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ROUNDTABLE FORUM

FOCUS ON GENOMICS STOCKS

Transforming the economics of pharmaceutical research

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From the Corporate and Consulting Sector:
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As drug targets multiply, the gradual adoption of genomics and other sophisticated biological technologies is transforming the economics of pharmaceutical research. On June 23, 2004, Wall Street Reporter Magazine hosted a genomics forum to update on how genomic breakthroughs are impacting drug development.

WSR: *Bill Kridel, could you start off with some introductory comments on how genomics and proteomics companies are moving the drug discovery process along toward product development?*

KRIDEL: I think there are two overarching issues that people in the genomics and proteomics field are facing today. Number one is the demand-pull for their services in either a collaborative mode or a fee-for-service mode. Second is the reaction of investors, both private investors for venture capital rounds and public investors for either IPO or follow-on rounds. And these two overarching issues are actually interrelated to the degree that there is an enormous demand pull for this type of expertise. You will find more enthusiasm amongst both classes of investors. But I think that the world is awash in raw targets and a couple of the companies here today — and in general in the field beyond the scope of this roundtable — are actually capable of delivering a greater quality of target or target validation or workup than in the past. For example, I am going to pass the buck quickly over to Lloyd because his company, Caprion Pharmaceuticals Inc., does not deliver raw targets; they deliver highly qualified ones, given the technology they deploy in the world of proteomics.

SEGAL: Thanks for passing that ball, Bill. I guess I have to be able to put that one in the net! I certainly agree with Bill that not all targets are created equal. And without tooting the horn of Caprion's capabilities and finding cancer targets in solid tumors that others haven't been able to find — using proteomics in our case — I think the key barrier for us is finding clients and collaborators in pharma and Big Biotech who can understand that we can do something on a scale that they not necessarily can't do, but would have to spend far more to replicate than would be economical for the number of targets that they could take forward.

KRIDEL: Because the proposition that I have advanced here is that not all targets are created equal. Take a second and tell your fellow roundtable members what is different about Caprion, because this is what I am suggesting makes the difference both with the demand pull and to the investor. **SEGAL:** What we do is to apply expression profiling at an unprecedented level of resolution. So we can see in looking at normal versus tumorgenic samples actual expression of proteins at a very precise level and at a resolution level that hasn't been seen before. That just allows us to understand what proteins are there — presumably expressed on the surface, because we are doing some very proprietary biology upfront to look only at cell surface portions of the cell, which is about 1 % of the cell by mass, but it's all we look at. That allows us to get at antibody targets, which are by definition cell surface, and do that in a way that cuts for our clients — which include Abbott Laboratories (NYSE: ABT $39,83) and Biogen Idec Inc. (NASDAQ: BII8 $59,44) — probably about two years from the development cycle in terms of time and probably (we estimate) somewhere between $15 and $30 million in terms of fully burdened cost. That is value, but you've got to be able to be convinced that someone, even if you're Abbott, can do something you can't. And we find that that's the biggest barrier to getting there.

WSR: *Charles, within the universe of biotech and genomics companies that JMP follows, where do you see the interest?*

DUNCAN: We first of all are currently covering 19 to 20 biotech stocks at JMP Securities, which is a pretty big list on Wall Street. We expect that to expand by 50% over the course of the next three months or so with the addition of another publishing analyst, so we are making a big investment in biotech. I have long been an advocate of what I'll call the platform-enabled drug developer thesis, wherein certain biology/genomics-driven platforms can result in multiple therapeutic product opportunities. That has been my focus throughout at least the last four or five years of my career on the Street; prior to that, I was more of a generalist biotech analyst. I'll tell you that most of the institutional investors that I talk to have become pretty much technology-agnostic and have stopped using the words "genomics" or "proteomics". They have realty started to primarily focus on certain specific therapeutic products because those are the kind of investment opportunities that they have long become comfortable with analyzing the risks associated with. So, unfortunately the words "proteomics" and "genomics" to a large percentage of institutional investors (at least in public companies right now) have not only lost their meaning, but also to some extent lost their luster. So, what I refer to these companies as using is platforms — biology-driven drug discovery and development. Now I could tell you that there are certain investors who are more forward-thinking — longer-term investors, less kind of trading-oriented investors — who are very keen on knowing where product opportunities come from and knowing that therapeutic product opportunities are driven with very, very sound biology and technology (genomics, etc.). And these types of investors can give some insight as to first of all, mechanisms; secondly, the design of clinical trials; and third, can really use this information to handicap the probability of success for products. But at this point, I think that in general, institutional investors, at least in public companies, have enough to handle

with regard to keeping track of all those interesting therapeutic indications that are being pursued. And they have lost sight of some of the more interesting technologies that are being used to develop the drug opportunities.

