give you the whole lecture, because you have heard it before.

CL: Are there new technologies, or do you see something that others don't?

VON ESCHENBACH: Well, if you take the premises that I just laid out, that we are in the midst of a biomedical revolution, and the strategic inflection, and exponential growth is real, and that we have intellectual capital and financial capital that is greater today than it ever has been, and there is more money being invested in cancer research today than ever before, that there are more people engaged in the process than ever before. So if you take that as a given, and then we step back from it and ask the question, "So where is it leading us? Where can it take us?"

One of the things that came out of that is the conclusion, in my opinion, that I don't know when we will eliminate cancer. I think some day we will eliminate cancer, but I don't have any idea when that's going to be.

But I think that there is a more proximate step, and that is, we may not eliminate cancer, but we can eliminate the burden of the disease by being able to control and modulate the disease. That is the implication of this biomedical revolution, and this paradigm that I talked about; moving from seek and destroy to targeting and control.

If you think about what we have learned about cancer, what we have learned is that cancer is a disease process. It has a pre-initiation, an initiation, and then it has a pattern of progression. Ultimately, it results in people suffering and dying.

CL: But 5-FU is a target and control drug. It's 50 years old. The most recent drug to be approved, Iressa, is helping one [lung cancer] patient out of a hundred, and we don't know how much it is helping them.

VON ESCHENBACH: Think of it this way. Don't think in terms of single individual interventions and whether they are or are not the magic bullet. There is no magic bullet. There is no single intervention that is going to do this. But, first, let's step back in terms of thinking about 2015. The goal is to eliminate the suffering and death due to cancer. I never said we would eliminate cancer. I said we would eliminate the suffering and death due to cancer. The point of that is, is that if you look at what we are dealing with, we are dealing with a disease process. There is some point in time where we begin to become susceptible to the development of cancer. It may be because we smoke. It may be because we are just getting older. It may be for a variety of things.

There is a period of susceptibility and then there is a moment of transformation. Then, at that point, there is a period of time in which that malignant process evolves in a subclinical way to the point where it actually becomes clinical disease that is able to be detected or diagnosed.

At that point, it actually then goes through a series of processes to the point where it becomes a lethal phenotype, almost always involving a metastatic phenotype.

People, with rare exceptions, do not die of primary tumors. It's the metastatic phenotype that is lethal. So you have a cancer burden phenomenon of increasing to the point of death, and you have a time frame over which that occurs. If you look at this then as a process, as a cancer process, you realize that there are multiple distinct steps that have to be involved in this process, steps that involve all the mechanisms that you are well aware of, from proliferation, to evasion, to dissemination, et cetera, et cetera, et cetera.

They are all processes that are associated with this ultimate outcome of suffering and death. We can begin to think, not of a magic bullet. There's not going to be one single intervention that is going to solve this problem. But we can think of multiple interventions that can be applied to essentially pre-empt this process from occurring. If you can pre-empt this progression curve, you can do a couple of things. One, you may even delay the time—what we will have at 2015, is there may be many people by virtue of things that we are doing and have been doing with regard to what we think of as prevention strategies, be they behavioral modification or chemoprevention, or whatever, where you may even shift this curve long before they even develop it.

CL: You are making it into a diabetes, or—

VON ESCHENBACH: Exactly.

CL: —a chronic disease.

VON ESCHENBACH: Chronic disease is the better word. You are doing two things. You are exploiting, one, the opportunity for the fact that there are many of these diseases that, if we detected them early, just the simple fact of being able to move our intervention point to the left. Let's assume, for example, that spiral CT works.

CL: But you are making assumptions.

VON ESCHENBACH: What assumption? Pick an assumption.

CL: Where are the modalities for, say, chemoprevention intervention? If you hit that one, you have hit 2015, but with what? You are assuming a cure.

VON ESCHENBACH: Do I have them today? Do I have all of the—

CL: Or some of them.

VON ESCHENBACH: Sure you have got some of them. I mean, you have got proof of principle with these things. In other words, I don't have to prove to you that chemoprevention is, in fact, a viable strategy. That has already been done.

What I have to do is get more of them. I don't have a full palette of those things, and so we need many, many more. For example, pick a couple. I mean, there are trials underway with prostate cancer

and finasteride. You have got vitamin E and selenium. Will those things work? Will there be other things we develop and design?

CL: But you are out on a limb now.

