Conference Summary

Pharmaceutical Executive Summit: Emerging Strategic and Financial Issues in the Pharmaceutical Industry

November 9, 2023
In-Person and Virtual Conference from 11:45 am EST to 5 pm EST
Yale Club of New York City

Agenda

12:00 p.m. **Welcoming Comments**
- **Peter Young**, CEO and President, *Young & Partners*

12:20 p.m. **Luncheon (in person) and Virtual Networking (virtual attendees)**

12:30 p.m. **Keynote Speech and Fireside Chat:**
Brave New World: Adapting to Change
- **Peter Stein, M.D., Ph.D.,** Director, Office of New Drugs, *U.S. Food and Drug Administration*
- Moderator: **Peter Young**, CEO and President, *Young & Partners*

1:15 p.m. **The Pharma and Biotech M&A and Financing Landscape**
- **Peter Young**, CEO and President, *Young & Partners*

1:45 p.m. **The Pharmaceutical Market: Trends, Issues and Outlook**
- **Doug Long**, Vice President, Industry Relations *IQVIA*

2:30 p.m. **Virtual and In Person Networking Coffee Break**

3:15 p.m. **Disruptive Innovation: Research Manufacturing and AI (Fireside Chat)**
- **Dr. Stephen P. Spielberg**, MD PhD, Senior Adviser, *Young & Partners;* former Deputy Commissioner for Medical Products and Tobacco, *FDA*
- **Eli Weinberg**, Partner, *Bain & Company Life Sciences*
- **Peter Young**, CEO and President, *Young & Partners*

4:00 p.m. **Speakers Roundtable: What Does the Future Hold?**
- **Doug Long,** Vice President, *IQVIA*
- **Peter Stein, M.D., Ph.D.,** Director, Office of New Drugs, *U.S. Food and Drug Administration*
- **Dr. Stephen P. Spielberg**, MD PhD, Senior Adviser, *Young & Partners;* former Deputy Commissioner for Medical Products and Tobacco, *FDA*
- **Eli Weinberg**, Partner, *Bain & Company Life Sciences*

- Moderator: **Peter Young**, CEO and President, *Young & Partners*

5:00 p.m. **Conclusion of the Conference**

Young & Partners

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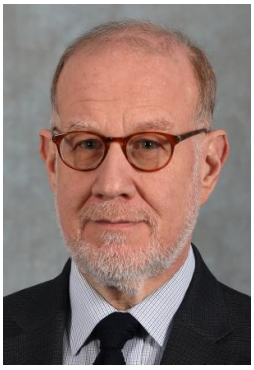
Brave New World: Adapting to Change



PETER STEIN, MD, PhD
DIRECTOR
CENTER FOR DRUG EVALUATION AND RESEARCH, OFFICE OF NEW DRUGS, FDA

I will try to give you a bit of a view from the FDA on the changes in the types of drugs being developed, some of which, you all are familiar with. We are seeing a shift to rare disease development and I want to talk about some thoughts and challenges for developing drugs for rare diseases and as well as the current context for common diseases. I want to talk more about the approval standards and how one will have to adapt and how clinical trial programs have been developed. We seen changes such as the shift to more applications in rare diseases and also narrower sub-populations in oncology versus for broader common diseases. 20-25 years ago when I first joined the pharmaceutical industry there were multiple drugs approved for common disease such as diabetes. Even with this shift, there are still many unmet needs in rare diseases. We need to make progress in both rare and common diseases.

Genomic drivers, molecular drivers have made huge differences in oncology but also understanding the genetics have made significant progress in cystic fibrosis and led to targetted new therapies. As we understand common diseases, we can divide patients into relevant sub-populations that has led to molecular targetting of those as well. There are still opportunities for common diseases, but those require truly differentiated therapies that leverage our understanding of the background diseases pathogensis and the utilization of new platforms.

There has been interest in using confirmatory evidence rather than a standard well-controlled trials. That includes performing more extensive work in animal model work and human translation work that companies are not currently doing. There is an increased interest in using surrogate endpoints to support approval and certaintly more interest in accelerated approval as a pathway to get drugs approved with not always the background support needed. Reguatory flexibility comes up when dealing with rare diseases where innovative designs are needed and intended to create efficiencies in how the data can be reliable. Another challenge coming to the forefront are "N of 1" programs. There has certaintly been a push from the FDA Commissioner on new ways for evidence generation using decentralized trials, pragmatic/point-of-care trials, master protocols, digital health-enabled endpoints and real-world evidence.

