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

October 26, 2022
In-Person and Virtual Conference from 12 pm 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*

12:10 p.m. **Luncheon (in person) and Virtual Networking (virtual attendees)**

1:00 p.m. **Keynote Speaker**

Gene Therapy- Unlocking the Promise
- **Peter Marks, M.D., Ph.D.,** Director, Center for Biologics Evaluation and Research, *U.S. Food and Drug Administration*

1:40 p.m. **Fireside Chat – Latest Development in Complex Biological Products**
- **Peter Marks, M.D., Ph.D.**, Director, Center for Biologics Evaluation and Research, *U.S. Food and Drug Administration*
- Moderator: **Dr. Stephen P. Spielberg**, MD PhD, Senior Adviser, *Young & Partners;* former Deputy Commissioner for Medical Products and Tobacco, *FDA*

2:00 p.m. **The Pharma and Biotech M&A and Financing Landscape**
- **Peter Young**, CEO and President, *Young & Partners*

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

3:00 p.m. **The Pharmaceutical Market: Trends, Issues and Outlook**
- **Doug Long**, Vice President, *IQVIA*

4:00 p.m. **Dealing with the Disruptive Environment**
- **Lisa Henderson**, Editor-in-Chief, *Pharmaceutical Executive*
- **Evan Loh,** CEO, *Paratek Pharmaceuticals*
- **Doug Long,** Vice President, *IQVIA*
- **Peter Young**, CEO and President, *Young & Partners*

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

Young & Partners

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Gene Therapy- Unlocking the Promise

PETER MARKS, MD, PhD
DIRECTOR
CENTER FOR BIOLOGICS EVALUARION AND RESEARCH, FDA

In the current state of cell and gene therapy, there are 10 approved gene therapies in the United States. These therapies are expected to expand into solid tumors as there are second and third generation of chimeric antigen receptors T cells developed. There is a robust global pipeline tackling diseases (with genetically-modified T cells) such as hemoglobinopathies, Hemophilia A and B, Lysosomal storage disorders, Neuromuscular diseases, and retinal disorders. One recent successful gene therapy treatment developed is Onasemnogene abeparvovec-xioi (Zolgensma) for spinal muscular atrophy Type 1 generating positive results never seen in untreated children. There are thousands of diseases that could be treated with gene therapy right now if we can develop a framework for these therapies in a commercially viable manner. We can also learn how to scale up the manufacturing to address more common diseases such as heart disease. In the field of individualized medicine, we have customized products where there is the same indication but we have a certain type of personalization to it such as using a specific person's cells. Then there are created products where someone may have a gene defect and we will create a product to address the specific defect. We have discovered recently that with genome editing that we can reach a balance in this paradigm.

The largest challenges of individualized therapies are manufacturing and product access. Other important issues are clinical and nonclinical development, however these processes are being improved through using new study designs to address issues in replicability and control. Commercial viability within the U.S. is quite interesting because one has to sink money into facilities and equipment, and figure out a way to recoup their costs on a net present value basis. In gene therapies where one could sell 100-10,000 doses a year, there is enough revenue generally brought in over the course of time to balance the costs out. In practice, the setup costs for therapies at lower doses is almost as much as those within the 100-10,000 doses per year range. We believe that a lot of the steps in creating gene therapies can be automated and in theory the optimal small batch gene therapy platform may be a device that can be repurposed for different parts of the manufacturing process. Since genes carry similar backbones in delivery, a machine can be used for various manufacturing processes. Other concepts in development by the FDA include making a regulatory framework for uniform processes in gene therapy to speed up the approval process. Many of the current developments come from academics who are using local processes available to them and result in developments that look different from one patient to the other. The gene insert is the business side of a gene therapy whereas the vector delivery is the backbone which doesn't need to be characterized every time for a specific treatment. Generally the pathway to access are through Investigational New Drug Applications but we expect more expanded access programs to help recoup the costs of production for these cell and gene therapies. Accelerated approval pathways are also being determined through effects on a surrogate endpoint or an intermediate clinical endpoint due to these effects being reasonably likely to predict clinical benefit.