VON ESCHENBACH: The assumption is not that chemoprevention will work. The assumption is, how many effective interventions can we develop and create and apply. So that's one piece. Early detection—I don't have to prove the assumption that early detection works. I just have to increase the palette of options and opportunities. Will proteomics and the work that Petricoin and Liotta are doing with the protein signatures that have looked tremendously exciting in ovarian cancer, and are beginning to be applied to other cancers, will that continue to play out? Will we be able to exploit the opportunities in proteomics for early detection, and be able to shift this curve in certain diseases? Just think of what we could do if we shifted the curve in lung cancer, where the greatest burden of death is right now for us.

CL: How would you shift the curve? That's the question. What are you going to give them, Iressa?

VON ESCHENBACH: No. Don't get trapped in one thing. That is my point. That's why I have got multiple arrows here [referring to a slide showing a cancer progression curve with arrows noting points of potential intervention]. Let's take lung cancer, OK? Look at how many places along this trajectory you have an opportunity to make a difference in lung cancer.

You have got opportunities down here with regard to pre-malignant transformation, OK? That stuff has already been in the bank, for the most part, in terms of smoking cessation, and things of that sort. Look at what you could do with early detection, of being able to exploit "son of spiral CT scanning," OK? I don't think spiral CT scan is the answer to early detection, but it can be, and may very well be, a major step. But we may have other things. Maybe the proteomics. Maybe what Lance Liotta is doing with proteomics will work. Think of what we could do if we could just develop more effective interventions for advanced disease.

CL: It's not as if scientists have not been working on this for some time.

VON ESCHENBACH: That's right.

CL: That's what NCI does.

VON ESCHENBACH: Right. It is not new. It is the realization that we have come to a point where we have the opportunity to now integrate and coordinate all of this opportunity in a way that gets us where we want to go to change the shape of this curve. This is doable. To eliminate the suffering and death due to cancer is not a pipe dream. It is a natural extrapolation of the progress that has been made. What we have got to do is to recognize that goal is within our grasp, and not only continue to rapidly accelerate the development of all of these various opportunities and interventions, especially around our exploiting the phenomena of metastasis and our understanding of the fundamental mechanisms. But, every time we understand one of those mechanisms, to rapidly begin the process of developing and getting available—and that's the FDA story again—approve an intervention, and then be able to strategize the integration of these interventions based on the tumor and the host. And if we apply them in an integrated fashion, some of these diseases we will eliminate, and other diseases we will modulate to a chronic disease. This is doable by 2015.

CL: It's almost like you are discussing this as an engineering problem. Is it?

VON ESCHENBACH: Basically for me, I think it is both. That's why the discovery, development, and delivery piece is important, because as you look at this, there are so many places within this process that we have got to intervene, and we have got to get things aligned.

The clinical trials infrastructure needs to be reengineered.

CL: Why did you feel that you needed to say 2015? Because what you are describing is non-controversial. The controversy comes in when you say 2015, because you are out on a limb. Your two predecessors in this office have specifically said, "I am not making any predictions." Other predecessors of yours have made predictions, with not the best outcomes for themselves.

VON ESCHENBACH: I have established that we have to set a time line and we have to drive to that goal and make the commitment. Every part of this community, I am asking people to commit to doing what is necessary to rapidly accelerate this progress and the integration of the pieces. There is a lot of work that has to be done in so many of these arrows, OK? It's doable, and the NCI is committed to providing the leadership and to try to catalyze and to work collaboratively and cooperatively, and to bring us to the focus of driving to that goal.

CL: Covering FDA, I am trapped thinking

of the interventions that are out there that are in the pipeline, and maybe I am missing something.

VON ESCHENBACH: I don't want to overplay the FDA. I mean, the FDA is one opportunity. I think there are multiple places in which we have to collaborate and cooperate. I mean, you know that when you first came to see me that one of the questions you asked me was the Dialogue, and why the Dialogue? There lies another mechanism, and it is another place, and it is another opportunity for us to engage in cooperation, collaboration, and integration, where we can find ways to bring this process to the fore.

