Key Issues Dialogue
Featuring Peter Turner and Vicki and Fred Modell
From left to right, Peter Turner, Dennis Jackman, Vicki and Fred Modell
DENNIS JACKMAN: Welcome Fred and Vicki. Our talks today mark the beginning of an effort we are calling Dialogue with ZLB Behring. We’re hoping to conduct public conversations on key issues and concerns with different leaders in the patient and professional communities we serve. Our company President, Peter Turner, sees this as a top priority and a way that all concerned will benefit from information exchange.

We would like to address a wide range of topics today including product supply, innovation, and changes in diagnosis and treatment for primary immunodeficiency disease (PI). Let’s start with understanding the basic nature of the partnership between ZLB Behring and the Modell Foundation.

The Partnership between the Modell Foundation and ZLB Behring

What has worked well in the past and how might it evolve in the future?

FRED MODELL: Well, first, let me say that this partnership is very active and tremendously productive. The Foundation is involved in four areas: research, physician education, patient support and public awareness. And I would venture to say that in each of those areas, ZLB Behring has vigorously participated with us. With respect to research, together we have established diagnostic centers at UCLA and at the Children’s Hospital in Philadelphia in the U.S. We’ve established a diagnostics Center in Munich, Germany. And each of these initiatives has had extraordinarily impressive results.

With respect to physician education, we’ve run a wide range of Continuing Medical Education (CME) physician symposia and ZLB Behring has been for years a vigorous supporter of those CME Educational Events. ZLB Behring has been supportive of our K.I.D.’s Days all across the country. These spirited family days bring patients together from the same community. And finally there are programs that we’ve partnered in terms of public awareness, such as the ten warning signs poster and other efforts. The net effect is that for the past 18 months, our field surveys indicate a

An active partnership produces results...

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48 percent increase in diagnosed patients, a 46 percent increase in patients on immunoglobulins, a 28 percent increase in referrals and a 26 percent increase in diagnostic tests performed. This has been a powerful, vigorous, and constructive partnership.

**Look into your crystal ball please. What might you like to do in the future?**

**FRED:** Frankly, I think we are onto a very effective model. I would love to take this program, expand it in the U.S. and replicate it in other regions of the world like Eastern Europe, Latin American and Asia. I think we’re onto a really demonstrated and supportable hypothesis. Physician education and public awareness will help us reach the undiagnosed.

**Diagnosis of Primary Immune Deficiency**

**PETER TURNER:** I have a question for you, Fred or Vicki. Do you feel in the areas where diagnosis has improved dramatically that you’re getting all the potential patients with immunodeficiency?

**VICKI MODELL:** I think we are just getting to the surface. I think there are many, many undiagnosed patients. I think that what what investigators and physicians have discovered is that there are so many ranges of these diseases. In addition, some of the more serious forms of the disease in turn have ranges of severity. I think we have not even scratched the surface with the very mild cases of some of those diseases. These patients can go undiagnosed for 20 to 30 years, and then fall into serious trouble.

**FRED:** And, doctors can miss it during the first weeks of life. About four or five months ago, we heard from a family in Long Island, not very far from our office. A woman had gone up on our Web site and wrote to Vicki, saying that her child, her first child, was born in a large, important hospital in Long Island. The baby had a slight fever and was kept in the hospital for about two weeks. Eventually the fever subsided. The family went home. She said the baby was happy, eating, sleeping, laughing, completely normal, skin color was wonderful—a normal baby. About the fifth week, the fever returned and, at seven weeks old, the child tragically died in the hospital. That child was never picked up with severe combined immunodeficiency. Only on autopsy, only on autopsy, did they even know what happened.

**VICKI:** The physician admitted he did not know to look for severe combined immunodeficiency (SCID). They were looking for meningitis and other kinds of infectious diseases for the cause of the fever. This story and others like it, have accelerated our research initiative in new-born screening.

