

**Spaulding & Slye Colliers International
Pharmaceutical Achievement
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Nancy J. Kelley: Well first of all I want to thank you all for coming and wish you a very happy St. Patrick's Day. I am sure you will be relieved to know that I am not going to tell you a long corny joke about that. I hope you had a good day anyway. Thank you all for braving the weather.

I am Nancy Kelley and managing Director of Life Sciences for Spaulding and Slye Colliers. We are here tonight to discuss how to recognize and reward excellence in the process of moving from science to discovery to the treatment of human diseases. I hope that you will all participate freely, ask our panelist questions, and ask Adam questions. Our goal is to have the very best people, organizations, and their work recognized at the Third Annual Pharmaceutical Awards. This event is being moved from London to Boston for the first time this year. It will be held at the Boston Harbor Hotel on August 8th. We also hope to create a forum in which to inform and educate the public about the importance of applied research. The issues raised by it, and its importance for improving human lives. The key to avoiding misunderstanding and to achieving public acceptance in this area is better communication about ways that biomedical technology can be harnessed to practical applications in order to improve human health. We've assembled an accomplished panel of your peers tonight to lead this discussion. I want to thank all of you for taking time out of your busy schedules for coming. I also want to thank Adam Smith, Editor of Nature Reviews Drug Discovery, for graciously flying in from London to moderate this event.

The very first question you might be asking yourself is, what is a real estate development company doing sponsoring an event on excellence in biomedical science? That is a really good question and believe me it is a question that my company asks me all the time. The answer is that we finance, develop, build, manage, and lease the buildings that you work in. We try to create environments that will bring out the very best and most creative thinking in all of you. We understand that what goes on inside these buildings is what's important, because it has the ability to transform human health across the globe.

The mapping of the human genome ushered in a new era in applied research and medicine. With this spectacular accomplishment scientist now have the blueprint to build and run the human body. The next challenge will be to use this information in order to discover new treatments and cures for both inherited disease, as well as for those vast majority of disease whose causes are influenced by genes.

I am not a scientist, so I am going to leave it to our distinguished panel, and to the clinicians in the audience to discuss how we might recognize excellence in biomedical science. I would however like to open this discussion tonight by reflecting on a few of the personal qualities that I have observed in the very best scientists that I have known. The reason is that I believe that it is these qualities that help them to accomplish what they do. The qualities are curiosity, creativity, conviction, courage, and compassion.

Curiosity prompts an individual to move beyond the mere observation of a natural event. To ask the empirical question, how does this happen? Why does this happen? How can the answers to both of these questions be used to create something useful? I was on a date with a scientist once and at the beginning of the evening as we settled down to drinks, he leaned forward with great excitement and he said, "so do you want to know how bacteria communicate with each other?" Not necessarily your average pickup line, but I was intensely engaged by the quality of

curiosity and excitement of which I speak.

Creativity is defined as the process of bringing something new into being. It involves a different way of looking at things. A new way of perceiving the world, that does not occur to others. In our context, it is the discovery of new forms, new patterns, new formulas, and new ways of working together that will bring forth a new and personalized medicine. In the midst of radical scientific change, we sorely need scientists, business leaders, and clinicians that can demonstrate creativity in their own personal work.

Conviction, the path to scientific discovery is neither linear nor smooth. It involves false starts, failure, and doubt. The best scientists have the ability to move ahead in spite of this. It is called inner certitude. Alfred Whitehead wrote, "In formal logic, a contradiction often signals defeat, but in the evolution of real knowledge, it often marks the first sign of progress towards victory."

Courage is the ability to face risks that carry dangerous personal and professional consequences. In this context great scientists, exhibit two types of courage: the courage to face their own internal demons and the courage to face the outside world. Internal courage gives one the ability to persevere on convictions against overwhelming odds over long periods of time, even when one is discouraged and full of doubt. Rollo May wrote a book called *Courage to Create*. If you haven't read it, I would absolutely recommend it to you. It talks about the intense anxiety produced by the true creative encounter, and the ability of the artist, or in the this case the scientist, to express and advance that encounter in the outside world, in the reality of that world. Rollo May's conclusion: "If you do not have the courage to continue to express your own original ideas, if you do not remain true to your inner being, you will have betrayed yourself and, ultimately, the world, in failing to make a contribution to the greater good."

Then there is social courage. A good friend of mine, who played football in college and later rose to some prominence, always tells me, "Kelley, life is a contact sport." It requires social courage to advance convictions in a professional environment that is extremely competitive and often unforgiving. Especially when others are not entirely supportive.

Compassion is sensitivity to the suffering of others. The desire to alleviate human pain. Anyone who has ever had a mother or a father, a sister or a brother, a son or a daughter, or friend who suffers from a disabling disease, or from a disease for which there is no cure, knows of this unspeakable pain. If we let ourselves fully experience that suffering, than we are forced to do something about it. That is why we are here tonight. To talk about how the best in applied research can help people and their families in order to alleviate their suffering.

Many awards, such as the Nobel Prize, primarily recognize breakthrough advances in basic research. However, there are relatively few awards that recognize advances in applied research which transforms basic discoveries into therapies that can dramatically transform lives. In his book, *Racing to the Beginning of the Road*, Robert Weinberg wrote that one of the most brilliant scientific minds of the 20th Century, Otto Warburg, had a clear vision of the solution to the cancer problem crafted with precision and powerful logic. He knew how the cancer problem would be solved and he knew it with absolute and almost total certainty.

He started this all, years later, we are fated to finish it.

Now I will turn it over to Adam.

[Applause]

Adam Smith: Thank you very much Nancy and I would like to thank you, and your team, for giving us the opportunity to spend some time discussing the subject of awards for scientific achievement in drug discovery and development.