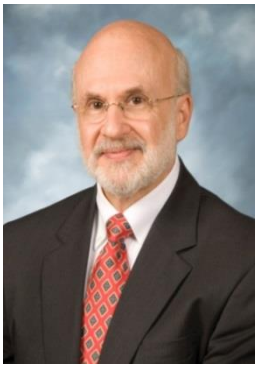
Global regulatory convergence is important for the cell and gene therapy treatments due to the need for robust commercial viability. Many products may not be commercially viable unless there is an aggregate marketing effort across high income countries. For low and middle income countries, gene therapy may also be the most effective treatment as there is a lack of access to general supportive care, and relying on a provided regulatory framework may facilitate access to these therapies in those countries. However, with the science of gene therapy evolving faster than the manufacturing capabilities, the effect of a poorly conceived product could be chilling globally to the industry. Areas in which global regulatory convergence could be possible include preclinical study requirements, environmental assessments, manufacturing information and clinical outcomes. US, EMA, PDMA and others are currently working together towards regulatory convergence. At the Center of Biologics, we are currently reorganizing the Office of Tissues and Advanced Therapies into the Office of Therapeutic Products with goals to increase interactions, improve timelines and enhance consistency of responses.

Fireside Chat – Latest Development in Complex Biological Products

PETER MARKS, MD, PhD
DIRECTOR
CENTER FOR BIOLOGICS EVALUARION AND RESEARCH, FDA

DR. STEPHEN P. SPIELBERG
SENIOR ADVISOR, YOUNG & PARTNERS
FORMER DEPUTY COMMISSIONER FOR MEDICAL PRODUCTS, FOOD AND DRUG ADMINISTRATION

Dr. Spielberg: I would like to take a look at three things: new vaccines, new diseases and new ways of communicating amongst ourselves, patients and the public to establish a degree and confidence. Any thoughts from a FDA point of view as we are moving to new vaccines such as RSV vaccines?



Peter Marks: There has been a priority problem with vaccines over the years. Until recently with the onset of the pandemic, vaccine research have been overlooked compared to other drugs due to financial issues related to profitability and product sales. We now realize what funding vaccines, even if the cost is high, if critical if the problem is large. The cost of Operation Warp Speed was $15 billion, but that is only a sliver compared to the significant cost of shutting down the economy for 6 weeks. To address the RSV vaccine problem, it is not knowledge of immunology that we are lacking. We will not see any progress unless we are willing to fund the research that is necessary. I believe that unless the government puts support behind these efforts, we will not see companies running to develop these vaccines. A new generation of these vaccines is necessary to deal with the coming years of diseases.

Dr. Spielberg: These topics bring up other issues with regard to credibility and confidence. I think we need new social paradigms to get the message across and to bring money into these new vaccine developments.

Peter Marks: There was a recent commonwealth fund study done that concluded the lack of vaccine confidence would cost 50,000-75,000 lives. It has been challenging as politics have become intertwined with science and social media, causing an echo chamber of conversations. The biggest issue is that these conversations have cost lives. Coming into the Thanksgiving and winter season it is crucial we try to protect as many lives as possible.

The Pharma and Biotech M&A and Financing Landscape

PETER YOUNG
CEO, PRESIDENT AND MANAGING DIRECTOR
YOUNG & PARTNERS

Business Conditions

The current business and financial environment is both positive and negative for the pharma and biotech industry. There have been a higher number of FDA approvals and regulatory changes that have been favorable to the industry. The biopharma industry's efforts related to the pandemic have been a positive for the public's perception of the industry. However, there are an equal number of negative factors, such as pressure on pricing, the stubbornly high cost of drug development, and periodic safety and manufacturing issues that are putting negative pressures on the industry.

The Y&P U.S. BioPharma Index and the Y&P European BioPharma index have both outperformed the broader overall market indices but Biotech shares have suffered on a year to date basis.

M&A

On the Pharma M&A side, there were 31 transactions completed for a total deal value of $33.7 billion, with an increase in the number of deals but a decrease in the dollar value annualized, compared to 2021. The reason for this slowdown has been the relative focus of large pharma on acquiring biotech drug candidates using M&A, strategic alliances, joint ventures and licensing. For Biotech M&A, there were 33 deals worth $21.6 billion completed in the first 3 quarters of 2022, slightly higher on a annualized dollar value than 2021. The number of deals have slightly softened as buyers have held back from the valuation uncertainties and a flurry of failed phase 3 trials. Within biotech deals, earn-outs have become increasingly common for bridging the valuation gap between buyers and sellers.

Financing

Biotech equity financing has historically been very small. In 2020 and 2021 there was a significant uptick in equity financing/ Activity has fallen in 2022 to levels similar to 2019 and the years beforehand. We can see this trend in both the dollar value and the number of deals. When we look at IPOs, there is a similar trend in 2022 where the number of financings and the dollar value fell significantly. This has an enormous impact on the industry as IPOs have been an important source of financing for biotech companies and liquidity for investors.