**IVIG Supply**

**DENNIS:** I’d like to turn to another topic now, if I could please. Peter, there’s been some talk in the news media about access to therapy issues due to reimbursement problems and perceived intravenous immune globulin (IVIG) supply shortages.
What is your view on this subject? What initiatives are ZLB Behring taking to address these issues?

PETER: I think overall there isn’t a supply shortage at this point. I accept that supply may be tight, certainly tighter than it’s been in recent years, but there are selective shortages in some product categories. And I think that these selective shortages relate to changes in reimbursement that have seen cost shifting in the system, which has placed huge demand on the hospital sector to take patients that were formerly treated in the outpatient environment. Hospitals, being under extreme cost pressure, have looked mostly for competitively priced products, and that’s put a lot of pressure on manufacturers of those lower priced products to find supply. The data suggests that supply has not decreased. It may be a little flat at the minute. I don’t know the reason for that because clearly each company is producing its own volumes of product, but essentially there is a lot of product still being distributed. And if we look at the difference between, say, 1999 and today, supply has grown from something like 15-16 million grams to 27 million grams in the U.S. today.

DENNIS: That’s a huge difference. In saying that, of course, the ability to create supply is critical. So, as a company, does ZLB Behring believe it will have consistent supply of product over the next three to five years? What are your supply plans?

PETER: In terms of 2005-2006, we will have a similar supply to the last 12 months plus we hope to have a new product, which is a subcutaneous immune globulin infusion, the first of its kind in the U.S. That will bring additional volume. We also have a liquid product in development in the U.S., in fact it is registered in Europe now. We’re looking to get a registration here in the next 12 or so months. That will be additional volume also. So, if you look at the status quo, we will continue to supply the equivalent volume that we’ve been supplying to the U.S. market with upsides in new products that are in development.

What are the implications of the announcement of the non-renewal of the agreement between ZLB Behring and the American Red Cross on the production of their therapies and supply of their plasma?

PETER: We chose not to renew the American Red Cross agreement so we could use that capacity to manufacture more of our own products. The expiration of this agreement allows us to manufacture more of our IVIG to help meet demand.

Fred and Vicki, how do you see the issue of product supply shortages and access to care?

FRED: We are delighted to hear that ZLB Behring has a real sensitivity to increasing the availability of product. We do make a distinction, however, during a tight supply market, between FDA approved and off-label indications. We think that there’s got to be special consideration for the approved usages. If the supply can support the approved and the off-label usage, that’s great. If that’s
not possible, then we are going to fight very hard for special consideration to the PI patient community. This community desperately needs the product, cannot do without it, and I just hope that we’re able to deliver on that.

**PETER:** It’s very difficult for manufacturers to control the channel of where these products get used. After all, it’s really the medical profession that determines who gets the product. And clearly they, through their experience and knowledge, hopefully use the product where it’s best applied. We clearly, however, do not promote off-label use.

**FRED:** I think that’s a critically important notion. Some patients say, “Well, if they suddenly find out immune globulin is effective in treating Alzheimer’s disease or neurology disorder, what’s going to happen to Johnny, my ten-year-old?” And if industry can say to us that we’re worried about your ten-year-old and we’re going to pay attention to that and we care about that and we will continue to care about that regardless of how broad the usage is, that’s a great comfort.

_Fred and Vicki, what are you hearing about perceived IVIG supply issues at this point?_

**FRED:** Well, so far we are finding about the same level of concern in the past 6 months as the past 12 months. We have tremendous traffic on our Web site, over 600,000 hits a month and 60 or 70,000 visitors. We are not finding patients or physicians who are unable on a continuing basis to get access to product. They are getting access to product, they do know there’s a concern, they do know there is a reimbursement issue, but they look to people like the ones in this room to advocate on their behalf. They cannot go to Washington, but we can. All of us.

**VICKI:** The patients are very grateful for IVIG. That we do hear constantly. “Well, thank goodness, they finally found out what’s wrong with me and I’m being treated with immunoglobulins. I’m feeling a million percent better.” So, you know, we hear only good stories.