My hope is that we will be able to have a productive debate on whether we should go about recognizing scientific achievement in drug R&Development with specific awards, and if so, how best to go about doing this, with an outstanding panel to lead tonight's discussions. From the opposite end of the table, Steven Holtzman is CEO of Infinity Pharmaceuticals. Judah Folkman is Andrus Professor of Pediatric Surgery and Professor of Anatomy and Cellular Biology at Harvard. Tom Maniatis is Thomas H Lee Professor of Molecular and Cellular Biology at Harvard University. Ken Kaitin is the Director of the Tufts Center for Drug Development. Fred Goldberg is Professor of Cell Biology at Harvard.

We have a lot to cover in the allotted time so my intention is to direct questions one at a time to selected members of the panel and then to open up debate to the floor. Since we only have about 65-70 minutes left, I think my main role this evening is to make sure that nobody hogs the microphone for too long. Once the debate has run a little bit on one question, we can then move on to the next question as appropriate. Obviously, some questions will be generated from the floor and you can direct those at the panel. The only point that I would make is to please introduce yourself before saying anything. There are two people very helpfully standing around with microphones so if you want to say anything you can just raise your hand and one will arrive. The discussion will be recorded and we plan to circulate transcripts of the discussion to all participants. That's it for me and I will pose questions from now on. To kick things off I was going to ask Judah and Tom to address the starting question of what role do they think that awards play in promoting scientific excellence? Judah.

Judah Folkman: Thank you. In preparation for this, I polled my colleagues at Harvard Medical School. About half of them expressed espoused enormous modesty. They said they didn't care about awards. They showed no interest in it. That thought you should take the medals home and not brag about them, and never mention it. They thought that they didn't work for awards. The other half said they preferred honest conceit to false modesty. [Laughter] They thought that awards in fact had helped them in their career, and it is very interesting, especially when they were young. They felt the first award they got greatly increased their self-confidence. If you have a lab with younger scientists in it and post-docs and they have begun to get grant rejections, somewhere along the way an award really is very helpful for self-confidence. Many of our young scientists begin to recognize that a life in science is to live with relentless criticism, especially if you have a very good idea. Then it gets even worse. However, an award says that the imprimatur of the award committee somebody did their homework and read those papers. People recognize that as very helpful and they can remember the first award or the second one. Bob Langer at MIT told me that an award also helps a field. Chemical engineering that was not a field that was highly recognized as other areas of biology. When he began to get some notable awards he noticed many bright young people coming into chemical engineering saying this is a really good field and didn't know about it. Therefore, it's a recognition of a field.

The other thing is that if you look at scientific careers, if we watch our post-docs and then they become young faculty, probably there is not such a career with so much failure as there is in scientific research. It's a huge amounts of failure punctuated by the occasional uh-ah moment. An

award really helps to sustain through all those kinds of tough times in science because you are in unchartered seas. I would tend to agree with the colleagues that it really has changed their self-confidence and has helped their own science. It is the same, I think, in the pharmaceutical industry because I have seen it from that side also. An award within the company, or one that is published outside, brings very high moral to the team and also to the awardees.

Tom Maniatis: I really believe that the great value of an award like this is communicating science and discovery to the public. I would disagree a little bit with the motivation of doing science for awards. I know few people who really are motivated by that. They are motivated primarily by the discovery and excitement of discovery. I think that prizes can be negative in some ways. It can elicit behavior that is not the most admirable. If the process is fair, careful, and very thoughtful, and I think that is the most important thing, exactly how are these awardees chosen, then I think it's good for everyone. I think it is very positive for the people who are recognized. It recognizes tremendous amount of hard work, insight, and creativity. I don't think it should be the incentive for what we do.

Adam Smith: Fred if you want to make a point.

Fred Goldberg: I just want to comment on, I agree with what Tom just said. I think the military gives awards for courage not because you expect a person on the battlefield to go to help his colleagues in a heroic way because there is going to be some purple heart or cross out there for them to win. It's a way of the society saying these values and behaviors are the ones that we most respect. It gives these people who will receive the awards the stature that the society recognizes this is the highest achievement. I think in giving awards to this area of science or other awards to basic science, the committees that choose are saying this is the kind of achievement we most applaud. This is the highest achievement in the field. I think each society recognizes different areas of achievement. This helps the field be recognized widely. It is not a motivating force, it's an affirmation.

Adam Smith: Okay, thank you. The follow up question to that is if we think awards play a role in promoting scientific excellence, should we separate out a separate category of award through applied research rather than basic research? Specifically, I suppose, applied research in drug discovery and development. Steven would that be something that you would like to talk to?

Steven Holtzman: Sure. I agree with the perspective, I think, that Fred just articulated that the purpose of awards, outside of a company giving awards, is a motivator and promotes certain kinds of behavior. When a broader group gives an award it is because we are saying that the activity itself has a certain nobility, which we wish to encourage. Therefore, it's less about motivating the individuals in it than saying this is something that is good for society that others in the future ought to pursue. To that extent, you still, though less than in the past, have a certain view of pharmaceutical research as the dark side verses academic research. To the extent that we can acknowledge that, it's a noble activity to take basic science discoveries and direct them to better medicines, that that in itself is a noble activity. I think that is something that is important to communicate to younger people and that it should be held in esteem. I do believe that you should separate the different kinds of awards. We can get into this further, I could do it now or later in the questioning, of the difficulties of choosing accomplishment in drug discovery versus basic research.

Adam Smith: We will get onto that soon, yes. Ken did you want to say something?