WSR: *Are there any technologies that really stand out to you that you think are very important, but maybe the investors aren't focused on?*

DUNCAN: Yes, there are. We believe very much, for example, in what we refer to as structural proteomics for lack of a better term. These are companies that are using kind of an old concept in drug discovery and development, but bringing their new intellectual property and/or equipment and/or know-how to catalyze drug discovery and development, and that is in the area of structural proteomics or crystallization information. So, for example, knowledge of protein structure across classes that can be used synergistically with good medicinal chemistry to really catalyze the discovery, but also the development of drug opportunities. The other area that we find interesting is kind of more broad and that is the area of pharmacogenetics (if you will), with regard to geno-typing cancer patients and identifying patients that are more amenable to therapies that are more highly targeted than those in the past. So, the most obvious example of a drug that is currently being sold is Herceptin for certain patients that express the HER2/neu receptor. There are several other drugs that are currently in development — most of my other panel members could speak to this in much greater detail — that are being developed successfully because patients can be identified that should be exposed to these drugs. And anytime that you can identify a patient that perhaps should be exposed to a drug, although that creates consternation within the marketing organizations with regard to the market sizes that could be really pursued with those technologies, we think that information can revolutionize the discovery, but more importantly, the development, possibly the commercialization of the drug.

WSR: *David Moskowitz, if you could introduce GenoMed Inc. (OTC: GMED $0,1,6) and your disease management genomics work?*

MOSKOWITZ: Well, I'm a practicing physician who happens to feel that the knowledge of disease genes is the best thing I have seen so far to take better care of people. And our focus remains patient outcome-driven and we will use anything to get there. So, in that way, we are a little different from the biotech and pharma sectors that want to create new products, usually at high expense. We try to do things cost-effectively and I think they are probably more in tune with the political atmosphere. In fact, the first thing we've got is kind of a master disease gene that is nothing more than angiotensin-1 converting enzymes [ACE]. So we are trying to commercialize new uses, about 150 new common diseases, which ought to do better with effective tissue ACE inhibition and receptor blockers. We are very connected to the clinical world, probably more so than most biotech companies, so we're trying to find predisposition genes for early diagnostics and then just use of conventional medicine because our goal really is to improve outcomes in our lifetime. And the problem with new drug development, which is extremely cool and technologically very neat and so forth, is that I can't imagine raising $800 million for 3,000 drug targets, which is how many we hope to have in the next two years.

WSR: *Are you working on a very broad basis, or are there a couple of very narrow targets that are highest on the list?*

MOSKOWITZ: Well, what we found from the ACE gene is that it's silly to be narrow. Since there are only 35,000 of them, the genes themselves tend to be pleiotropic and used in lots of different diseases. So in fact, what we would like to do is really solve the top 250 common diseases, and it's just a matter of money. I mean you use the same SNPs, you just increase your genotyping load by 250 instead of just one and the same process should work for all 250,

HEDGPETH: It's a very interesting model. Are you looking mainly at expression or also polymorphisms from a functional point of view, from the mutation point of view?

MOSKOWITZ: We are looking actually at regulatory polymorphisms that are likely to be functional. Expression profiling is extremely valuable. But what I found in looking at renal hypertrophy, I wanted to define the trigger for making one kidney bigger by surgically removing its mate, because then I want to give the trigger to renal-failure patients and make them grow their kidneys bigger and stay off dialysis. Even 30 minutes after taking out one kidney, it is impossible to tell what the trigger was. And since we are looking for the beginning steps in the pathway of 50 to 100 genes that ultimately lead to disease, we are probably going to mostly do association studies and stay away from expression profiling. I think expression profiling is great for treatment, but for what we want to do (which is really early diagnosis and basically identify targets by how early they appear in the pathway), I think we will probably stay with association studies.

SEGAL: Are you concerned that just by working at a genome level, and it sounds like doing it in an animal model, that: (A) you don't know if you are getting, ultimately, an expressed protein at all. (B), if you are, you don't know if it's expressing in humans and (C) if that's even the case, you don't know if there is a post4ranslational modification or some slight glycosylation that is actually affecting the way the protein is working. Isn't that the Achilles heel of a purely genomic approach?