I have created a mechanism here—well, not created, but I have emphasized the mechanism here—where all of the major organizations come in for meetings, and there is an opportunity to engage with various staff based on the agenda, and then I have a face-to-face meeting with [them]—AACR, ASCO, and on down the line. Because, we have got to work and find the places where we can interact and synergize, and work towards accelerating this. We have looked the cancer centers, and we had the P-30 and P-50 working group, which has brought its report forward. I am now launching a very active recruitment to bring in another deputy director. We know and recognize that we have an enormous opportunity with regard to the cancer centers, not in terms of just what their individual contributions are, but what our opportunities are with regard to more effective horizontal integration of the cancer centers working with each other, and more vertical integration of the NCI supporting the cancer centers, and the cancer centers becoming much more embedded into the community programs. So, if we can really effectively drive and maximize that kind of integration, and cooperation, and collaboration, that accelerates our ability to get to this endpoint.

CL: You are recruiting a deputy director for clinical research?

VON ESCHENBACH: Well, the deputy director, you know, Anna Barker [NCI deputy director for strategic scientific initiatives] came in, and she brought with her, her background as a Ph.D. basic scientist, and especially in looking at things from the perspective of how could we more effectively accelerate efforts that go from discovery to development. What I am looking for in this other deputy director is a clinician who has great experience in terms of development to delivery, more of a translational effect, if you will, but particularly looking at the delivery component, where we have to bring those pieces together. So that is the kind of effort, and that is the structure.

CL: Would that person also direct the Division of Cancer Treatment and Diagnosis?

VON ESCHENBACH: No, that is a separate recruitment, and that is just about final.

CL: What about other recruitment? You have acting heads of the Office of Communications, the Division of Cancer Control and Population Sciences—

VON ESCHENBACH: Well, again, Bob Croyle [acting DCCPS director] is the designate there, and we are going through the final processes with him on the approval of his position, but Bob Croyle brings a tremendous set of skills to the DCCPS. I mean, his personal investment in behavioral science and his ability to orchestrate the full dimension of that, and he is going to be—and I should let him speak to his plans for the division, but I am really excited about a lot of the things that he is going to be doing. He brings a wonderful mix of leadership to the organization. I really believe very strongly in shared governance, and the role and importance of the Executive Committee and the senior leadership team working effectively as a team has been a part of what we have been working on this past year. We have been through a strategic planning effort, which is really to kind of lay out the broad portfolio, and to really define what our strategic initiatives have to be in terms of getting us to this goal.

So, you will be hearing about specific initiatives that we are going to be undertaking. I mean, part of what's going on is a systems problem, that as you pointed out, it is an engineering problem.

CL: I am not sure it is an engineering problem. I was asking *whether* it is an engineering problem.

VON ESCHENBACH: Well, I think it is.

CL: I mean the biology part of it. Is it an engineering problem?

VON ESCHENBACH: Well, I think it is an engineering problem, if we are saying the same thing and by what we mean by an engineering problem.

CL: Gleevec is an engineering sort of drug, but—

VON ESCHENBACH: Oh, we may not be saying the same thing.

CL: I was wondering whether cancer as you are showing it here—I mean, you are talking

interventions, and people working together, and that is sort of an engineering of a system.

VON ESCHENBACH: Yes.

CL: I am thinking of engineering in biology. Is the underlying biology an engineering problem?

VON ESCHENBACH: Let me answer it in this way and see if we are using the right concepts, and maybe not exactly the right word. Cancer is a systems problem, and the solution to cancer is a systems problem. Cancer in itself is a systems problem, in that it isn't simply the identification of the individual pathways and processes, the identification of the genes, the identification of the circuits, or the signal transduction pathways. It's also the understanding of how those pathways and processes are interrelated. What is the role of robustness and redundancy, in terms of how these systems work? So, one of the things that we are going to be emphasizing programmatically is the whole area of systems biology, because now, it is not only a matter of identifying the various components and pieces in a reductionist way, it is also the need to help figure how they link and integrate. Maybe when you interfere with one particular mechanism, there may be other pathways that also are important if you want to get the desired outcome, because there is redundancy in the system, or robustness in a way that is difficult to do.

So, if that is what you mean by an engineering problem, the answer is yes. It is a problem and it is a challenge for us to do the integrative biology, as well as the identification.

CL: I guess the reason I was asking is that when you come up with a Moon Shot sort of approach, which was a pure engineering problem, you could in principle set a goal. Here, you are setting a goal based on something that is one of the greatest mysteries of the universe.