One thing I mentioned before has been the increase in the number of applications for approval of rare diseases. Looking at the number of NME's, the proportion was 25%-30% designated towards rare diseases 12 years ago. It has increased to around 50% of applications today. There has also been an increasing year-over-year number of rare disease/orphan INDs. We expect to see more of this proportionally.

In rare diseases, we are facing small populations of varying sizes that require novel study designs. These rare diseases are often progressive, serious and life-threatening diseases that lack approved therapies. This means that they must be dealt with properly to ensure trials are well-designed. There is often a lack of precedent for the drug development and genotypic and phenotpic diversity despite similar genetics and different versions of the disease may exist. This makes trial design very difficult including factors such as the rate of progression of the disease affecting the time of the clinical trials. Drug development tools are not necessarily available among all these diseases with, at times, no established endpoints. Many of these cases involve children and are under very different regulations.

A year ago, we have launched CDER's Accelerating Rare disease Cures Program which is a multidisciplinary, multi-office program to work with sponsors and stakeholders to help accelerate drug development for rare diseases. On issues related to common chronic diseases, there are still opportunities with inadequate treatments. Only recently, in areas such as diabetes and obesity, we have seen drugs that are quite effective and we expect to see more drugs that are effective for areas such as in obesity. Drugs for heart and Alzheimer's disease are beginning the field

treatments that are novel therapies that are effective. We are also focusing on treatments for common diseases targeting subpopulations of patients that have defined subtypes by genetic, genomic or mechanistic phenotypes that were previously seen as large categories (breast cancer, small cell lung cancer, varities of lymphoma). On the other hand, we also see a lot of proposals for subtypes that are not really subtypes. Subtypes do not mean there is a greater or less effectiveness of the drug, but rather a different pathogenesis where the targeted drug is only effective with that subtype. This has lead to more drugs for resistant diseases or late-stage diseases.

I want to talk more about the new methods of evidence generation and it is hard not to give credit to the impact of COVID-19. It certaintly accelerated our thinking about drug development and the use of decentralized trials because patients often could not come to the investigational site. The use of DHTs, which enables the use of decentralized trials, became increasingly important as we looked to see whether we can gather investigational data at home. The increased use of master protocols allows us to test multiple therapies concurrently. It underlines the need for innovative approaches for rapid development and use of RWE to inform regulatory decisions.

The FDA "standard" requirement is for two A&WC studies to fairly and responsibility evaluate effectiveness. This is flexible, for example, p-values <0.05 is not required in the statute, but is our interpretation of the statute. The historical approach was effective for chronic common diseases but there is also the use of one adequate and well controlled study with "confirmatory evidence". This ranges for the types/sources of evidence and the level of convincing support for the A&WC study. A less common method is a single A&WC control that is often a large, multicenter study that provide similar persuasiveness as two A&WC trials. There are a variety of tools for regulatory "flexibility" where the FDA can exercise the broadest flexbility. There is also an acceptance of uncertainty within regulatory flexbility for rare and serious diseases where two A&WC trials may not be feasible. There are two components to approving a drug, demonstrating effectiveness and mastering the benefit-risk approach.

I want to spend the last few minutes talking about the changing "face" of clinical trials. Clinical trials will evolve dramatically in the next 10-15 years , but our focus on substantial evidence of effectiveness will not change. It will be important even if the way the evidence is generated will change. Decentralized clinical trials will see some or all of visits done remotely with investigators at a central location and drugs at local depots or sent to the patients. This will be useful for simplier Ph3 or post-approval trials and not for trials with complex procedures or drug aministration, or limited safety information. Digital health technologies will make it a lower hurdle and help improvement measurements of current endpoints. The ways we can use safety monitoring, look at blood pressure and engage with patients will also be enhanced. A few words on pragmatic trials. Whereas traditional trials were very strict and very dedicated and thus not very generalizable, I believe more and more we have phase 3 trials with broader inclusion criteria which will push sponsors to be as broad as possible. Certainly, the dedicated research sites were more on-site and were strictly monitored, whereas the pragmatic trials will have fewer visits and reduced data collection. There is great value in using the data to identify trial populations and potentially use it to support an aproval decision as confirmatory evidence. This is important because you can take information from a much broader and diverse patient experience. If you can download data and develop a proper protocol to analyze it, you can get data in months rather than years. In some clinical trials, the endpoints could come from real world data and real world evidence. On master protocols, this is an area that has seen a lot of growth. This has been able to leverage efficiencies in enrollment and other aspects that was utilized in situations such as COVID. This allows for a more efficient approach than starting new trials to test drugs that could be dropped in or taken out. The challenge of "N of 1" is what type of evidence needed before exposing a human to a new drug. How persuasive should the data be to permit a clinical study, dosage and regimen, CMC characterization, an assessment of the urgency of the patient's situation with regard to efficacy and safety. When addressing the importance of diversity with legislation like FDORA, we want to understand the differences and responses between different populations. We want patients to know that we are studying patients like them so that the data is relevant.