Kenneth Kaitin: I would say it's not just that the award should be separate for applied and basic research, because as has been brought out already there are awards for basic research, but that the time is right now for awarding applied research. I run a group that some of you may know that tracks trends in pharmaceutical development. Over the past 28 years we have looked at the time, cost, and risk to bring new products to market and one of the trends that we have noted and has gotten a lot of attention in the press in the lack of productivity in the industry now and the dwindling pipelines. Many of you are familiar with some of these issues. What we are hearing more and more is to move away from the blockbuster model of drug development. Which is the type of drug development strategy that focused on market considerations for choosing products to develop, as well as large indications or large populations. We are moving more towards a science driven approach to R&D. I came with a quote as well that I share because I have been talking on these issues for quite a while. It is a quote by James Bryant Conant who some of you may know from his most famous quote which is, "Behold the turtle who only gets ahead by sticking his neck out." You may have heard that quote. But, he has another quote, by the way he was the Harvard President in the mid 1900s, and he said, there's only one proven method of assisting the advancement of true science, that of picking men (and presumably women) of genius, backing them heavily and leaving them to direct themselves. I think that embodies the essence of non-blockbuster R&D within the industry, and the move that we are seeing of large firms interacting more with smaller firms. Something that has benefited the economy in the Boston area and has lead to a lot of the larger firms putting offices here. All of this relies on individual scientist giving the opportunity to advance their area of expertise, and their research interest. Not just the basic research, but the applied research that will eventually many years down the road lead to advances in therapeutics.

Adam Smith: Thank you. Does anybody in the audience have any comment on the split between applied and basic research in awards? Yeah.

Dennis Goldberg, Nexus Therapeutics: I think it is an important comment about going from academia into industry. When I left academia where I had anticipated my career and then went to Pfizer in the industry, I was roundly abused by my colleagues in academia for selling out. If you are a talented person, going into industry has been considered stepping down or moving away from the pure science and so you don't get those awards and you are discouraged from what you are doing. Then as one of the people who recruited me at the Pfizer said, putting a drug on the market changes people's lives and that is the important part of it. We don't get recognized for that and I think that is very important to recognize applied science. It is very hard in big pharm companies that want to manage creativity to be a creative person. You have to fight against a system.

[Unknown speaker:] I would like to comment on that because I think the point you made is an important one. When I was a student, or a junior faculty, yes the social climate of Boston academia would be one of condescension. For instance, an talented person would go into industry because basically pharmaceutical research was pedestrian research. I think that has really changed in many respects in many areas of science there is a very close continuity between the cutting edge and

applications. My colleagues now a days, as soon as you discover something you are mentioning how it might be utilized for therapeutic applications. I am talking about basic scientist in the [inaudible] community. I think a big change, and it should be reflected in awards, happened probably in the '80s when people took the lead in developing biotechnology companies. There was really a premium on taking information and putting to the good of the citizen hood through better drugs or rash of drugs. That's a very important niche to recognize whether the creative step is in academia. in biotechnology, or pharmaceutical industry.

Adam Smith: Tom.

Tom Maniatis: I serve on the Lasker Committee for the Lasker prize for the last two years. Three prizes are given, but two primary prizes, one in basic science, and one in clinical research. The clinical research prize tends to go to individuals who have been really a part of the basic discovery itself. There is no recognition by the Lasker Committee for the kinds of activities we are talking about here today. I think to convey the excitement, energy, and the complexity of bringing a drug from a discovery to a patient is spectacular. I agree that that has not been recognized in any formal way and I think it should be because of one of the reasons you mentioned. It provides recognition of an area and allows people to go into that with pride and enthusiasm. I feel very strongly that it is a very different process, if you want to call it translational medicine, than discovery and even strictly clinical research. There is a niche between clinical research and basic discovery that really is not recognized.

Judah Folkman: Why do you think that is? I see the same thing on the [Gardner] Committee. Is it because it simply is not accessible to the committee?

Tom Maniatis: I think it is partly that it is not accessible so it is hard to identify individuals. In addition, the enterprise is so different than basic or clinical research. It is often times very difficult to identify an individual that one can recognize. I think that is what we are going to discuss that later. I think that is one of the problems that we have to deal with. What is really amazing about biotechnology companies or a big pharm is that a very large number of people have to work together as a team to make something happen. How do you recognize this effort? That is what I find is the most difficult.

Adam Smith: One point from the audience?

Bruce Cohen, McClean Hospital: And I am also a psychiatrist so people should be careful about interpreting what I say. Perhaps just to follow up on some of the points. In my own career I have noticed that people get awards, some of them because they hang around with societies a long time and you give them credit because they go to all the meetings. Then there is this other type of award that I think we are talking about, which is that you are making a statement that what someone has done is worth great credit for society. In this distinction between basic and clinical, to me, my father was physician and that's probably the reason I am, it is very easy to appreciate someone who cares for you directly. Equally, it is very easy to appreciate someone who comes up with an intellectual advance that you could have never of come up with yourself and thereby that person gets the Nobel Prize, or some such other award. It is not so easy in the middle ground. I think if there is a point for this award, which to me is very strong, it's that we are on a threshold where not

just in the pharmaceutical companies, but throughout science, we can now take some of these basic technologies and do what was properly called translational research for the benefit of society. If we are to advance that maximally and to give credit properly to the people who are able to do this, such as the people on the panel in front of us, we ought to give awards for it. It may say a social comment as to the value of the activity and the effort that goes into it. It seems, I think, on that basis relatively clear that this is a good endeavor to encourage and acknowledge.

Adam Smith. That brings neatly onto the point of how we best identify excellent research in this field. Speaking as science publisher, I can think of one reason why it is hard to identify, there are just so few papers coming in. There are many other reasons. Who on the panel would like to address this issue? Anyone jump in? Tom do you want to go? The question is what are the problems that one faces in identifying applied research in drug discovery and development? Why is it different from identifying good research and basic research?

Tom Maniatis: Well I think I more or less answered that previously.

Adam Smith: Okay.