VON ESCHENBACH: Yes, but where I think there is a critical threshold here is—just like I said, I don't know how long it will ever take us to eliminate cancer completely. I don't know how long it will be before we ever fully understand cancer. We may never. We don't need to know everything about cancer. We need to just know enough. Now, you might ask the question, "So what's enough?" But, the point is, don't set the problem in the context of cancer being so complex and so overwhelming in its biologic profundity, I guess, that it, therefore, is an insolvable problem.

It's not a question of solving the problem of cancer. It is a question of managing the disease process, to preempt it from ultimately taking someone's life and creating the suffering.

People don't die because they get cancer. If that were true, I would be twice dead. People die because they get cancer and we don't preempt it. Either we don't detect it until it is too late, or we don't have the weapons to change or modify its behavior, et cetera, et cetera.

Our goal is to ultimately understand cancer, but our goal right now is to understand it enough, and exploit that knowledge effectively, which is the real part of it, to be able to preempt the disease's ultimate expression of a lethal phenotype.

CL: But it's still really a major goal here.

VON ESCHENBACH: Of course it's a major goal! Of course it is. But in 1971—and so you ask, well, what is this? Another Nixon thing, with the National Cancer [Act]? In 1971, when that goal was established, we didn't have the tools, nor did we even have the fundamental rudimentary knowledge. Just think of what has happened, and think of what has happened even in increments, such as if you just think of what has happened in the past decade.

The point that I am making is, what I have asked the community to do is, to step back and look at the problem from that perspective. Look at the problem from the perspective of the tremendous progress that has been made. Look at it from the perspective of the tremendous investment that we have today in intellectual capital, in resources, in enabling technologies. Look at what we have learned about cancer as a disease process.

The various places along this pathway that we now have real—not imagined, not hoped for—real opportunity to impact and to make a difference. Proof of principle has already been established. We just need to drive the expansion of that principle, whether you are talking about chemoprevention, whether you are talking about mechanistic-based interventions, et cetera.

Just look at all of that, and then recognize that that has positioned us in a way that in 1971 was unimaginable and unfeasible, and being positioned, now in what I expect and look forward to us doing, is to rapidly accelerate and catalyze the effort to pull this all together.

We have got to keep moving with regard to discovery. Of course, we don't know enough about cancer, and we need to know a lot more. Of course, we have got many more things to learn and discover.

Of course, all of those things are true.

But, at the same time, having said that, just think about what is within our grasp. So, what the NCI is going to do, is to commit to continuing to drive the research agenda, and at the same time provide the leadership to bring the components and pieces together in a collaborative and integrative way that really get us to the point where we have made a difference in people's lives. That's the vision.

CL: Who do you look to for advice on the science?

VON ESCHENBACH: I am working through a lot of various ways of doing that. This is to be an embracing kind of effort that brings the entire community together. So, with regard to science, we have tremendous resources within the Institute itself, and even today, later this morning, I have a group of the intramural scientists coming in—Steve Rosenberg, and the usual players, and Carl Barrett [director of the Center for Cancer Research], and Dinah Singer [director of the Division of Cancer Biology], and people like that are fabulous.

Outside the Institute, we have been working a couple of different agendas. Eric Lander [director of the Whitehead Institute's Center for Genome Research] comes on the National Cancer Advisory Board, and shortly, even before I arrived, I went up to Boston and met with Phil Sharp [director of the McGovern Institute for Brain Research, MIT], who at that time was the chairman of the National Cancer Advisory Board, and while I was there, I met with Bob Weinberg [Daniel K. Ludwig and American Cancer Society Professor for Cancer Research, MIT], and Eric Lander, and Tyler Jacks [director, Center for Cancer Research, MIT].

Eric took on some responsibility for helping to drive a lot of discussion of the focus groups that will look at the various scientific challenges that you have been alluding to. We have put together focus groups that Dinah Singer and Carl Barrett have been developing and working, bringing people into the institution to help. I am really looking for a variety of ways of gleaning that real intellectual talent to bear in helping to think about the next step. We have reached out to a number people around emerging technologies, and what we ought to be doing capitalizing on things like nanotechnology, systems biology, the whole area of imaging is extraordinarily exciting, and we have to be sure that we are positioning ourselves in a way to nurture and develop that.

CL: Is the National Dialogue on Cancer serving as kind of an advisory body?

VON ESCHENBACH: No, the Dialogue hasn't really been an advisory body, as much as it has just been just that, an opportunity for dialogue and discussion. The one place that I think we have really had tremendous experience has been with the research team, and Anna Barker has been heading that up, which has made a nice link. But, the research team has really been focusing people on the issue of how can we accelerate the process of the development of these interventions, and I think it has been great to be a part of that discussion, and great in terms of trying to bring all the pieces of the community together.