MOSKOWITZ: Well, I certainly know about Achilles heels since I have already torn one. But, no we use people. We are doing genomic epidemiology, so we start with the disease and then the proof of the pudding in terms of how significant the polymorphism is; "is it useful clinically?" Can we improve patient outcomes by using that polymorphism? That's the proof of our pudding. And all the stuff in between — like the other partners that that protein interacts with, all the modifications — except from the pathway that you correctly allude to, we will leave it to other people to work out.

SHEN: So, you are really cherry picking that.

MOSKOWITZ: We are cherry picking in the sense that we are doing public health. I mean, yes, we are cherry picking because we want to improve outcomes as quickly as possible and not so much get beautiful drugs. I mean, we'll use bleach if it works.

KRIDEL: And what is investor reaction to this?

MOSKOWITZ: Well, we are in St. Louis and nobody's ever heard of us. So, one of the ways we are trying to get attention is, this is the second year we have been running a trial for West Nile virus. We got a 100% success rate. We are hoping, maybe people will hear about us this way, But, we are buried in the Mississippi River Valley and investor

reaction (the little bit that there has been) has been quite positive. Our investors on Raging Bull feel like they have signed up for a mission.

KRIDEL: Why not deploy your platform into things that have sort of immediate funding capability in biodefense?

MOSKOWITZ: Oh, because biodefense won't listen! Although the truth of the matter is, I have been told I would be disinvited if I mention it, but I have been invited to Washington to talk about it.

KRIDEL: I would hope so.

MOSKOWITZ: It only took about a year of press releases before I did get invited. Vector, the Russian virus lab, has already picked up on what we are doing.

KRIDEL: You know, that does give you an edge in approaching investors because the funding for that is substantial and the contracts are relatively long-term and stable. Just keep it in mind.

MOSKOWITZ: Well, it will be great, except I'm not on the inside track and you tend to have be on the inside track to get government funding. We think we are going to bypass the establishment really, and just go straight to patients. We would like to become a household name when people get sick from a virus (whether it's because of an air attack or a mosquito attack) we want people to go straight to our Web site regardless of funding.

SHEN: You will need a lot of good PR then in that case, to get the mass population aware of what you are doing.

KRIDEL: And a good catchy corporate name.

MOSKOWITZ: We've got the name. We can't change our name, and we are getting the PR actually by being on shows like this one.

WSR: *All right. Joe, would you like to further introduce Complete Inc. ?*

HEDGPETH: Certainly. Complete is an early-stage, developing-stage company that is in point of fact a new molecule drug discovery company that uses a platform that is applicable to "genomics." I have never really understood what genomics meant and I have been doing this for over 30 years — before there was even a term biotechnology — and I could never figure out what genomics is. But nevertheless, we've generated an incredible data- base of potential targets for drugs, and CompleGen's goal is to be able to use those targets to find those drugs in a very, very high throughput, broad-based way. And not only to deal with pharmaceutical discovery, but one of our bigger clients in fact, is DuPont Crop Protection [a unit of E.I. Du Pont De Nemours & Co. (NYSE: DD $42.60}], so in a rather competitive low-margin field, our technology can compete and we can find products. As a consequence, our business model is to discover new compounds and patent the families that those would belong to. This includes in some cases discovering new targets with our system and providing the compounds in a bottle to pharmaceutical companies to do testing directly using the compound as the Occam's Razor to validate targets and/or to take targets that are already validated and find new compounds that work more specifically or more potently on those particular targets. And we do this by taking genes from essentially any organism, putting them into yeast and forcing the yeast to be dependent on the product of that foreign gene. So then, any drug that acts on that particular foreign gene product will act only on the yeast dependent upon that gene, and depending on what gene products we

compare, we can identify products that are more and more specific. Our model is more specific, less toxic and quicker, so we anticipate that we can shorten the front end of drug discovery (as was just discussed) by a significant amount of time and then money. Arguably, one can pick different numbers for both the time and the amount of money that we could save the pharmaceutical industry, but I think it is going to be significant. And we have already demonstrated that with a couple of clients; the most difficult one actually was, as I mentioned, DuPont Crop Protection, because their research is very cost-inhibited and their regulatory hurdles are almost as bad as the pharmaceutical industry. We have been able to demonstrate that the system has allowed them to discover products that are very specific in a very, very short period of time — a matter of months.