Tom Maniatis: I think that it is going to be difficult because most of these endeavors are not transparent. One sees at the end of the road what happens. I am not sure how we can do that, what mechanism we have of actually looking inside of a company that developed a great drug and recognize the appropriate people. One could image that one could have a category in which you actually recognize a group in a company for a drug. That probably would be the appropriate way to do it because, as I said, the enterprises differ so much from basic research it is really hard to give credit to a single individual. I think there are cases in which there is a champion in a company that takes a product or a drug that no one believes and he or she fights for years and finally it happens. In that case, if it is generally known that that occurred, it would be appropriate to recognize that individual.

Adam Smith: I think one could segregate out two things. One is recognizing individuals versus teams. Then the other is recognizing the research at all because it is all done behind closed doors in many cases.

Tom Maniatis: I think that unfortunately, there is an end result, and there is an impact on the human health. That can be the starting point to work back from to try and identify how that accomplishment should be credited.

Obed Cepeda, Transkaryotic Therapies: First of all, I want to say that it is an honor to be in a room with all of you. I recognize a lot of your names from when I was in med school.

Adam Smith: Can you identify yourself?

Obed Cepeda: Yeah, my name is Obed Cepeda, I am at Transkaryotic Therapies and I am also an MD by training. I just would like to say that my perspective on it when I was at Yale in the '90s there was a lot of pharmaceutical biotech companies spinning out of the University. There was a huge wall between the academics at various institutions and a lot of the leaders in biotechnology

and pharmaceuticals. One of the important things that would have to be done, it seems, and I am sure that a lot of you are thinking of this also, that what ever committee was awarding this recognition would have to be a very careful mix of academics. Also, a balance of people in these companies, so if it was 12 people, maybe 6/6 I don't know the exact number. That would balance off several issues. One of which historically has been issues of resentment because there have been a lot of financial awards granted to people and who have spun off into business. I am thinking about people such as Voyeur at [inaudible] Tech who is able to bridge the science and business. Jonathan Rothberg who founded CuraGen, he for example has an interesting perspective. The committee that was formed that granted the award would have to be a very careful mix of both industry people with strong science backgrounds and then academic to validate the science they are proposing for the award.

Adam Smith: That is an important point. I think we will get onto the criteria for selection a little later. Fred do you want to speak about problems identified?

Fred Goldberg: I was just going to make one comment. The problem that we are trying to face is how to best to honor people who have major achievements in development of therapies of applied drugs. Some of those people would be recognized by the usual scientific criteria. Many or most will be and some areas will be academics who saw opportunities and developed the science in a direction that lead to therapies. One can think of topics like angiogenesis, where insight was linked to pushing for therapeutic applications. It is much harder of course because the pharmaceutical industries there are these large barriers to visualize from outside what goes on. You will have to depend on companies to nominate their own distinguished leaders. If there is a spark of leadership there and insight, they are the only ones who are going to say it. Teams, I don't see how you can honor, especially if they are large teams. I think you are going to have to depend on big industries to select their own special intellectual leaders. In biotech companies, it is a little easier because there are often people who are running the companies, seeing the applications, immersed in the science, and pushing the therapies. There I would suggest you look for major achievements such as beta interferon, gamma interferon, erythropoietin, and ask was there an individual in this major achievement who lead intellectually in the applications of basic insights.

Judah Folkman: Tom mentioned champions. It is interesting, when there is a champion that had to overcome a lot of difficulties in a company that often reaches the public awareness because you have Receptin and you have Pulmozyme, and you know the names that go with that. Those are easier than if there was no champion. There is no equivalent either of the Dean in the company who goes around and says we would now like to select who we should honor in the University. I don't think there is in a company, but that would probably help.

Adam Smith: Steve?

Steve Holtzman: It is very striking to me that the examples that were all thrown out were biologics. Largely where it was the case where you clone the gene and you clone the drug. It is almost as if there is an infection of the academic model of research and it's a pharmaceutical research. When we move to small molecule drug discovery, we are into a whole other world. It may be true that Tom Maniatis elucidated the role of NF Kappa B, but NF Kappa B wasn't the drug. That's the anti-cancer drug. You have to start to think about the paradigm of the discovery

differently and then the key discovery differently. What we will also have to focus on, is the key discovery or the key discoverer taking place at different parts in the chain. For example, it is easy if you have got the person who said damn it this target, I made the molecule, drove it all the way home, mortgaged my house, and made it happen. Some of us know one of those guys. What about the person who said gee this molecule which failed in this syndication and is sitting on the shelf could be repurposed for this alternative indication. I don't know a wit about basic science. Yet, that can be the billion-dollar drug or the drug that can make a huge difference. The person who observes that AZT which is a failed cancer drug that can be repurposed into anti-virals. Depending on which hypocritical story you want to believe, the statistician or the nurse in England, who noticed that that failed cardiovascular drugs that the guys didn't want to give up because they were enjoying taking it. That is the Viagra story, right? You are going to have to be open to the awardee having different flavors. Individuals or teams from different parts of discovery and development in the spectrum.

Adam Smith: One has to really reinvent the criteria for an award?

Steve Holtzman: Say again?

Adam Smith: You will have to reinvent the criteria for an award.

Steve Holtzman: If what you are recognizing at the higher sort of abstract is the human activity that takes a piece of science and makes it into a medicine, that is maybe not sufficient, but the necessary condition that got it across. That insight can take a lot of different forms.

Adam Smith: Good point.

Tom Maniatis: This may just argue for different categories for awards. An award for translational research. An award for mechanistic research. Everything that you are saying would suggest that you can't pick one person or one area of the chain and say this is the one that lead to the product at the end. It could be anywhere along that chain so why not award at several levels?

Adam Smith: Yes.