The Pharma and Biotech M&A and Financing Landscape

PETER YOUNG
CEO, PRESIDENT AND MANAGING DIRECTOR
YOUNG & PARTNERS

Business Conditions

Pharma and biotech are marching to a much different beat financially, but it is clear that there are ways to explain the drivers between those differences. There is a lot of innovation currently by pharma and biotech with regard to their ability to invent new drugs, inspite of challenges such as the high cost of development. The biopharma industry's efforts related to the pandemic have been a positive for the public's perception of the industry.

Stock Market

The biopharma industry has generally performed well in the stock market, with our indices increasing. We can see that the only one that didn't do so well is the NBI. As a result, because the biopharma industry has had good performance recently, their multiples are trading relatively well. The generic industry has had somewhat of a recovery this year after a long-term period of decline. However, in terms of multiples, the generic companies have not done as well.

What about biotech? The bottomline is that the broad NBI index fell by 5.3% compared to the general market indices that increased. Only our group of small-medium cap stocks increased. Historically, the NBI has significantly outperformed the marke, but not recently.

M&A

On the Pharma M&A side, there were 20 transactions completed for a total deal value of $9.6 billion in the first three quarters of 2023 versus 42 deals worth $59.9 billion in 2022. The are a number of reason for this significant drop. Large pharma have not focused acquiring other pharma companies. They have focused on acquiring biotech companies and drug candidates using M&A, strategic alliances, joint ventures and licensing. There are a few big pharma deals in the pipeline but not enough to create a high volume year for 2023. This year will not be as strong compared to last year. In the late 80s and early 90s we can see that the volume then is similar to today before big spikes from big pharma mergers. Pharma CEOs have come to realize that merging two pharma companies does not necessarily produce an ability to invent faster and as such they have shifted their strategy away from large Pharma acquisitions.

For Biotech M&A, there were 59 deals worth $55.8 billion completed in the first three quarters of 2023, significantly higher on a annualized dollar volume and number of deals basis than 2022. One of the deals in the was a rather large deal, the acquisition of Prometheus Biosciences by Merck, but it does not dominate the total numbers or dollar volume. Much of the M&A focus has been in the U.S. due to the concentration of the biotech industry in the U.S., Part of the reason for the high M&A volume is because biotech companies are having trouble going public. When IPOs were plentiful and at high valuations, biotech companies could wait to sell their companies.

Financing

On the debt side for Pharma, big pharma generally has a lot of cash and can generally only borrow when they are trying to adjust their balance sheets after M&A transactions. The volume of debt has fallen through the first three quarters, consistent with the volume of deals slightly decreasing. Equity offering volume has been reasonable.

If we switch to Biotech, generally debt issuance is modest due to their lack of positive cash flows. However, the story regarding equity issuances is interesting. The total equity issuance market is healthy, at a similar pace to last year. However, most are secondary offerings, not IPOs. The volume of IPOs has collapsed, with only 13 in the first 9 months of 2023, much lower than last year's pace.

Outlook

The business outlook for pharmaceutical companies is positive. It has been a good time for innovation. In addition, Pharma companies have been able to fill up their pipelines with promising products. Overall development activity has been strong and will continue to be strong, with new technologies being developed. The only group that is challenged are the Generics, with fierce competition.