KRIDEL: How tough a sell is it to stress the cost-saving, time-saving feature and use that as the wedge to open the door? **SEGAL**: It's a bitch, to use a technical term. Bottom line is that there are a thousand early- to advanced-stage biotech companies who are talking about how they can shorten the drug discovery pipeline and the reality is there is a very low single-digit percentage of companies that can actually do it. And that's the challenge, The challenge is getting your technology capability, your data to prove it, because you have to be able to prove it in front of the right people in pharma who have the authority, the budget and the will to be a champion for what's best for their respective organizations. That's a lot of moons and stars to align, and it's just really, really hard. And for us, we have decided to apply our capability as we always envisioned from the beginning: to engineer and to ultimately develop our own products because it is organizationally intensive for too long to continue to try to sell your capability to other parties. And we have been fortunate with the kind of partners we have that include Wyeth (NYSE: WYE $34.79), Abbott, Biogen Idec, and Merck & Co. Inc. (NYSE: MRK $44.71) and others. We have been able to generate enough cash to have the luxury of now being able to say, "you know what, our capability is good, is excellent in identifying targets and ultimately drugs. We are going to use this ourselves, and isn't that the proof in the pudding?"

HEDGPETH: Well, there is a lot of pudding going around. The figure for drugs that have been developed by the entire pharmaceutical industry is 500 over the last 150 years. What my big question for you is, Bill — given that are 35,000 genes and maybe 10% of them are going to be involved in various diseases, we've got maybe 3,500 drug targets that are going to come pouring out, and isn't that going to overwhelm business as usual?

KRIDEL: I don't think it will ever be business as usual again. I think that the days of business as usual are rare to find. We are going to find markets fractionating down to smaller subpopulations. Reference has already been made to polymorphisms and SNPs being able to be addressed to those subpopulations. Diagnostics will be more precise. I mean, anybody just has to think about Herceptin and the over expression of HER2/neu, which is about a 30% to 35% causal factor in women's breast cancer. You are going to find that that may be a very large subpopulation in the future, that we are not going to be having blockbuster large-scale drugs. We are going to have more and more targeted therapeutics that the smaller companies with their genomic and proteomic tools not only

will be able to discover and bring forward, but also enter into lucrative marketing arrangements with the larger companies that have already invested in infrastructure.

HEDGPETH: The bottleneck for me is to figure out who is going to pay for all this. I mean, I see there only being one or two drug companies in the future, basically just marketing stuff. And they may be the banks, but I would see large VCs like Warburg Pincus, who like to do $100 million deals and up. I would see VCs actually coming in and the biotech companies themselves kind of organizing like ribosomes on a messenger RNA and essentially pushing the product as far as they can, getting into consortia of other companies that want to push that drug target. Then ultimately going into clinical trials with the financial backing of a VC. And ultimately, maybe getting into distribution agreements with pharma.

KRIDEL: I think you are ignoring the existence of specialty pharmas, companies that have recently been formed and bought out in Europe that are and marketing organizations: the Innovex [a unit of Quintiles Transnational Corp.], the PDI Inc. (NASDAQ: PDIl $28.61), the smaller members of the Big Pharma community. For instance, Schering AG {NYS& SHR $59.20) — all of these companies have an insatiable appetite and they do have cash based on test-positive financial performance. You are going to find an awful lot of people competing to get their hands on what they perceive to be the mid-sized as well as the large-sized blockbusters of the future. But, whatever it is, you can bet it isn't going to be business as usual.

SHEN: I want to make some comments on this very topic of personalized medicine. I definitely because since the Genentech Inc. (NYSE: ONA $52.23) drug was developed (Herceptin) and the linkage has been identified where you will only get benefit for those patients who have over-expression of the HER2 gene. We have seen a prime example of linking the diagnostic with therapeutics. Recently there has been approval for an additional test for HER2 over-expression, which is the FISH test coming from Abbott from their acquisition of another company. So, more and more companies are going to get into that space and I personally believe that pharmacogenomics is going to be there to stay. As we get a deeper and more thorough understanding of the disease and the biology of the disease, we are going to identify more biomarkers that will indicate which group of patients with what particular genotypes will truly benefit from therapeutics that will be developed from these kind of collaborations. And I also believe that from what we have seen in several of the multinational pharmaceutical companies where they have a major business in the diagnostic area — like those in Roche Holding AG (SWX: RO CHF 124.25), Bayer AG (NYSE: BAY $27.55) and so forth — they are going to put more investment in trying to identify such diagnostic pharmaceutical therapeutic pairs. And the PDA also has taken a stance in supporting this future pharmacogenomics initiative by providing guidelines in how to conduct clinical trials where you can indeed compare the data and integrate the therapeutic tests into the pharmaceutical development. So, I think the future is quite promising in that area.