Dennis Goldberg: Dennis Goldberg again. I would like to comment on the idea of big pharm companies nominating their own awardees. Very often the person who stands out from the group, as we talked about the champion, is the one who has to fight the hardest against the establishment, the gadfly who is politically incorrect inside the big pharm company. I will give you a specific example of Al Albert who was at Merck and he was responsible for the development of Mevacore. He was told very clearly that if he didn't stop this he was going to be fired. He persisted and finally got them to develop it and changed the entire spectrum of how we treated atherosclerosis. I don't think that a lot of people at Merck for a very long time were going to nominate Al Albert for the award that he deserved. It is very difficult particularly in big pharm to get them to nominate the guy who forces the breakthrough against the grain. That is the person who perhaps needs to be given the award the most.

Adam Smith: Someone at the back there.

Judah Folkman: I think I feel the need to put in a word for that end of applied research which are the enabling technologies. It is so easy to just leave them out of the spectrum of the discussion. I think that we can count on the fingers of one hand the sort of notable cases where awards at the level of the Nobel Prize have been given for CAT scanning, more recently for magnetic resonance imaging, PCR, [Carrie Melus], but so few times for such powerful cross-cutting issues. Maybe that is an argument for having categories just so that they don't get neglected by being regarded as somehow intellectually less important to work on. End of point.

Adam Smith: Yes, please. Don't forget to identify yourself, please.

Upendra Mishra, The Mishra Group: My name is Upendra Mishra for The Mishra Group. A lot of us who have kids we know the well the work of awards. They get their certificates in the school and it is framed, and they are excited. They get very motivated. It is beyond dispute that awards are very good for kids, the scientific community, or anyone. The key question is we see that in those people who really make a lot of noise and have a big mouth, they really get the awards, but those people who really do the genuine research they really don't care whether they get an award or not. They are so focused on their research and what their mission is. I think for the community, which is really trying to encourage people by getting awards is how to recognized those people. They are the ones who really make a difference. Is there anyway to encourage them and recognize them? Second, when we give this drug discovery or give them their awards, what person did receive the awards all by accident?

Adam Smith: Tom.

Tom Maniatis: I would like to respond to that. I think that in basic and clinical research those questions are answered by scholarship, by carefully reading the literature, by knowing your colleagues, and finding out who really did what. I presume that the same thing could happen in this case. It gets back to the issue you brought up, that having the right set of people making these decisions. A thoughtful and careful debate is important to distinguish the braggers from the doers. I think it is possible. Certainly, it has been possible in other awards. It is a matter of process and a matter of bringing the right people to the table that have the ability to distinguish between those.

Adam Smith: Is it the point though, that we can only ever make awards for done deals? For drugs that have reached the market, because, as you say, then you can then go back and investigate what happened. Is there anyway to recognize scientific excellence along the path, do you think?

Judah Folkman: [inaudible] manufacturing advance that are very important that the drug ever makes it to a patient. There are synthesis changes. In fact, there are big advances in taking the toxicity out of a drug that make it much better for patients. Those are all along the way. I can think of many examples, but I can think of any awards for them. Yet, they relieve suffering in many places.

Tom Maniatis: I would say that if you want to think about awards in the roles that was described as enabling technologies, then you could certainly do that, so to speak, along the way because it's been applied. There is the primary focus here of drug discovery and development. You don't

award medals to people who lead the 100-yard dash at 50 yards. You can only decide after you have gotten across the finish line.

Fred Goldberg: Yes and no. I think the Nobel Prize emphasizes a single major contribution. Often there are individuals who have had a lifetime of important contributions that are fantastic scientists who have changed the field. However, they have not done one singular contribution which those awards tend to recognize. I think it would be very appropriate for a series of lifetime achievements of leadership and in a number of therapeutic areas or drug development, that those individuals be singly recognized.

Tom Maniatis: But Fred, I guess what I would say is that is either going to take the form of the drug that they made or more than one, or a piece of enabling technology that's broadly used. I am perfectly fine with the latter, but let's not confuse that with the goal of getting a drug across the finish line. As soon as you lose that, you are now getting into awarding public ... [cuts off]

Judah Folkman: --one of them is Sir James Black and the other is Paul Greengard. In both cases, they said that the Nobel Prize changed their life immensely. In fact, Paul's comment was that before he got that award he had no friends. [Laughter] Shortly afterward, he said that it was amazing how many people became his friend. Jim Black pointed out that until the beta-blocker business became a business, became a billion dollar industry, nobody really cared, and he didn't get his award. His point was is that at the end of the day, there are many, many great ideas but until they mature into something that is fiscally or financially valuable, it doesn't seem to be acknowledged. I think that you have a real challenge here in all of that. Certainly, the Nobel Prize granting group is widely acclaimed. I think that it is an interesting challenge as to how to go about making that determination.

Tom Maniatis: I should say that also has a very negative affect on many people. The perfect example is Dan Nathans who felt that it ruined his life. He felt that it distracted him from what he really was interested in doing and put him into a situation where he has to constantly fight lectures and commitments to not embarrass people or himself. It works both ways. It can change people's life in a positive way, but it can also change people's life in a very negative way.

Bruce Zetter, Children's Hospital: I want to bring up the point of what is a good prize and what is a bad prize? Do we need another prize? The ones that we've heard mentioned tonight are the Nobel, Gardner, and the Lasker. Prizes that are very well known and that most people would say are important in some way, and well recognized. There has been an enormous increase in the number of prizes over the last 20 years. It is going up exponentially. There is clearly some advantage to the prize giver to setup a new prize. Is there an advantage to the scientific community? The question that I want to bring up is what are the metrics by which we analyze whether a prize is an important prize? Whether it is worth giving, or worth receiving. Whether it will be known except to the giver or the recipient, or make a difference to the public, or to the science that is being undertaken.