The stock market will continue to be kind to Big Pharma, but biotech companies will likely continue to be punished. On the M&A side, pharma companies will continue to go for small to medium-sized companies on the pharma side.

Biotech companies are doing a good job of continuing to invent new drugs and treatments, but their challenge is the financing market. The IPOs will continue to be depressed and biotech companies will struggle to get funding and, if they do get funding, at attractive valuations. Partnering, licensing, an M&A transactions will continue to play an important role..

The Pharmaceutical Market: Trends, Issues and Outlook

DOUGLAS M. LONG
VICE PRESIDENT, INDUSTRY RELATIONS
IQVIA HOLDINGS INC.

COVID is appearing to be more in the rear view mirror with the passage of time. Deaths to date are down and I am not expecting a great increase in vaccinations. The flu vaccine season is consistently strong and we see similar numbers this year. What you can also see is that we have had big flu seasons before. We have developed a Health Services Utilization Index before COVID. It was 100 based on the first 8 weeks of 2020 and we are back there with office and telehealth visits as well as new prescriptions. However, what is concerning to me is screening and diagnostic tests aredown. Elective procedures are down and lab test are also down which may be explained by COVID deaths of those 65 and older.

In the use of medicine report, the first trend we see is greater antibiotic use and rising antimicrobial resistance. ADHD medicine has also grown 11% over the last 5 years with women leading this change. Mental health prescriptions have gone up and particularly in young wmen. In GLP-1s, there was the approval of Zepbound yesterday with over 500k GLP-1 aganoist new prescriptions across diabetes and obesity in February 2023. Opoid use has been down but opiod over dose are up significantly. Contraception use is down, but I do not exactly know what that means. If you look at what contributed the most growth to specialty therapies, the big three are immunology, oncology and diabetes, but we do not refer to diabetes as a specialty therapy area. We are back to similar growth as what we had pre-pandemic. Prescriptions are up on adjusted and unadjusted basis.

This chart looks at dollar growth in the market with total market growth, retail and mail growth and non-retail growth. When we break down the non-retail to clinics, hospitals, home health care and long-term care, clinics are doing fine, hospitals are having a bumpy road with examples such as antibiotics, long-term care has recovered.

We move to specialty compared to traditional growth, with diabetes being classified as a traditional class. The acceleration of growth was historically been driven by specialties, but that percentage has gone down. The biggest class for specialty therapies in retail was HIV and immunology. 10 specialty therapy areas dominate the market and are growing at 13% per year and accounting for 43% of the market. Multiple sclerosis and respitory are the two classes that are down. In sales dollars specialties are growing in all channels. In non-retail Keytruda is the largest product showing tremendous growth, in mail the largest product is Humira, and in specialty retail we see Biktarvy and other HIV products there.

In GLP-1s, Mr. Stein talked about how changing this potential is. 70% of the United States is obese or overweight and 50% worldwide and obesity is linked to additional health problems. There may be a decline in the future in cardiovascular drugs and other products as obesity drugs are being seen as preventative care. Treatments in obesity are a game-changer. Mounjaro from Eli Lily in late 2022 had the second best performing rpoduct sales launch since Harvoni.

As an example, Hepatitis C is a curable condition that affects 3 million people in the United States. The treatments can cure 95% of the patients but are also expensive at $20,000-$25,000 a course. The obesity map in the United States has also significantly changed as America has become more obese in the last 10 years. Ozempic and Mounjaro drove most of the volume growth. In 2018, this market was about $9b, was worth $35b in 2022 and will be worth $61b in 2023. Almost 2/3 of retail growth is driven by GLP-1s.

The peak of the opiod epidemic was in 2011 and the use of opoids since then have been down 64%, at a level similar to the early 2000s. Fentanyl overdose deaths are up 1000% since 2015 and are the leading category of overdose deaths. Generally overdose deaths have plateaued since the increase during COVID-19. Generics have been up on a volume basis, but the sales have been relatively flat representing a smaller share of the total market. Generic prices

have also been eroding. There are a number of smaller players that are being approved that cannot compete truly in the marketplace with the larger players.