**Reimbursement Issues**

**DENNIS:** I’m sure you’re aware of recent stories in the Associated Press and The New York Times about patients being deprived of access to therapy for PI because of reimbursement issues.

**What do you think of those accounts?**

**FRED:** As you know, in early May, a press release on this issue was put out by two non-profit organizations and a distributor. That press release was never reviewed or discussed with us prior to its launch. We thought it would have been appropriate to at least have some dialogue with our organization. I think it is very important for this community to have a uniform voice.

**DENNIS:** Reimbursement by federal programs and insurance companies keeps coming up as an issue related to access.
Peter, from an industry point of view, what is being done to increase access to therapies in the U.S.? How would you like to assess the success of the efforts with Medicare, insurance companies and other payors?

Peter: Well, certainly our company, ZLB Behring, has a very strong commitment to increasing access to therapy through our own efforts and also with our industry association, The Plasma Protein Therapeutics Association (PPTA). We do work with Capitol Hill to seek access for therapies. I think in terms of success, clearly achieving avoidance of IVIG going under the Competitive Acquisition Program (CAP) next year was the big win. That program would have allowed a contractor not to cover all brands or all offerings of IVIG.

I think also it’s important for us as a company to demonstrate social responsibility in this regard. We run reimbursement services for people who are having trouble getting insurance and we have an assurance program to help ensure that people who rely on our therapies can continue to receive them even if they experience a lapse in their health insurance. And that’s a commitment that we have to the patients.

Fred and Vicki, what’s your view on what is being done to increase access to therapy and what is JMF (Jeffrey Modell Foundation) doing in this regard?

Fred: Well, we have been going through the different layers. We have visited with third party payors. We’ve met with Aetna and with Blue Cross and we’ve had discussions with HIP (The Health Insurance Plan of New York) and with Kaiser. And I think they’re certainly aware of what is happening in this community and look to us to lead the way—us being industry and the patient organizations. So, to a degree, they rely upon us to fight the fight kind of for them in this particular area. We had a meeting at CMS (Centers for Medicare and Medicaid Services) and brought three of the leading physician immunologists. I think they made a very compelling case on the value of therapy and the importance of reimbursing physicians properly.

Fred and Vicki, does it seem to you that some insurance companies and also some states are moving toward a model that would allow a contractor only to cover certain competitively priced brands of IVIG?

Fred: We are absolutely convinced from the patients and the physicians that access to all preparations in all sites is critical to the care of the patient. There must be availability and choice of all of the products; it must be available in a doctor’s office, in a hospital, home care. It must include the availability of intravenous immunoglobulins and hopefully, with approvals, subcutaneous delivery as well. Every option has to be made available for patients because all of the patients are really different.

Vicki: Right. And not all of the products are the same.
DENNIS: So, from a manufacturing perspective, limited reimbursement is going to freeze out some products.

Peter, what does that do to you as an executive of a company looking forward and making decisions about investments and supply?

PETER: Well, limited access programs are essentially about price control. They’re not about access to choice. Apart from the potential disservice to patients, we’ve seen what discounted product has done to the industry. The latest round of consolidation in the biotherapeutic industry is all about economics. When companies are losing money, you get more consolidation to get to a new point on the cost curve where the industry can find enough return to continue to invest in product development and research that’s necessary in this industry to create the products for the patients. We see these limited access programs in other countries too and they are a threat to the very viability of the industry.

I guess the classic case would be the flu vaccine industry, which basically went away. There used to be ten manufacturers in the U.S. There’s now one. Maybe two. The reason? Well, the price of an influenza shot got down to $2, and companies said the risk/reward ratio is clearly not balanced here, we’ll stop investing in this, we’ll go and do something else. And what is government doing now? It’s throwing hundreds of millions of dollars at the flu industry to try and resurrect it. So, there’s a natural balance in all these things. Providers have to understand if they go too far, industry will struggle and patients will suffer.

IVIG Prices

Related to that, Peter, why are IVIG prices at the levels they are? How do IG prices get set in the marketplace?