Because, as I said early on, long before I ever came here, cancer is not just a medical and scientific problem. That is what we are critically focused on here. But it is a societal problem, and it has got all the other components. Just looking at maps the other day—death rates from cervical cancer in Appalachia, which we need to be concerned about, and how can we be thinking strategically about addressing that? Because that's not an issue of, we have to develop a new therapy, and we have to develop a new intervention. We have adequate tools—and we need better tools—but we have adequate tools with regard to cervical cancer, but we have to be sure that we are applying them.

CL: Do you ever see opening up the Dialogue to coverage? What happens now is, you have to be a member to be there. So, it's a problem.

VON ESCHENBACH: We can come back some other day and talk about the Dialogue in a different context. I can't speak for that, because that is not my decision.

CL: Do you see the National Cancer Policy Board as something that is useful to NCI?

VON ESCHENBACH: The National Cancer Policy Board has been useful. I think, like with everything, we have been engaging in conversations, discussions, as to how we can most effectively utilize that opportunity, and with Harvey Fineberg coming in as the head of the Institute of Medicine, he's just really been a great asset.

CL: So it will continue?

VON ESCHENBACH: Well, we are engaged in conversations and discussions, and that is still a work in progress.

CL: I guess the interesting thing about that

group is that it is advisory to Congress, and is funded by NCI, but just looking at the reports, they are interesting.

VON ESCHENBACH: Well, I think the point that you are asking, in terms of a work in progress, is that the work in progress for everything that we do is to try to ask the question, "How can we most effectively utilize this mechanism in a way that really adds value?" What Dr. Fineberg and I have been talking about is, how we utilize this process in a way that really gets the maximum impact. That's what I mean by a work in progress. We are discussing and working through how that might come about and how that could best serve.

I am looking at all of these things as tremendous assets, and asking the question, "How could they be even better?" I am looking at the cancer centers and saying, "This is an incredible asset. How can it be even better?" I am looking at clinical trials infrastructure, and the cooperative groups, and everything else, and saying, "This is a phenomenally important part of our agenda. How can it be even better?"

We need to come up with a bioinformatics platform that will enable the clinical trials infrastructure to be even better. We have got a great relationship with FDA. How can it be even better? So, we are always striving to ask the question, "How can this mechanism be even better and more effectively employed?" I don't have the answer for that yet.

CL: Would it be wrong for me to conclude from what you have said that it will probably be around at the next renewal?

VON ESCHENBACH: I don't know about that. I mean, that just has not gotten to that level of discussion. I don't have an answer for you. I don't want you to misconstrue from my lack of an answer that that means it is not. It would be inappropriate to send a signal one way or the other that, yes, it is definitely going to be this or it is going to go away, or whatever. I think the answer to the question is that Dr. Fineberg and I are engaged in conversations and discussions, and I have met with the National Cancer Policy Board. So it is a work in progress.

CL: Is 2015 a goal or a promise? Is a goal the same thing as a promise?

VON ESCHENBACH: Eliminating the suffering and death due to cancer is a goal. It is a goal that is attainable. The promise is that as Director of the NCI, I will be steadfast in the committment to make the goal a reality.

Cancer Letter Editor A Finalist For Journalism Award

Paul Goldberg, editor of **The Cancer Letter**, was selected as a finalist for the Gerald Loeb Awards for Distinguished Business and Financial Journalism, the highest honor in business journalism.

Goldberg was named one of four finalists in the "small newspapers" category—newspapers with circulation of less than 150,000—for his coverage of ImClone Systems Inc. and its development of Erbitux for colorectal cancer.

In late December 2001, ImClone disclosed that FDA refused to consider its application for approval of Erbitux (C225). Samuel Waksal, company founder and CEO, described the problem as resulting from a missing "train of documentation," a technical problem that would be resolved.

FDA is prohibited by law from discussing proprietary issues and does not release its official "refusal-to-file" letters in cases like ImClone's.

Goldberg obtained a copy of the confidential letter from FDA to ImClone. The letter revealed that the problems with Erbitux were far more extensive than Waksal had indicated.