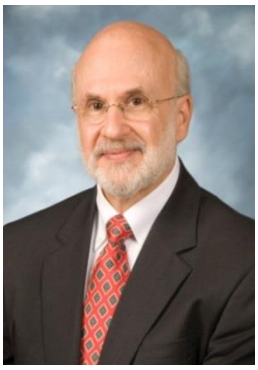
In 2018 it took 8 branded products to equal the total generic business. In 2023, it will only take 2. With Ozempic in the future, it may be just one product. The problem is that generics represent 87% of the total prescriptions but represent only 8% of the total dollars. Since the 2000s about 2/3s of the ANDAs launched and in 2022 it has been less than 20%. More commonly, we are bringing drug to approval without any commercial success. The fragmentation in generics has also been increased since the earlier days of a few big players. There has also been a lot of activity in biosimilars, with 10 set and approved to launch in 2023. There is some advantage to being a first mover in a biosimilars and expected launches and uptake will likely increase overall spending in biosimilars.

There are more drug shortages than ever before, partly because of the increased demand of some products (GLP-1s, ADHD drugs). We can see that psychiatry drugs have the greatest number of shortages and the reason this is important is because they are large and increasing with fewer being resolved. Some of this is driven by buyers increasing orders to buffer the expected disruptions. This chart of FDA inspections is very concerning to me, with the number FDA inspections on plants being significantly lower than the level pre-pandemic. Does this cause shortages when people come around to inspect the plants? One example is Akorn Pharmaceuticals, which decided to close their business. 86% of Albuterol used in hospitals was made by Akorn and there are only two players with the other also being inspected.

In product launches there were 50 launches in 2023, with the largest product being the RSV Vaccine. We can see that by comparison, we are running lower than 2021 and are right on pace in 2022. Alzheimers continues to be an untapped space with significant untapped needs. Amjevita, the biosimilar for Humira, was the second largest product launch in 2023. Looking at Q4 2022 to Q3 2023, the biosimilar penetration for Humira has been very small, which is concerning as we see biosimilars for Stelara.

We see growth in the marketplace, although we believe it will be stressed. We believe the growth rate will climb. The classes we believe will grow the most include obesity, who has seen great growth forecasted and historically. Oncology has also been big despite the fact that there are three biosimilars for big oncology drugs. We see that diabetes is forecasted to shrink as there is significant rebating of 60-70% of the cost. Spending on obesity drugs is only going to go up. The gross dollars tells a different story than the net dollars in diabetes spending as net spending is forecasted to decline. For autoimmune, we believe that there will prospective savings from biosimilars, although it hasn't played out as I expected.

GLP-1s, huge impact on sales and remember, retail pharmacies lose huge amounts on each prescription. Flu was mild, COVID vaccines have been weak this season. Mental health and ADHD drugs have been increasing in prescriptions. Several Adalimumab biosimilars are launching and their impact is to be seen. Branded generics and generics have had poor sales as well. They have an OTC birth control pill and OTC Narcan which we will see how that affects those markets. There are more resistance and reluctance on vaccines particularly involving pediatrics. Drug shortages are significant in oncology. About 10 million people have been disenrolled from Medicaid after the pandemic and where will they go? And what will be the impact of IRA, DSCSA and DIR on retail pharmacy? With that, thank you very much.



DR. STEPHEN P. SPIELBERG
SENIOR ADVISOR, YOUNG & PARTNERS
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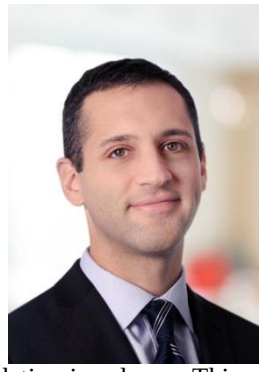


Young: We have a very nice group today to cover the areas of disruption that would be of the greatest interest to you. I will first ask Dr. Spielberg about which areas are being disrupted and I will also ask Eli some questions on AI and other areas that he sees are being disrupted.