PETER: Everyone knows that processed plasma is a very expensive raw material. It’s about half the cost of goods of a portfolio of products, which is quite unusual if you look at other industries. You have to sell a basket of products to get a return on your cost structure, and the pricing largely has to cover all those costs. Prices have gone up recently, but they’re only approaching levels where they were several years ago. So there’s been severe discounting in pricing in recent years, which threatens the very viability of the industry.

FRED: I would add that we are in favor of and will advocate for a fair level of reimbursement to the companies. The patients and the physicians are completely aware of some of the difficulties with industry and with government.

DENNIS: We hear reports about distributors marking up product prices by significant percentages above the wholesale price.

What is ZLB Behring doing to try to control that type of behavior?

PETER: This is of great concern to us because, one, it’s clearly unacceptable behavior. Secondly, I think in terms of what is happening here, you’ve got some
FRED: We have also heard of activities within the spot market in the industry in which the product was being sold and resold. There are genuine concerns about the chain of custody and the integrity of the product when this happens. We would only ask, again representing the patients, that ZLB Behring, your colleagues and PPTA put forth at least a statement that you are in favor of a code of conduct that makes clear that steps are being taken to monitor your customers. As far as the gouging, I respectfully look to ZLB Behring, your colleagues, industry to control your customer to play by the rules. You’re very strong. There aren’t too many places to go to day to get the product, and your customer must live by a code of conduct that’s appropriate. And if it’s going to be gouging, I mean our recommendation would be to just cut them out if that’s what they’re going to do.

PETE R: We don’t sell to the secondary distribution market.

FRED: Well, that gives us great, great comfort.

Product Integrity and Safety

Peter, what is ZLB Behring doing to address supply, chain of custody and product integrity fears in the marketplace?

PETE R: Well, clearly, we have worked to get tamper-proof packaging in place, and that’s a first step. We’ve also worked to get peel off labels and the like for traceability. One of the compliance issues is effectively tracking the product once it leaves the manufacturer. We do that, and we run compliance checks on our distribution channel. When it gets to the point of use, it’s also important that our medical colleagues track the product. They need to peel off the label and get it onto the patient’s record, making it easier to get that traceability.

FRED: One of the things that made me very pleased was when I heard that ZLB Behring had come through with new labeling and tamper resistant controls. I would hope that all of industry would do what they could to assure that the product is safe and is not being tampered with.

Peter, what steps has the industry as a whole taken to increase product safety?

PETE R: Clearly over the years, there’s been a huge amount of investment of improving the safety of the product, starting with the raw plasma material, where multiple viruses are screened for in the ongoing plasma donation process. Also, processes have been put in place that either remove or inactivate viruses, and
other sources of potential contamination such as prions. The industry is taking the approach, and certainly ZLB Behring is taking the approach, that we want to deal with known contaminants or infectious agents, as well as the unknown ones. And you can only do that if you have robust processes and procedures in place.

**VICKI:** This means it is very important that you are able to get a fair price for your product so that you’re able to take some of that money and put it into your research and development to constantly make newer, better, safer products for the patients.

**Regulatory Initiatives**

**Peter, in terms of product availability, are there regulatory initiatives that can be taken to increase the availability of immunoglobulins in the U.S.**

**PETER:** Well, I think first and foremost, the regulators have a tough job. They have to approve both safety and efficacy of these products, and that is a big responsibility. I do think there are steps that can be taken in times when more supply would be of benefit, and that generally relates to the speed of review of product that is submitted for registration. We work with the FDA and other regulators throughout the world looking to get prompt attention to clinical trial results that we submit and certainly to work with them to move products through the registration process very quickly.

**Peter, we hear about the need for “regulatory harmonization” on an international basis. What does that mean? How would that apply to products?**

**PETER:** I think there’s an opportunity for economy and efficiency in product development that can be attractive to patients, government and industry. Specifically, if you have a lot of your team’s time spent reformatting data to meet essentially the same safety review or clinical trial activity for a different country, it isn’t productive. It is expensive and inefficient. Yet, that’s what we often are compelled to do. So, from that point of view, international regulatory harmonization of requirements would enable the industry to spend money on other activities that could be more enhancing for patients.