Adam Smith: Does anybody want to tackle the question of metrics? Apparently not.

Bruce Zetter: [inaudible] there are people up at the table who have gotten many prizes and they

don't talk about all the [inaudible]. Clearly [inaudible] and if you are going to establish a prize I would think that you would want to think that that prize has a chance of being an important prize.

Tom Maniatis: I agree with that and that is why I keep getting back to this is the process. If the judgment of the grid viewed is fair, thoughtful, as apolitical as possible, that prize will reach a stature that is very important. If it is felt of the sort we have heard before, of being in a society for 20 years and you naturally are recognized because you've patted a lot of people on the back. I think that it gets back to whether you established the criteria in the process carefully enough that it's viewed as a very honorable thing to receive.

Judah Folkman: You mentioned what you called a good prize, the Nobel Prize for example, none of us would turn it down. What is interesting is why, because it brings a sense of society's respect for these achievements among the scientific peers. It has given a platform to some very talented people to voice their opinions to the larger community and to governments. It is respected as a good prize because it has maintained a standard of excellence. That is continually a point of interest. As has been the Lasker. If the goal is to continue to achieve, choose candidates, real excellence, then the prize will be respected as a major attractive award for a career. It would also tend to exalt itself in the future and give a certain influence to people whose influence we want to applaud, and increase.

Adam Smith: Ken did you want to make one?

Ken Kaitin: I think one of the factors in establishing a credibility of any kind of award in this category, which is a very good question that you bring up, it is how closely you can link the award with what the public and academic community considers to be a substantial achievement. The closer that the linkage is established between the award and that achievement, the more the credibility the award gains just by being linked with that advance. I guess this in part would argue some of the issues that have been discussed so far, when you start looking at critical parts earlier on in the process, a pathway discovery or something along those lines, where in the public mind there isn't a real—it is hard to see the value of that to a final product. Then the award sort of gets lost in there as an award that was given for something that not many people really understand except for a select group of people that really understand that degree, or that area of science. Whereas in the initial stages, I would think, there would be a high premium on establishing a linkage between an award and advances that are universally recognized as critical.

Steven Holtzman: I think the point is wonderful of course, it is sort of obvious in a very concrete way that it partly depends on how many prizes you give. As well as on who gets the award. I think that it is true that if you give the award to someone that everybody shakes their heads and says oh yes that was an appropriate awardee, then the prize actually gains luster. If you give 20 awards every year then the prize loses luster. I didn't pay too much attention to the materials but I think this is the third year of these prizes?

Adam Smith: Yes.

Steven Holtzman: Sorry, this has never been given?

Adam Smith: There are pharmaceutical achievement awards, which are in their third year which should be awarded in August, but this discussion is peripherally linked to those. We are talking really about the best-case scenario for starting awards in drug discovery and development.

Steven Holtzman: Which is why I was actually wondering exactly what we were talking about. Are we talking about a single award, are we talking about five awards, or are we talking about 20?

Adam Smith: I think that the question is open. It is how many awards should there be, and what should they criteria be.

Steven Holtzman: Fewer will have more impact.

Adam Smith: Okay.

Tom Maniatis: I agree with that and I also think fewer individuals as well. Most of the prestigious prizes go to no more than three individuals. The Lasker committee adheres to that very aggressively. It is the same thing there, too many prizes dilute the significance. Having a dozen people recognized also dilutes that. Then we get back to the issue we talked about before of how to recognize team efforts. I think that it is much more complicated with an applied award than it is with a basic research.

Adam Smith: Indeed because it probably becomes the case of recognizing a few teams.

Tom Maniatis: Right.

[Cross talk]

Fred Goldberg: We talk about what's a good award and what's a bad award. There are certain areas where the most valuable player in the baseball league, scorers, they continue to have an impact because the records was not—they might not be the best choice but they are outstanding choices and there is a continued interest in the criterion but with the best pitcher. These remove most of mediocre examples. Here, I think, the first steps, the first awardees, will set a pattern that can make it into an influential, what you call a good award, or something that nobody knows is.

Steve Holtzman: I think you are also going to have to consider the criteria that certain billion dollar drugs address very important medical needs. Certain billion dollar drugs arguably are lifestyle drugs. Fifty million dollar drugs interest important medical needs for a small population. How are we thinking about it? Which is the award? What are we awarding? Is it the thing that does the most advanced piece of elegant science that eventuates in a product? Is it a piece of, in retrospect pretty simple science, but it really made a difference in terms of something that was life saving? The fifth statin was Lescol, which did nothing. The sixth was Lipitor. It makes a difference in people lives. Yet in terms in the advance and the science, not a

lot of difference.

Adam Smith: Sure, but coming back to the point that was being made originally, the single goal of recognizing scientific excellence within the development of drugs is a big enough challenge, I would have thought. If you go ahead and recognize medical advance on top of that without science, that is a separate challenge I would have thought.

Steve Holtzman: What I am asking is what is the relevant scientific challenge? When you say scientific excellence, what are you thinking of it? What does it enable and what goal? You could have an incredibly elegant piece of science that gives you a lifestyle drug. Do we care about that?

Adam Smith: No, I understand.

Don Lombardi, Children's Hospital: I think the last comment is on target. I think I would see almost a three stage process where the first stage is to identify development which warrants the attention. It would be the focus for the award. The second would be to assemble a narrative about how that took place, not from the company, but through a panel such as this, to really get a validated story, because there is no one pathway that results in innovative drugs. In fact, going back to Nancy's introductory remarks, part of the overall process is to simulate public interest and awareness and how advances really do take place. I think generating that narrative of how a particular development did occur would be in itself a very interesting and useful result. Then only after that could the group maybe identify the three key individuals who played the right roles, or the key roles. The result of that kind of a process would be to highlight, as almost an exploratory piece of work by the committee, the kind of roles that really are effective in advancing this kind of translation. I think to try to set in advance what the criteria would be for selecting the individuals would be a mistake. It might be best to do it experientially based on what the narratives were that themselves were worthy of the attention of the group.