Spielberg: This is my 50th year as a physician, more specifically a pediatrician. I want to look at innovation, disruptive technologies from a historical point of view. Pretend we are back in the 1940s. It was a time when polio was rampent and was made more scary by having a president that had polio. And there was a scramble for new technologies and new innovations with technologies such as iron lungs. Boston Children's Hospital was designed in the 1950s around polio and desgined their facilities around being user-friendly for accomodating iron lungs. This had made it almost impossible to practice medicine in the hospitals. This led to the flu vaccine and all the iron lungs are now stored in the basement and are an exhibit of when innovation failed and understanding pathgenesis to make all of it irrelevant. Second example is when babies in the 1960s suffered from respitory distress where surfactants were developed to help premature babies, leading to a product and innovation where the latest technology respirators at the time became archaic. Next, a brief look at oncology in pediatrics. As I became a resident, there began to be treatments for acute lymphoblastic leukemia and over my career cure rates went from 20% to over 85%. But this was not necessarily due to innovations in chemotherapy. It was due to antinauseants, particularly in teenagers that were unable to complete their treatment because of nausea. That miracle had nothing to do with the treatment of cancer, it had to do with the ability for them to continue with the treatment of cancer. Cystic fibrosis had been mentioned, and because beautiful science led to the findings of the gene that led to cystic fibrosis, life changed. Because we understood the gene products that led to lung and GI problems, this led to incredible innovation heavily driven by patients and patient advocacy groups. So, we have entered the genomic era. We have gene therapy, gene editing, immunological approaches (vaccines for antibiotics and cancer), new approaches to immunology. These are all things I could of never imagined in my early career. They are in the process of approving a sickle cell anemia drug, with gene editing, where they are targetting the gene that regulates the sickle cell gene rather than editing the sickle cell gene. The issue now is can we get technology available to those who need.

Weinberg: I will talk about a very different kind of disruption which is the disruption to how people in mid-size and big pharma companies go upon their day to day lives. This has become much more of a critical issue with the emergence of foundation models and generative AI capabilities. Firstly, technology is no longer the factor holding back progress and impact and second, it will impact us in our day to day lives. On the first point, for previous types of models there would be great investments in training and the data. What we have now is an agent who may be a quirky person but is able to acculumate a lot of information in their fingertips and can work at the speed of light. And, because they come preloaded with information, it is incredibly fast to go from zero to generating meaningful insights. What we are not held by back is getting an agent to do something useful, it is whether the users and regulators are ready for that type of disruption, whether there are regulatory flexibility and whether patients are

ready for that. It is the choice of where do we use this technology and how do we impact people. The reason that it has such an impact, in contrast with previous technologies, is because it is very easy to point at areas where AI is not useful. I will point at two of these areas. Regarding the question of AI in clinical trials, there is no sign we will stop testing clinical trials on humans. We will still need to manufacture medicine and we cannot do this virtually. AI can be a wraparound but these things won't go away or change. The final changes are making trade-off decisions which are increasingly being impacted by AI. This work will be done sooner than people may think.

Young: I would like to comment on the drivers of pharmaceuticals which is new technologies and so forth. One side that doesn't get as much attention is the manufacturing side, and Peter Marks last year, talked about the problem on manufacturing and new technologies. These new technologies will help solve diseases otherwise untrue but also many of these are very hard to manufacture. In our work, if something is difficult to manufacture of expensive to manufacture, it is a problem. When this is the case, the number of people they can treat is very limited. AI everyone is very excited about but there is a cost to training the data and produce the answers with AI companies seriously subsidizing your use of AI. There are multiple purposes, such as attracting users but the cost to the company is moreso than what some may pay for their searches. The other problem is whether the cost allows it to be something viable in the marketplace. My feel is that there is not attention paid to that, if more companies were able to rationalize and make manufacturing less expensive, it would make more drugs economically viable and available to patients. There are disruptions in innovations to manufacturing but I do not think that there are enough relative to the innovations on the research side.

Spielberg: Another question that arises is that there is incredible technology and understanding of disease pathogenesis. Where we are strugglling are the interfaces, taking a great idea and making it into a molecule, turning the molecule into the drug, the ability to de-risk, and the ability to adapt to the innovations. Do you see a way that AI can make our inabilities to bridge these things to collapse? Can this make us wiser and well as smarter?

Weinberg: Good question, I am not sure if this will make us wiser, but AI wll help make some of the connections. Google was able to model any protein initially, and what was announced last month was modeling protein folding and docking. They have launched a company that focuses on the translation and identification of clinically ready assets. Once you start with one part you start expanding to other domains. This gives us the ability to look at the assessment, combine the genomics, the patients, the outcomes. Companies that started on the discovery side ended up finding a clinical biomarker or companies that started the other way to find biomarkers, after digging a bit, concluded that it is interesting drug target. The more technology can explore and link big datasets and find insights, the more we ineviability link from the initial signature of a drug target all the way to a molecule and the patients.