**Looking Forward**

**DENNIS:** Let’s look to the future.

**Peter, as President of ZLB Behring, what are your immediate priorities, and then also what is your vision for the company over the next three to five years?**

**PETER:** We came together as a company more than a year ago, merging the former ZLB Bioplasma and Aventis Behring organizations. We have tried very hard to put together a very strong company because we recognize from that strength you create opportunity to invest and to be creative in what we do. So, essentially we’re very much in the short term consolidating those gains, and effectively getting the benefits flowing through, be they efficiencies within our own structure or
providing access to more products that we make for treatment of people with serious medical conditions.

From there, we are very keen to grow our business and create opportunities both for patients and for the people who work in the company. And we want to be a leader in the fields that we operate in—and that involves investment, clearly, in research and development to come up with new and improved ways.

**Fred and Vicki, what are your views of what industry might be doing and how it looks from your perspective going forward? In other words, how comfortable are you with where the industry is heading?**

**FRED:** I recommend to ZLB Behring and to the industry in general that they increase individual company visibility. It is in our collective interests that a patient or family not say to us “ZLB Behring? What is that?” We want the familiarity with the corporation and with the company’s products. If a patient knows who the company is, if the patient knows what the product is, the name of the product and there is some visibility in terms of what the company is doing in the marketplace, I think that’s very, very productive.

We have a small community. Our community is in competition with many other diseases that are very important. We’ve got to step up and be recognized. Thanks to all the help that you guys have given us up on Capitol Hill, they don’t say “Primary what?” any more. In Washington on Capitol Hill, they know what primary immunodeficiency is because we have been so outspoken.

Does JMF have anything new coming up in this regard?

**FRED:** Yes, it’s something new that is very exciting. It’s not ready yet but it will be ready in about a month—and it’s called “PIN,” the Primary Immunodeficiency Network. We will be launching an additional Web site. It will be password protected just for physicians on one platform and just for patients on the other platform. It will include a comprehensive information center, message board, disease specific survey results, “best practices” report, developments on gene sequencing, newborn screening, disease specific specialists, educational symposia and much more.

For patients, there will be dialogue concerning access to therapy and any potential side effects experienced with IVIG. There will be an opportunity for patients to share dialogue concerning reimbursement and site of treatment. PIN will be password-protected for both patients and doctors.

**VICKI:** And, it will be worldwide.

**PETER:** I share your enthusiasm for awareness and creating if you like a big splash because we’re competing with a lot of other serious medical conditions.

**What do you think of potential new IG products? What’s on the horizon?**

**PETER:** I think clearly if you’re a patient, you’re looking for easier modes of administration. Primary immunodeficiency patients need to get a lot of protein...
infused into their body on a monthly basis, and that currently is quite challenging for some. They go into an outpatient facility, they have an infusion that basically takes half a day, and quite often they don’t feel particularly well for two or three days. That can be a real impediment to their life and getting on with their work and everything else associated with their very being. Being able to give a subcutaneous product where they give smaller doses on a more regular basis, but the adverse events that they experience are much reduced, is clearly a benefit to the patients.

You spoke before of SCID patients and being able to get a bone marrow transplant. I think with genetic technology over time, there will be cures for this condition. And it won’t be for everyone, but a lot of people will be picked up early and will be cured and that’s fantastic.

VICKI: We’ve come a long way.

Is there opportunity for great research do you think at the government level at NIH (National Institutes of Health)?

FRED: Oh, absolutely. We started with Congress and the NIH about seven or eight years ago. We asked them about the level of research monies going into primary immunodeficiencies. Immunodeficiencies was a general category divided into two pieces: acquired immune deficiency, $1.6 billion and genetic or inherited immune deficiency, just under $3 million. We were working with Senator Lieberman. We went back to him and asked “How can that be?” And he said, “Well, the answer is you’ve got to show up.” And we began to show up. And in a few years, we did six research collaborations with the NIH, with two of the Institutes, in which we put up $1 and the NIH put $4, and we did $5 million of five-year research grants all together.