KRIDEL: If you take a look at some of the differentially expressed proteins that are rare and are certainly disease-linked (or at least are acting as sort of

semaphores to say, "here I am, I only appear when there is a disease in mind"), sortie of the work that you are doing at Caprion can be used in both modes, both therapeutic and diagnostic, in this sort of subpopulation approach.

SEGAL: Absolutely. I think there is an emerging recognition, as several of us have pointed out already, that this idea of the so-called "theranostics" tied to the very early stage of drug discovery is the new paradigm. Like everything in pharma, it's catching on extremely slowly, but I think the encouraging signs that we see are when a de novo project is established in any pharma domain. We know at least three or four mainstream pharmaceutical companies (and there are at least three or four of them) that have a policy that you need a bio-marker when you establish a program in any disease area. They want to know that there is a marker of efficacy. They want to see a diagnostic or prognostic marker, and I think clearly the only ways they are going to get there are through both advanced genomics and proteomics tools that they don't have today. The question is; is it going to take them ten years to integrate those tools? A lot of these pharma companies have singed fingertips from their early experiences in genomics, where they led with their checkbooks instead of with their left or front lobes, and they are still paying the price. And frankly, companies like ours are still paying the price.

WSR: *Charles, I want to give you a chance to highlight a few investment ideas that you are looking at in the sector right now.*

DUNCAN: I think we can't spend a ton of time doing that with the time remaining, but I would echo a few of the thoughts that we had earlier on, that institutional investors are pretty much technology-agnostic. However, given that some of the panel members have made some really pretty compelling arguments for predictive medicine and personalized medicine, I do think that it makes sense to make a comment from an institutional investor's perspective. I believe very much that genomics and biology, if you will, can revolutionize the discovery, development and possibly commercialization of therapeutics in the future. The challenge that we have from a sell-sider's perspective in serving the buy side is trying to value the importance of those diagnostics in terms of being value-added and driving revenue. I think that at this point, unfortunately, one of the highest-profile examples that we have that other folks have mentioned on the call is the Herceptin example. And that is one where the diagnostic has unfortunately lagged the therapeutics. I believe that in the future as drugs are developed — maybe quicker, maybe better, maybe having much greater margins associated with them because someone has identified a marker for efficacy or because they have identified a marker for determining the patients that should be exposed to the drug — then I think that institutional investors will start to value these technologies more broadly. And I encourage any of you that are on the company side trying to put forth such technologies to really think through the pharmacoeconomic model that you can use to help to understand the value add of the technologies. In terms of answering your question, the one company that I have that is currently on my recommended list (for which we are non-investment bankers for and of which I don't own any shares) that plays kind of in this field is Myriad Genetics Inc. (NYSE; MYGN $13.83), about a $450 million market cap company very much involved in the

development of predisposition tests and marketing of those tests. In fact, they market currently four or five products based on genes that they found mutations in that convey a higher than usual probability of getting an illness, including breast cancer. And I think someone else on the panel can speak to the importance of those tests, but Myriad Genetics has a business in selling these tests of approximately $45 million. It's cash flow positive and it's a pretty interesting cash cow for the company. Now, the company is moving into drug discovery and development and so that's not the limit of their view in terms of moving forward and growing their company, but their predisposition testing business is a viable commercial entity. So that's an example where some of these technologies have been used in a public company format to drive growth.