Outlook

The business outlook for pharmaceutical companies is positive as innovation and productivity has improved. Combined with the contribution of drugs from biotech, drug development continues to be strong. The pandemic has improved the reputation of the industry, but has disrupted clinical trials and the manufacturing supply chain. One group that has continued to have a poor outlook are the generic pharma companies. They are struggling to be profitable due to pricing and competition. I believe that ethical drug companies will continue to be positively treated by the market although there may be a potential spillover of the woes in stock prices of the biotech into the pharma industry. M&A activity for the pharmaceutical industry will continue to be modest with most of the market focused on moderate sized deals. Deals will be focused on a strategic rationale, theme or technology that are needed to be acquired. I am very optimistic on the biotech industry as the development capabilities of biotechs continue to be strong. The funding outlook, on the other hand, is more uncertain. If historical trends repeat themselve, the trough of the biotech industry may continue for a a number of years. Valuations will continue to drop, backing up the chain of public company valuations up through the early stage equity placements. The venture capital players have a dilemma as they are looking at low risk companies, but cannot sit on money. This will change the biotech landscape as companies struggle to get attractive valuations and many go through down rounds or run out of cash. M&A in biotech will be strong as interest from pharma buyers will continue to be high and biotech companies have fewer options to go raise cash on attractive terms. We do expect that the lower public and private valuations will likely continue for an extended period of time.

The Pharmaceutical Market: Trends, Issues and Outlook

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

Starting off with a COVID-19 recap, self-testing has been the majority of the testing, but more relevant to its impact, hospitalizations have been down. COVID vaccines make up almost three of every 100 vaccines, down by half since last year with the RSV respiratory virus breaking out more recently. The Australian flu season has also been a predictor of the a strong flu season in the U.S. The Health Services Utilization Index indicates that U.S. is operating at almost pre-COVID-19 levels. To demonstrate the impact of COVID-19 on diagnostics visits, we saw almost a billion less visits in 2020. Depending on what speciality you were in, there were significant differences. Telehealth rose to the occasion, rising to 15% of all medical and health claims at the peak. It has dropped to 8% but is still relevant for diagnoses such as ADHD. Institutional claims have stayed flat in comparison to office claims, which have increased over 2021.

Retail channels were not affected by COVID-19, but the non-retail channels are now recovering. All retail channels show growth, but food stores had the largest growth with maintenance prescriptions. Specialty products have grown more than traditional products, with specialty medicine driving 55% of net spending, up from 28% in 2011. Autoimmune and oncology are the fastest growing specialty classes while diabetes is the fastest growing traditional class. When we look at all classes, pain, diabetes and immunology have strong short-term momentum. Simiarly, immunology and oncologics have grown the most in the last 5 years, with viral hepatitis declined due to vaccines. Specialty products are increasing in all channels in terms of sales dollars. The pharmaceutical industry has historically suffered from a negative image, including with regard to pricing. We see protected brand volume increasing , but offset by the loss of exclusivity. We can see that protected brands net prices increased 4.8% in 2021, but has increased at or below the CPI for the fifth year. Net drug spending averaged 15% across 12 countries with the U.S. at 14%. Hospital care has inflated the most in the last 20 years, inflating by 200%.

In terms of patient adherance, we see adherance declining and IQVIA's risk score increasing. The risk factors that are have the highest impact on risk scores are food security and income, along with culture and literacy elements. With regard to opiod deaths, deaths have climbed significantly during the start of the pandemic with prescription drugs only contributing to 12.4% of those deaths. We can see that fentanyls have represented the largest number of overdose deaths. Prescription opoid use also continues to decline, with the greatest decline seen in dentistry. Furthermore we see only 42% of pain relivers get their prescription from a doctor, with the majority getting them from a friend or relative. With generics and biosimilars, these drugs are facing value problems that I call the "perfect storm". Three generics pharmaceutical companies make up 91% of generic prescriptions. We can also see that 88% of prescriptions are generics, but they make up only 8.9% of total spending in 2022. In oncology, biosimilars range from 53%-73% of market share.