Young: I agree with you, I think there will be a ton of uses for AI that will not turn out not to work but I am confident that AI will have a significant impact on the speed and cost of drug discovery. I did a lot of work with companies in microfluidics which was a huge benefit for exploring the most promising molecules. And I believe it is working.

Spielberg: On the comment about protein folding, cystic fibrosis is a syndrome that is a mutation on the same gene, but there like 90 mutations of that same gene. Because of all of that, it took a number of years to get to a developed product. It is an interesting thought experiment with the technologies today, whether time or cost could be knocked off in the development process.

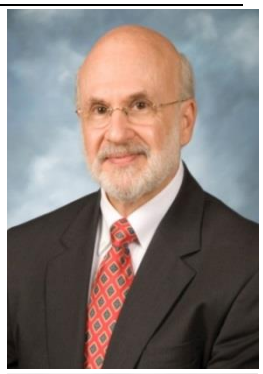
Weinberg: There is a lot of high science artifical intelligence in being applied to and it is hard to say. But for sure, we can reduce development time in regulatory documentation for example. There is a ton of value on dry stuff that is not very scientific but the generative tools are perfectly suited for that. Internal knowledge management, content generation and other things are going to look different from today.

Spielberg: If you think about the unbelievable wastes of time we go through and the frustration of the people affected, there is great benefit. I would love to have something that connected the FDA and the rest of the international regulatory community.

Young: Although this conference is dedicated to the pharma industry, I want to point to what Doug Long mentioned regarding the costs of the health care systems, and my hope that AI can help reduce these costs. It is already known that AI and other techniques can have benefits in radiology and other things that can reduce cost. Hospitals, diagnostics and testing chews up a significant portion of dollars. I am also very pleased that so many new drugs are increasingly able to cure diseases rather than just prolong life. For a time in oncology, it was known that it could only treat to prolong life. I am cautiously optimistic about this and prevention.

Spielberg: We struggle and have struggled forever with mental illness. How to define it, what it means? If we look at severe mental illness, these are diseases that present often in college, end of high school. Once the diseases are raging, people suffer, society suffers and families suffer. If we get smart enough, some of it is sociology, the issue is whether we can use technologies to look at early signs, where before or just as someone is about to lose it, we can help them. It is interesting, I view all of these diseases as developmental diseases and we do not necessarily know what to look for.

Young: On the preventative side, the statistics shown by Doug Long really show that obesity directly impact diabetes or other cardiovascular diseases. Thank you again for the combination of different angles. My hope is for any many positive disruptions as possible.



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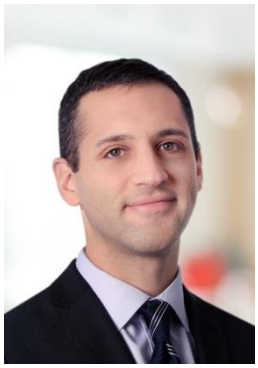

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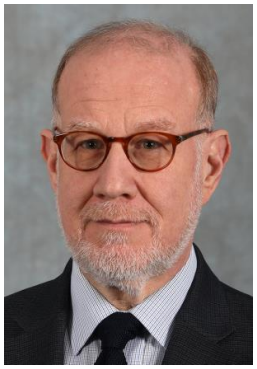
Young: The general question I would like everyone to address is "What does the future hold?"

Weinberg: I think we haven't talked as much today about patients and how their relationship with physicians has changed. I think that there is much more patient-friendly care and some of the biggest products this year are dispensed at retail stores. Patients are now going to One Medical, an Amazon subsidiary, so people are now getting care from Tech companies. It has been getting more complex as to where the physicians are, how they spend their time and how they interact with patients.

Young: Because of new laws that favor the hospital, they are really driving the independent physicians out of business. In addition, the current independent doctors are getting older.



Long: There has been significant staffing issues in home care, hospitals, and it is a big concern. Another big concern of mine is the state of the retail pharmacies with Rite Aid going bankrupt and CVS and Walgreens closing stores. One example of the problem is that fulfilling GLP-1 prescriptions is a big money losing proposition for them due to the pricing structure..