WSR: *I think one of the key things that has come up today is there are so many things that are going on in terms of all this targeting work and how we are going to pay for it. Bill Kridel and Zhu Shen, in terms of the work that you are doing with companies and how they are looking for things, how are you proceeding here?*

KRIDEL: I will take a crack at that. We do an awful lot of work in what we call the enabling technology field, which embraces genomics, proteomics, various types of combinatorial computational medicinal chemistry and all the Other discovery tools that are either organized separately or in an integrated fashion. What is happening in terms of transactions is alliances along the lines of what Joel from Complete has described and Lloyd has as well; there are deals that are being done that are either molecule-specific, possibly therapeutic-area specific. Also, you are finding that investors are attracted to the versatility and the speed of these tools because as there is a demand pull, if a company does have the data as referred to earlier — has the ability to do things faster, cheaper, better — more and more companies will find themselves under their own P&L pressure and turning to other organizations for outsourced help. And so you are not only going to find an increase in these collaborations, you are going to find investors willing to back that. I think the real issue; is the public markets near-term upsurge of public market investment opportunities to float companies through au IPO or an attractively priced follow-on, just because too many companies who have done this in the past have burned the fingers of the investors. Complete is private, Caprion is private at the moment and to the degree that they have a proprietary pipeline, they can look at the public markets. But to the degree that they are in these collaborative modes using their expertise and developing further collaborations, then they will be addressing mostly the private equity markets.

SHEN: I concur with Bill's comment here. I just want to add that it is a constant struggle to balance your own product development with what you can partner out. In the case of an example company, Nuvelo Inc. (NAS¬DAQ: Nuvo $8.55), which I know fairly well, they were able to transition out of truly focusing on the genomics discovery aspect and turn themselves into a product development company by successfully striking an alliance with Amgen Inc. (NASDAQ: AMGN $ 56.00) and develop a really robust clinical pipeline, while at the same time trying to derive value from their earlier days of genomics research and then focusing on the cancer area. I think a lot of companies can also possibly

benefit from a topic that Bill mentioned earlier, outsourcing. Mike, you and I have been to this US-China Pharma Opportunities Conference last week in New York. I think, for especially smaller companies in the earlier stage where financing is a major challenge, they could truly use some help from overseas from countries in the Asia-Pacific, And particularly in greater China, for example, where things can be done a lot cheaper and you can ensure quality by working with the right companies. That way, you can get some of your clinical development program both in the diagnostic area and in therapeutics moving forward. And then with human data, you can validate and reduce the risk for further development for the main major markets in the US and Europe, So, I think that's an area where companies, if they have the right resources, can truly generate a lot of savings and efficiency and be able to carry out their development efforts more productively.

WSR: *David, in terms of GenoMed, as a public entity how do you see your work going forward? Are you looking for many more collaborations?*

MOSKOWITZ: I think it's a truism of science that the bigger the project, the more collaborators you need. We have already outsourced our genotyping to the Montreal Genome1 Center, which uses an aluminum machine. It is a lot easier to just hire somebody at $0.40 a genotype than to train an entire lab. I mean, we would be down for two years, and even then we couldn't compete probably with what Montreal is already doing. So, we love collaborations and we will get into more and more of them.

WSR: *Lloyd, where do you see yourself going as a private company in terms of funding?*

SEGAL: I think our next step is the public markets and we are fortunate in that we have a pretty deep cash hoard, more than $20 million. And that's actually gone in the positive direction in the last couple of quarters by virtue of our collaborations, but I think others on this call have pointed to the challenge of being a platform company in getting access to the capital markets. So, it's been a driver for us to forward integrate. We announced just last month an acquisition of our first clinical program, a monoclonal antibody in hemolytic uremic syndrome, and we are accelerating two of our own oncology programs into development.

We are going to look a lot more integrated, and I think, a lot more friendly to capital markets so that we don't need an intermediate step before we get there.

KRIDEL: But will you continue with collaborations?

SEGAL: Absolutely. That is the driver of our P&L right now, and I think that is what allows us the freedom to go and develop our own programs without raising more money.

WSR: *I think it is interesting. On one of our previous conference calls, there was a discussion about all the interest in going into collaborations. Even some of the smaller companies felt that sometimes they jumped the gun too soon and ended up going into collaborations too early, in giving up too much of the end game, and that seems to be a growing concern for some companies.*

SEGAL: At least our perspective is that is the difference between a platform company and a one trick pony. If you are truly a platform company, your platform should be applicable (as ours is) to a sufficient number of disease or drug opportunities such that you don't mind selling one of the children, and that has been our case. Sure, I wish I didn't have to sell our lung cancer and

colon cancer programs as we did. But, frankly, we got a lot of money for them given where they were, and we delivered value for them and it's given us the freedom to pursue on our own prostate cancer, breast cancer, kidney cancer and so on. I don't think there is much of a debate; you've got to keep the lights on, you've got to pay your people and you've got to have some stability in your company, and that requires a bit of financial compromise.