The agency repeatedly warned ImClone about fundamental problems with the Erbitux studies,finally deciding that the data were uninterpretable and that new clinical trials would be needed. Goldberg's story, "FDA Says ImClone Data Insufficient to Evaluate Colorectal Cancer Drug C225," was published in **The Cancer Letter** on Jan. 4, 2002.

Days after the story appeared, a Congressional committee and the Securities and Exchange Commission began investigations of ImClone.

Waksal has pled guilty to charges that include securities fraud, conspiracy, obstruction of justice, perjury, bank fraud, and tax evasion. NASDAQ recently began "delisting" ImClone stock after the company failed to report its financial results. Erbitux is being developed with Bristol-Myers Squibb Co.

The Loeb Awards, established in 1957, are presented by the Anderson School at the University of California, Los Angeles. The award winners are scheduled to be announced on June 30.

Other finalists in the small newspapers category were Wesley Loy, Anchorage Daily News, for "On the Rocks;" Cadence Mertz, The Burlington Free Press, for "Anatomy of a Scandal;" and Eric Eyre and Scott Finn, The Charleston Gazette, for "A License to Steal."

HHS News:

U.S., Italy Sign Agreement For Scientific Cooperation

HHS Secretary Tommy Thompson and Italian Minister of Health Girolamo Sirchia recently signed an agreement to promote greater cooperation in health and medical science, including cancer research, between the two countries.

The countries agreed to cooperate on bioterrorism preparedness and response, oncology, and research and treatment of rare diseases.

"Each of these areas shows great promise, however the collaboration in cancer research may ultimately lead to the most hope for people around the world," Thompson said. "If we could end the threat of cancer as a death sentence for millions of people, we could truly brighten the lives of so many men, women and children walking on earth."

The agreement may be expanded to include other health issues in the future.

As part of the agreement, the U.S. and Italy are able to exchange scientific delegations, non-proprietary information and technology; organize meetings and scientific conferences; and coordinate scientific programs and government-sponsored research protocols, including clinical trials. This agreement will augment existing partnerships between the two nations.

The Memorandum of Understanding does not list specific projects in oncology, but does state that the parties will plan expansion of cooperation, said Joe Harford, head of the NCI Office of International Affairs. All activities will be subject to available resources.

"Italian scientists and NCI scientists have a long history of working together with several ongoing projects," Harford said to **The Cancer Letter**. "There are more Italian scientists in NCI labs in Bethesda/Frederick through the Visiting Fellow Program than from any other European country."

The components of HHS involved under this agreement include: HHS' Office of the Assistant Secretary for Public Health Emergency Preparedness, NIH, and FDA.

The Italian components involved include: the Istituto Superiore di Sanita' (NIH), the Istituto Lazzaro Spallanzani (Institute for Infectious Diseases), the Istituto CSS Mendel (Institute for Genetic Diseases), and the Alleanza contro il Cancro (Cancer Hospital Network).

Funding Opportunities:

Mesothelioma Research Grants

Mesothelioma Applied Research Foundation is accepting grant applications for developmental projects advancing pleural or peritoneal mesothelioma treatment. Grant amounts are $100,000 over two years. Projects may relate to benchwork or clinical research, must not be presently funded or pending review, and may be conducted through any not-for-profit academic, medical or research institution, in the U.S. or abroad. Application deadline is Aug. 15, 2003. Full details, review criteria and application form are posted at http://www.marf.org.

Inquiries: For more information, contact The Mesothelioma Applied Research Foundation (www.marf.org) executive director, Christopher Hahn, phone 805-560-8942, e-mail c-hahn@marf.org.

RFA Available

RFA CA-04-004: Molecular Targets for Nutrients in Prostate Cancer Prevention

Letter of Intent Receipt Date: June 19, 2003

Application Receipt Date: July 17, 2003

NCI Division of Cancer Prevention invites applications for R01 grants to define molecular targets for nutrients and further, connect those targets with phenotypic outcome in prostate cancer prevention. Candidate targets for examination should not only be influenced by a nutrient but also be closely linked to a significant proportion of prostate tumors, be relatively specific for prostate cancer across various genetic backgrounds, and be related to changes in tumor risk and/or behavior when modified. Investigators are encouraged to use in vitro and in vivo studies with various levels of target expression and to address confounding factors that influence the overall physiological response to changes in a given molecular target. The RFA will use NIH R01 award mechanism. The RFA is available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-CA-04-004.html.