Stein: I think the future will bring what the past has already tee'd up. A lot of the changes that the research has done has accelerated. There is a massive amount of data out there and the quality does not always capture the purpose and is a distraction. There is a ton of data out there that is not captured or is improperly recorded. We would hope that would drive us to a better data enterprise through more standarized and quality data collection. If we can do that, we have these engines that can look at associations across genetic and phenotypic data across history. The amount of information that we could gleam and model could allow this enterprise model simulation to design trials to determine whether a drug is likely to work, and change the nature of what you put your effort into. In the future we would like to know what are the likely manifestations and design a protocol that could save potentially a huge amount of time. We could go from a concept of a drug, design using AI and other

technologies to go to trials in 2-3 years, a much shorter timeline. From our side, we are looking at how do we should look at data and accelerate our analysis? How do we put all of this together to make a system that is much more efficient and shorter in development time?

Spielberg: Putting on another hat, as a former medical school dean, I am concerned that we face a very different challenge and sociology now about how to teach students. I have colleagues that quit medical practice when electronic records came out because they didn't know how to type and they weren't going to learn. Sounds funny but at that time you could not find an EMT surgeon in my neighborhood in Philadelphia. With things like AI, you do not need to memorize every metabolic pathway, but we don't teach our students to do that. We don't teach our students virtual visits, or teach visiting nurses or pharmacists. Medicine won't be the same as when I started or when my son started 10 years ago. We need to be teaching our students the skills that translate into real patient benefits. In addition to doctors, we need sociologists, teachers, and psychologists who are out there in the real world who are interacting with patients. The greatest mistake would be to have the best drugs in the world and not be able to deliver them to patients because they cannot afford them or because we do not know how to talk to them. One thing about cost, the therapy to treat sickle cell anemia has been discovered long ago and is currently about $2 million a patient. There are approximately 100,000 patients in the U.S. with sickle cell anemia and close to 10,000,000 patients in the third-world.

Long: Think of it this way, in pharmaceuticals they were biologics, then specialties, then biosimilars, then rare disease and cell and gene therapy. As you go left to right, you go to smaller patient populations. The challenge is how do you expect society to fund the cost of innovation for fewer people.

Young: If I take an even bigger picture view of all this, one of the concerns is the high cost of healthcare in the U.S. and the impact that has on our economic competiveness. We have the highest cost of healthcare and we are 27^{th} in terms of quality of healthcare. One of the problems is that we haven't tackled inperfections in the system and where the costs incurs. Instead, there are many unintended consequences. Often, they are looking at the wrong end of the telescope. Our primary problem is not insurance, it is the cost of the system.

Long: Some of the people writing this legislation aren't people who are in need of drugs.

Young: So the future seems mixed. I almost feel like the guy who once was interviewed as a leading producer of buggies who was asked whether he was worried about cars, and responded "No, we will just make horses go faster".

Long: I am not as worried innovation as I am worried how we pay for it.

Stein: I certainly agree with that. I wanted to make an additional comment, I was looking at news reports and a news on our new obesity drug approved and food companies are judging the impact of this drug on their business. The benefit risk calculation is always important and looking at what the opportunities that exist are.

Weinberg: If we talk about the general pharma company performance over the last 30 years with 17 companies representing total revenues in the $30b range, with now over 200 public pharma companies with over $2 trillion in market value, things clearly have changed. We have added medications and treatments since then and we are now entering the period where things will look different than the way they have historically.

Spielberg: I am a pediatrician so I have to be optimistic. I just hope going forward that adding AI to one of our tools will allow us to get smarter and wiser. We need to find where the impediments are and we need to find ways to address them. I am optimistic that having patient groups at many of these meetings will keep us honest and focused.

Young: I am also concerned with the financial side. It is my hope that the dysfunctional system for the biotech industry gets fixed. This feast or famine system where, if you moved into clinical trials in the wrong year, your ability to finance is significantly affected. Right now, there are some very good drug companies whose technologies deserve to see the light of day, that are being killed. This is not seen in every industry but is most particular in the biotech industry. I also happen to agree with everyone with regard to the cost issues, if you look at many industries,

as technology is introduced, often the cost also decreases. We need somehow to make improvements in the systems that favor innovation, but also work on the cost side.

I would like to thank the panelists and speakers for the amazing speeches they gave today and I thank the audience for participating and hope you found the conference helpful.