KRIDEL: That also goes to the point that Joel made earlier, that it also gives you validation.

SEGAL: Absolutely. You know, we have a snowball rolling in terms of our capabilities. The first sell of our program to Biogen Idec was tough; the second one to Abbott was less tough. Since we announced the Abbott deal in January, we can't meet the demand to come and visit or have people come see us to look at the next cancer program, So, I think Bill is absolutely right. Validation is important because pharma aren't known for their risk-taking approach to early-stage drug discovery.

SHEN: Right. I would agree with both of you gentlemen, and Lloyd, we've seen each other at the Oncology Partner Conference. Glad to meet you here again. I think it's a natural evolvement of the stages of the biotech company through their development process, you know, the earlier stages more focusing on licensing deals and partners giving out perhaps a little bit more value so that you can get the validation. But as you move along the pipeline, so to speak, you gain more experience and you have proven yourself, so later on the deals would have more attractive terms for the biotech companies themselves. And that would also allow you the kind of support financially to develop your own products and then generate more value. So, it's just the natural progression of the company,

HEDGPETH: That's Genentech. That was Genentech's model right from the beginning. So, I don't think it's anything new to sell your technology early on to finance product development later and I don't see what the real worry is about that. But it's precisely as Bill said before, yon have to have more than one shell in your gun, otherwise you would be indeed selling out too soon.

MOSKOWITZ: Are you going to follow that mixed business model and have a proprietary pipeline as well?

HEDGPETH: Absolutely. I mean, our notion is to have a proprietary pipeline as early on as we can, proprietary in the sense that we will have small molecules that are specifically active, patented and in our possession when we go in to talk to people. Right now, we are just at our stages of development where our shtick is to say, "okay, we've got these targets, do you have interest in the targets?" and library screening begins. That is only going to last for a little while longer for two reasons. One is that it's not only a business; it's a way to get some cash and validation. But the other reason is that we will have our own resources to do that and generate in the long-term both relationships and revenue.

SEGAL: And it's probably not a bad idea to remember (and I have to give Karen Bernstein of BioCentury credit for this) that this isn't a new model in terms of using partnerships and licensing out early intellectual property to bet on the longer-term therapeutic opportunities. You know, little early-stage companies 15 years ago in our business like Genentech did that, as did Chiron Corp. (NASDAQ: CHIR $44.34) among others. It's a very old model.

MOSKOWITZ: Chiron still does it,

SEGAL: Yes, it is a very, very old model. Build your skills, your cash flow, your capabilities at your partner's expense, but always focus on the goal of being more integrated and having your own therapeutic compound. And I think that if yon can use that as a model, it is certainly tried and true.

MOSKOWITZ: Our goal here as companies, it seems to me, is to have our own products, and that your product is not your technology. The product is something that a "broad" consumer base is going to use, and then at least there is a significant patient base for a given drug and it's going to be worthwhile. And the idea is if we can do things that will reduce the cost barrier and the time barrier so that pharmaceutical companies can take on the $100 million, $200 million product rather than have to live and die with a blockbuster, I think that we have a reasonable niche to fulfill. But if we have to simply sell our technology, I am not sure that very many of us here would want to stay in the business very long.

SHEN: Oh, that's right. It's hard to survive in these days; to have the company purely based on the platform. Even with Affymatrix Inc. (NASDAQ: AFFX $29.97), you know, they have products to sell. It is not just technology to sell.

MOSKOWITZ: One of the things that we haven't talked about is the healthcare system on the other end. Everybody is assuming that if you come up with a good mousetrap that people will use it.

HEDGPETH: And pay for it, and we are finding that even if we have a great mousetrap, the health system is perverse it's hospital-based, and keeping people out of the hospital and improving patient outcomes is not what it's in business for.

WSR: *I'd like to open the door for any of the companies if you have anything you'd like to put on the table*.

HEDGPETH: First of all, we're a very small company, so some of the things we do are mainly to keep ourselves going and enhance our .business. It might not sound like a very big deal, but the way we look at the picture is that we have a system that is kind of like a search engine that can query any database, both the genetic database and the drug database, and put these two things together to generate useful drugs and to treat significant disease. So, I think we are going to be able to announce in the near future an arrangement with DuPont that will give us the wherewithal to expand our discovery program significantly. I can't really talk about it, but one of the things we really need is access to very, very large chemistry libraries. Our system is set up so, that we can do a high throughput screening on the order of millions of compounds per week. We finished last year a screen of 750,000 compounds with Schering AG to assess their activity on a target that they had discovered by genetic profiling — by expression profiling in certain tumors — and this is a case where we had to use our technology to find their drug. We are going to be in the position where we have our own chemical compounds at our disposal to find our own drugs in the near future, and I think we will be able to announce that within the next couple of weeks.