Inquiries: Young Kim, Division of Cancer Prevention, NCI, 6130 Executive Blvd., Rm 3156, Bethesda, MD 20892, phone 301-496-0126; fax 301-480-3925; e-mail yk47s@nih.gov.

In Brief:

Friedman To Head City of Hope; Bigner Wins 3rd MERIT Award

(Continued from page 1)

Institute. In 1983, he moved to NCI as chief of the Clinical Investigations Branch of the Division of Cancer Treatment, and went on to become associate director of the Cancer Therapy Evaluation Program. He was recruited to serve as FDA deputy commissioner and eventually tapped by President **Bill Clinton** to serve as acting commissioner of the agency. Friedman is credited with helping to streamline the FDA's approval process and for spearheading the highest level of approvals for products, devices, and food ingredients in a four-year period. He became senior vice president of clinical affairs for Searle/Monsanto, and then senior vice president for medical and public policy for Pharmacia Corp. He also served as chief medical officer for biomedical preparedness at the Pharmaceutical Research and Manufacturers of America, in response to the events of Sept. 11, 2001.

"An outstanding individual with impressive credentials in clinical, executive and academic leadership, Dr. Friedman is well-suited to steer an effective course for City of Hope in the prevention and cure of cancer and other life-threatening diseases," said NCI Director **Andrew von Eschenbach**.

"City of Hope is recognized nationally and internationally for humanitarian biomedical research and for its profound contributions to modern medicine," Friedman said. "I am honored to work with the organization's visionary scientists and leadership team to accelerate medical discovery toward cures for life-threatening diseases."

Friedman received a B.A. from Tulane University and an M.D. from the University of Texas, Southwestern Medical. He received postdoctoral training at Stanford University and NCI, and has authored more than 150 scientific papers.

* * *

DARELL BIGNER was awarded his third consecutive grant from the NCI MERIT (Method to Extend Research in Time) Award program for his application to continue research and investigation on the immunological and biological studies of brain tumors. Bigner is the Edwin L. Jones, Jr. and Lucille Finch Jones Cancer Research Professor and leader of the Neuro-Oncology Program, Duke Comprehensive Cancer Center. Approval for the award was granted in February by the National Cancer Advisory Board. The grant provides Bigner with $3.2 million over the next five years. . . . **BOB WOOD**, chief of staff to HHS Secretary **Tommy Thompson**, is leaving the department to join the public affairs firm Barbour Griffith & Rogers as vice president and director of state affairs. Wood has served Thompson since 1994, when he joined the then-Governor of Wisconsin as an education policy advisor. . . . **RONALD HERBERMAN**, director of the University of Pittsburgh Cancer Institute and UPMC Cancer Centers, was honored by the Carnegie Science Center for achievements that have led to business, economic, and societal benefits in the biomedical industry throughout the region. Herberman will receive the Carnegie Science Center Award for Excellence in the biomedical category. . . . **MICHAEL SHARP** has joined the Emory University Winship Cancer Institute as clinical trials director and chief regulatory officer, said **Jonathan Simons**, director of the Winship Cancer Institute. Sharp was clinical director for regulatory affairs at AAI Pharma Inc., of Wilmington, NC. . . . **RAVI SALGIA** has been named director of lung cancer research at the University of Chicago. He was assistant professor of medicine at Harvard Medical School and the Dana-Farber Cancer Institute. . . . **SAID SEBTI** has been awarded a $1.2 million grant from the NCI Cancer Therapy Evaluation Program to develop drugs for breast cancer clinical trials. He is director of the H. Lee Moffitt Cancer Center & Research Institute drug discovery program. Sebti is developing farnesyltransferase inhibitors as anti-cancer drugs. Patients in the trial will be treated with a combination of Zarnestra and Adriamycin and Cyclophosphamide. Sebti will work with **Stacy Moulder**, assistant professor of oncology and member, Moffitt comprehensive breast cancer program, **Mokenge Malafa**, associate professor of oncology and surgery, also member of the breast cancer program, and **Joseph Sparano**, of the Albert Einstein Cancer Center in New York. . . . **SHELLEY BERGER** has been appointed to the Hilary Koprowski Endowed Professorship at the Wistar Institute, said **Russel Kaufman**, director and CEO, Wistar Institute. Berger was assistant chairman of molecular genetics at Wistar for four years. She holds adjunct appointments at the University of Pennsylvania in biology and the in UP School of Medicine in genetics.

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