Through September 2022, there have been 39 launches in 2022 versus 57 in 2021. The top therapeutic areas are oncology, infectious disease and dermatology, with each being 18% of product launches. Launch trajectories have not been as strong as previous years with positive performances hinging on patient acquisition and practitioner engagement. With these launches, there have been margin pressures in diabetes and immunology. The complexity of the industry has increased with declining efficiency in research, research spending growing faster than revenue, indirect program costs skyrocketing, and diminished patient access. The path to immunology consists of 97% of patients with initial rejects and 68% being a durable rejection. High cost treatments have accelerated and which is why we need generics and biosimilars. The average cost of these high-cost treatment products in the last 3 years is $435k. Growth in late stage pipeline slowed down in 2020, bringing total expansion to 68% since 2016. We expect the market to return to pre-pandemic levels by 2023. New generation biotherapeutics are expected to grow significantly into 2026. Autoimmune, oncology, and diabetes will be expected to grow as well.

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PETER YOUNG
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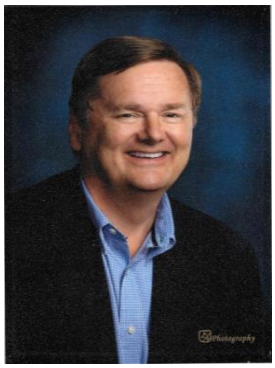
Young: I would like this panel to reflect on a number of issues that are disrupting the industry currently and those that are most relevant to each panelists' work. Some issues include pandemic, legislative action, stock market changes, interest rate changes, geopolitical tensions, supply chain problems, etc.

Henderson: In our November issue, we saw G1 Therapeutics face difficulties conducting clinical trials in Ukraine. They had to navigate to move out their treatments to another CRO with the logistics of moving patients, their drug supply and the regulations regulations around that. Some of their sites on the ground faced difficulty communicating but they were able to recognize it and adapt to the difficulties.



Long: Some of the things that are of interest to me are issues regarding vaccinations and supply chains. Many of the problems forecasted with COVID-19 have not come true and there needs to be a discourse over regulations. Supply chains are also of interest to me, and there needs to be much greater visibility companies have in their supply chain. There needs to also be more redundant planning, as you do not want to put all your eggs in one basket.

Loh: In my role, my belief is that every day is an uncertain day. I think that if you can live through adversity, you will never allow yourself to return to a place like that. First of all, always build credibility with whoever you work with: the people you raise money from, your employees and the board. It is also critical that you maintain a strong balance sheet. A strong balance sheet is one that is able to weather a storm, not matter how severe it is. An example this year has been the rapid increase in the cost of raw materials and other costs that cannot be passed down to the customers. There are significant penalties in place also for increasing drug prices greater than the CPI that we have to deal with.

Young: From the point of view of our clients, each company is different in how they have been affected. Up until 2021, problems were mostly operational, with disruptions to clinical trials or supply chain issues. In 2022, it became a financial issue as well with funding drying up, affecting mostly the small and medium sized biotechs. What this means is that you have to be resilient and be open to different strategies. You must also recognize that many of these issues also cannot be forecasted. With so many different scenarios that cannot be planned, it becomes important to be able to pivot and adapt to the environment.

Loh: One problem we faced that we could not forecast happened during our launch in Feburary of 2019. Antibiotics generally have to be launched to the hospitals first and due to the pandemic everything was shut down shortly thereafter. As a result, we had to learn how to rely on the prior relationships and operate with a salesforce that was

fully remote. This made it even clearer that you have to be able to have a balance sheet to weather these difficulties and to plan for different strategies when you are in a situation where the team is trying to survive.

Long: The best term I have heard is “adaptation”, whether in personal life or business.

Young: Last question for the panel, “What were the two biggest disruptions that you had to face?”.

Henderson: I believe the effects from the pandemic were the greatest disruptions. Clinical trials were delayed, hospitals were shut down and decentralized strategies had to be implemented immediately. A lot of people liked the hybrid model and there is a more patient focused model for clinical trials. Strategies are now more difficult with the digitilization and omnichannel distribution becoming more complex.

Long: You walk around New York City and a number of the shops are closed. We have no understanding of what the long-term effects of lockdowns are with mental health, test scores and so forth.

Loh: I think COVID allowed people to rethink their priorities. We went 100% virtual in a day and our business was okay. What I learned is that CEOs set the culture and drive the tone. Zoom is strictly a transactional form of communication and we miss the small interactions 5 minutes before and after meetings. One of the things we have been working on is how to get people back into the office without mandating it. Solving problems is one of those things where being together in an office is more effective than being on Zoom.

Young: A lot of the topics you raise up I can relate to at my own firm. 7 or 8 years ago we adopted Zoom as it helped connect our team and clients across different locations. There have been many benefits associated with the use of virtual meetings. However, our staff believes that when it comes to solving difficult problems or trying to develop creative solutions, being in-person can be very important.