Adam Smith: Okay. Francine.

Francine Benes, McClean Hospital: I think this type of award does present a unique challenge in terms of assessing scientific excellence, because of the profit motive that is inherent in the development of new drugs. This is something that, because of human nature, can influence the behavior of scientist. In some respects, degrade the scientific process. It has been known that hoarding of data is practiced to prevent competitors from having results that might help them get to the finish line before oneself. This of course is going to represent a delay to the entire scientific undertaking that is perusing a new drug for the treatment of a medical disorder. In evaluating scientific excellence in the applied sciences, I think, it is absolutely critical to take into an account the behavior of the scientist who are being considered for the award. Not just the science that they have done or the discoveries that they have made, but how they have acted along the way, and how their behavior has influenced the rest of the scientific community.

Fred Goldberg: In terms of the Lasker or the Nobel are those considerations at all at stake, or is it just assumed that it is all very noble and it's [cross talk]

Tom Maniatis: That is the point that I was actually going to make, I have worked on both sides, and I can tell you that ego is more powerful than money. There is more bad behavior to go around in academia than there is in almost any other enterprise. I wouldn't simply state because there is a profit motive that somehow that leads to bad behavior. I think ego is equal to or greater than money as an incentive force for bad behavior.

[Cross talk]

Ron Newbower, Partners: I never disagree with Bruce Cohen or maybe it is just because as a psychiatrist he makes me feel I am never disagreeing. I just push back on the idea of the only way to get the impact is with small numbers by using the MacArthur Awards as an example of the so-called genius awards. What engages people about that is that I think that they are imaginative. They identify people who would have not have been obvious. They are not just the ones that would be on everyone's short list, and therefore it doesn't have that much value. They certainly make a difference in individual's careers in remarkable ways, and they certainly make statements to the public that do all of these things by identifying people who are not at all on the radar screen. They do it with a fairly large number of awards and do it in different areas, different fields, and disciplines. I offer that mainly again away from the top of the pyramid.

Judah Folkman: Can you image a MacArthur Award system for the pharmaceutical industry worldwide? Multiple?

Ron Newbower: I think the key words are that it has to be clear that it was not political and it was a thoughtful process. However, it doesn't have to be the obvious short list. It is clear that a lot of homework went into identifying who those people were, then it has legitimacy and it's imprimatur. I don't know if that is responsive but—

Tom Maniatis: I think that it is important to recognize why the MacArthur Award are so popular. I don't disagree with you Ron, [cross talk]. I would never want to make you feel bad, but the MacArthur Awards have—anybody who writes newspapers will tell you that the story is human interest. Accuracy is less important. Sorry about that too, Francine. In this particular case if you are trying to establish awards you can do it a number of ways. One is to give it to people who are clear exemplars of interesting people. The people who win the MacArthur Awards often, as you suggest, they don't have money to do what they are doing. I think it is an important side to what Francine was saying too, that they are getting these awards, they are often people without a lot of money, they would be able to do what they were able to do without it, but they make good press. Really good press because of what they are doing. They don't give a lot of them away. There are multiple Nobel Prizes too, but there are not that many of them. I think that in a situation like this if you can find some people that, everyone will agree, are well worth awards and they make good stories, and there are not too many of them, you've got your strongest case that all those things matter. The MacArthurs aren't given for the same kind of enterprise.

Adam Smith: Let's move on to the question of how we would identify such people, and what the best process for getting these awards moving would be? Do you have any feelings, Ron, on how one should pick the unsung geniuses that you are talking about?

Ron Newbower: You mean out of the MacArthur? Is there any— Certainly I don't know how they operate because part of their strength is that they don't want to give any impression that there is a back door into the process?

Tom Maniatis: I know the process and basically, they send out as many nominations as they can to people who they respect and trust, and ask people to nominate. Then they have a very diverse committee go through these applications and narrow them down to a short list. Then they have a committee to make judgments on them. It is a very systematic and very careful process. It starts with just going out to the community and trying to find these people. In their letters of nomination, they establish criteria that they wish people to write their nomination letters on. I think that is basically the way that it works. That is how you find these rare individuals because they are out there, but they are hard to find.

Judah Folkman: I am not even sure why the analogy is attractive. That is a wonderful award to—it is quite different from pointing to leaders who have really influenced the development of drugs. Who have influenced the thinking about areas and who have lead in applied applications of knowledge. These people are usually visible and they are recognized by their peers. They are looked up to by their peers. They may have been catalysts in a field. I think to look for hidden gems is a very different role than the kind of awards that we are talking about.

Adam Smith: That is a good point.

Steven Holtzman: I think that they are not hidden gems, but I think that you have to deal with the fact that since this is science that takes place in corporations which are the larger corporations who have big PR machines and have the kind of politics that were discussed, you can't trust the official story from the top. If you read the story of Gleevec today, a lot of people invented Gleevec, but a lot of people who invented Gleevec we've never heard of. I wonder if there isn't a process of actually going out into the rank and file of the R&D of the corporations, because they know. The scientists know who are the people who really made the difference. [Cross talk] Readership might be an interesting award.

Adam Smith: We seem to be talking about a process of investigative journalism and reconstruction of the case history of all stories, and only then being able to nominate.

Ken Kaitin: Steve made a couple of good comments, one is about the importance of the sixth statin versus the first statin. You talk about a breakthrough drug versus a drug that really has greater impact, but one setup the stage. The second is going and finding the people that really were involved. The question becomes, perhaps, you identify not the people, but the product first. Then go in and you nominate the breakthrough products. Then you go to those companies, advisors, and people involved and find out who was really the key players and the important people associated with the product. You work your way backwards, the important drug, the breakthrough, to the people who were the creative force behind it.