It was wonderful science that would never have been funded had we not triggered it with our funding.

DENNIS: I think there’s another question that comes up once in a while from people who see the economic importance of generic prescription drugs.

What potential, Peter, might there be for generic biologics?

PETER: Well, I think first of all you’ve got to recognize that biologics are much more complex than chemical entities, and whilst there is a generic industry in pharmaceuticals, the very products that we make are all different, and that’s part of the reason for maintaining access to all products because some patients do not respond well to one particular product and are fine on an alternative product. So, I think the issue of generics is complex in biologics. I really think that there isn’t the potential to develop generics like there is in the chemical drug industry, if you like. The nature of the plasma, the complex processes, I think you’ll find that government regulation will not easily be simplified for those types of products. A generic drug maker can chemically show equivalence to an existing product and then they
don’t have to do the clinical trials and can go to market at a lower cost. I don’t think that will happen with biologics.

DENNIS: We’ve covered a number of important matters today. Thanks for joining us, Fred and Vicki.

FRED: I would just summarize by saying, and I guess you could hear it sometimes when either Vicki or I talk, we are essentially optimistic, very positive about the future. We would ask industry hopefully to believe in this mission and accordingly as you do your planning three years, five years, seven years down the line, think in terms of increasing capacity in order to meet the demand. We are going to find the patients and these patients need to be treated. We desperately need to rely on you to be able to produce product that will help these patients.

PETER: Fred, please be assured we are looking to increase our capacity in the next five years if the product demand is there.

DENNIS: Well that’s a very good note to end upon. I would like to thank all of you for coming to the introductory session of Dialogue with ZLB Behring.
About the Participants

The Jeffrey Modell Foundation

The Jeffrey Modell Foundation was established by Vicki and Fred Modell in memory of their son Jeffrey, who died at the age of 15 of a Primary Immunodeficiency. The Foundation is dedicated to early and precise diagnosis, meaningful treatments, and ultimately cures of Primary Immunodeficiencies.

The Foundation’s Focus:

■ To affirm its absolute commitment to clinical and basic research in order to better understand and treat Primary Immunodeficiencies.

■ To serve as a national and international source for the dissemination of information and education into the diagnosis and treatment of genetic immunodeficiencies.

■ To serve as a tireless, compassionate advocate on behalf of patients and families to assure their access to excellent and comprehensive care.

■ To promote public awareness of the Primary Immunodeficiency diseases through programs involving our lawmakers as well as lay, scientific, and medical communities.

■ To affirm its commitment to turn pain, despair and suffering of immunodeficient children and adults into comfort and hope.

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ZLB Behring

ZLB Behring is one of the world’s leading pharmaceutical companies specializing in the manufacture of plasma products. Its comprehensive line of therapies include products for the treatment of hemophilia and other coagulation disorders, immunoglobulins for the prevention and treatment of immune disorders, treatments that inhibit the formation of blood clots, wound-healing agents used during major surgical procedures, and plasma expanders for the treatment of a variety of conditions such as shock, burns and circulatory disorders. Additionally, ZLB Behring operates one of the world’s largest, fully-owned plasma collection networks.

ZLB Behring is committed to developing the next generation of therapeutic proteins to meet the demands of the evolving market. Products under development include subcutaneous immunoglobulin treatment for primary immune deficiency and fibrin dressings for use in cases of severe hemorrhage.

At plants located in Bern, Switzerland; Marburg, Germany; and Kankakee, Illinois, ZLB Behring manufactures therapies in accordance with international safety and quality standards. The products are distributed worldwide.

ZLB Behring is a subsidiary of CSL Limited, a pharmaceutical company which operates worldwide from headquarters in Melbourne, Australia.

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