SEGAL: We are pretty well established in finding new targets for pharma companies. What we'd love to do is use our expression profiling capabilities to look at failed clinical trials where groups of clinical developers at pharma feel that there was a responding group that was clearly there in a cohort. And let us look at the plasma in those patients and see if we can find the

markers of responders and non~ responders, which is an interesting way to rescue drugs. And that's what we are looking for; opportunities that could really add value to where we are not working today.

HEDGPETH: How easy is it for you to get access to both the data and to the samples?

SEGAL: That's the impossible part. Generally in pharma, you know, if there is a Phase III trial that failed even if it was really close to the line, people are running away very fast from those freezers.

HEDGPETH: Absolutely. They bury their dead quicker than any army I've ever seen.

SEGAL: Yes, and just given that, that's why when we are asked what are the product opportunities, that is one that we love. We could imagine going right back to the Phase III trial, and that's a nice way to skip a lot of time.

SHEN: Right. So, I think, Lloyd and Dave, perhaps, one approach you may want to think about is to get smaller samples of a bigger trial or reassemble that somehow where you can prove something in a short time.

HEDGPETH: I think the model is a wonderful model from a hypothetical point of view. I think once the dam is broken and a pharmaceutical company says, "we don't have to look at this as a failure that several vice presidents are going to lose their bonus over, but a way that we've generated a significant amount of useful data," to provide it to someone like a Lloyd to use. I think that then we'll see a lot of data from these clinical trials.

KRIDEL: I think your best bet is to go after the medium-size pharmas that failed trials and not big pharmas.

SEGAL: Those clinical guys bury their dead just as fast.

KRIDEL: But they are smaller dead and you won't get the nickname of Don Quixote there.

SEGAL: If Ray Gilmartin, rather than spending $20 million upfront on a pre-clinical molecule that's a year away from an IND, would say, "I will give a million-dollar bounty to anyone who can rescue one of our many failed clinical programs," then if that kind of direction came out from above, we'd have a lot more customers on that end than we do now,

SHEN: Yes, I personally believe that would probably be one of the most immediate market opportunities for pharmacogenomics, because you've done a lot of work already in those areas and it's just a matter of identifying if there is a way to rescue those drugs.

MOSKOWITZ: Mike, you asked the companies for projects and I would just like to close. We have two projects. One is that we've already shown that we can prevent 90% of kidney failures in this country and delay emphysema by a significant number of years. That was announced two, three years ago and went nowhere. So, now to get some attention, we are running a global trial for West Nile. Maybe people will realize that we can also prevent dialysis.

SHEN: Lloyd, actually I have a question for you. You were talking about pharma companies, when they start their de novo drug development programs they want to incorporate the biomarker into the picture. Do you work with those companies also in your collaborative efforts? Do you guys work with the PDA in terms of trying to get some more guidance on the processes of getting the diagnostic and therapeutics companion tests approved? And what are the requirements and how to go about it, in short?

SEGAL: That's a whole other conference call. But, you know, to the extent that anyone works with the PDA, we do have an open1 channel to several thought leaders there. They have issued something recently which broadly included pharmacogenomics, proteomic and genomic markers in what I think opened a huge door for pharma called the Safe Harbor Statement for that kind of data. It allowed pharma companies to apply pharmacogenomic tools like proteomics and genomics and not have to disclose those into their clinical trial files. That has suddenly opened the door for many pharma players to start to use the tools because before that they were scared of what they might find and not understanding that would hold up a clinical program. So, again, pharma, they aren't early adopters of technology. They are looking carefully at how this works, but the PDA, I think, has made a very important step in the right direction in creating a safe harbor for this new form of data.

KRIDEL: In closing on the subject of bio- markers, there are a number of conferences around the world that are taking place on that subject. I chaired the BIO panels in Europe last year on the use of biomarkers in cancer, where I had the pleasure of a number of world experts sitting in on the panel. So if anybody on this roundtable wants my sort of introduction to the subject and some of the specialized speeches, send me an email and I will pass them along.