Adam Smith: Yes.

John Potts, Mass General Hospital: I just found this a very stimulating discussion. It is challenging and everyone has brought out very interesting points. I finally decided to say something, I was going to before. It seems to me that it is not necessary in the early days of awarding such a prize to assume that it could come only to those in a pharmaceutical company. I can think of some notable examples of people who have understood, some of whom are in this room, a mechanism or an approach to disease, and the cure of disease, that they have followed through their entire academic career. It may even be in the earlier stages of awarding such a prize that looking in that direction may be as productive in shaping the award, as necessarily going to pharmaceutical industry to make the award. Which isn't to say that I am opposed to that at all, it wouldn't matter if I was, but I mean I am not. The point is that it is very difficult to decide how this going to be done and the impact of it. You want it to have an impact. I think it may actually be easier to identify some major academic leaders who have pushed the whole field. I could list a few and you are all aware of them. That is another direction. Every time I hear it coming back to the pharmaceutical industry it seems to me, while that is a very legitimate area, it's necessary too narrow.

Tom Maniatis: I agree with that, but I think that the formula just proposed that you start with an accomplishment or a drug and work your way backwards. You go wherever it takes you and it may take you to academia rather than—

Steve Holtzman: I am not sure if I agree with you John or not. I love the idea of starting with the drug. Yes, you might go back and there might be a group of people including academics who were essential to it, but I don't think that you should start with the notion that the person who elucidated Pathway X, if they never eventuated in a drug, or has not yet eventuated in a drug, it might have an award of a different type, but that is not this award.

Adam Smith: Sure. I think it is almost drinking time again. The last question I would like to pose would be how ideally would such an award be administered and financed? I guess the Nobel and the Lasker stand out as examples of how it is done in basic research. Does anyone have any strong feelings about that?

Judah Folkman: There are awards that are just started up like the Albany Medical prize. It is only three years old. It has a very interesting committee that goes through this same debate. The donor wanted the prize to be \$500,000 a year, which is a large prize. The donor also said that he would like the committee to think about translational not only research. That immediately made it a difficult committee to be on because the committee decided that it maybe three years before the award has the kind of recognition as the Lasker. As you pick the people that determines what the nominations are that come in. They are trying to decide if there is a ratio between translational and others. It is really difficult to do this, so they are going through all of this for a single donor.

Tom Maniatis: The Lasker is a good example of why the prize doesn't have to be big financially. It is a relatively small award and very prestigious. I think that the most important component of establishing a prize like this is to have an endowment that independently established and not linked to any particular pharmaceutical company or individual so that it is a completely neutral non-conflicted source of funds. I don't think that it has to be a lot, but there has to be

some kind of continuing endowment so that this prize can be given every year. Obviously the worst that is if it is given for five years and then dies, then all the receipts— It is a matter of getting the proper endowment and attracting the right group of people to be on the committee to give the first award so that you establish a precedence of excellence.

Adam Smith: Yes did you want to make a point?

Steve Holtzman: The top pharmaceutical companies each with a capital around 50 billion dollars, each contributed 5 million dollars in stock which would be .001% dilution. You could have a 100 million dollar endowment, and you could do 5 million dollars a year in prizes.

Adam Smith: We've got the solution there. Start writing letters. Yes.

Unknown: I was afraid you would want us to write a check.

Jeff Krasner, The Boston Globe: This may be putting the cart before the horse, but when you look at all the awards in other areas like the Nobels, Oscars, Emmys, or the MacArthurs, they all have these nice snappy names. Has anybody given any thought [laughter] to what this award is going to be called?

[Cross talk]

Adam Smith: There you've got it there. Do you have any suggestions?

Jeff Krasner: Well if you were to name it after Dr. Fokman, it would be the Foke.

[Laughter]

Fred Goldberg: I noticed, and I am using a feature of this nice discussion, if you actually went out to the public at large or our congressman, they would be wondering well why give an award to basic research, because translational research that benefits patients is what the focus of the motivation is for the NIH and most foundations. They want to rush into patients before they even have a rationale for their therapies. We are almost an esoteric group of academics, intellectuals, and people bound to pharmaceutical industry because we recognize the exclusive emphasis amongst our peers on basic research, and want to go back to what is the layman's version what science should be doing. It should be an easy niche to fill and raise money for.

Adam Smith: That is a nice point to wrap up with, thank you Fred. I just wanted to thank all the panelist and the audience for making this work. As I said, we are going to circulate transcripts of what has happened and also some details on how we intend to proceed. Now I just pass it over to Nancy.

Nancy Kelley: Thank you gentleman. I really appreciate your participation in this event and all the audience for participating as well. As a follow-up, I would like you to think about your colleagues who might be nominated for awards in the scientific achievement category this year. There are three of them. The first is the Lifetime Achievement award. The second is the Chief

Scientific Officer of the Year award, and the third is the Academic Scientist of the Year award. Please feel free to log onto the website that was included in your invitations, or to call Adam or myself on the business cards that you received when you came in, with people who you think should be considered. The nomination deadline is April 30th for this year. If any of your colleagues that were not able to attend today would like to offer their suggestions or their thoughts on this important topic, we would welcome them. We have actually scheduled a conference call on March 22nd at 12 o'clock noon for those people who weren't able to participate this evening.

Before we break for final drinks and food, I want to recognize two groups of people who made this evening possible. First, I want to recognize IBC who is actually organizing the Third Annual Pharmaceutical Awards, and the team from Spaulding and Slye Colliers who made this evening possible. Thank you very much. Now I invite you to have a final drink.

[Applause]