The 15th Annual Young & Partners Pharmaceutical Executive Summit

"Emerging Strategic and Financial Issues in the Pharmaceutical Industry"

Agenda and Speaker Summaries

October 23, 2019
The Yale Club at 50 Vanderbilt Avenue - New York City

11:45 a.m. **Luncheon and Welcoming Comments**
Peter Young, CEO and President, *Young & Partners*

12:00 p.m. **Keynote Luncheon Speaker**

Making Individualized Gene Therapy a Reality
Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

12:45 p.m. **Dialogue Luncheon Discussion (Moderated Discussions over Lunch)**

1:30 p.m. **The Pharmaceutical Market: Trends, Issues and Outlook**
Doug Long, Vice President, *IQVIA*

2:15 p.m. **The Pharma and Biotech M&A and Financing Landscape**
Peter Young, CEO and President, *Young & Partners*

3:00 p.m. **Coffee Break**

3:30 p.m. **Deal Makers Intentions: Where Are We Heading?**
Bill Shew, Managing Director, *Syneos Health Consulting*

4:00 p.m. **Fireside Chat: The Voice of the Patient – Issues and Impact**
(defining patient-centric outcomes, QOL issues, "right to try", clinical trial design)

Dr. Stephen P. Spielberg, MD PhD, Senior Adviser, *Young & Partners;*
former Deputy Commissioner for Medical Products and Tobacco, *FDA*
Moderator: Peter Young, CEO and President, *Young & Partners*

4:30 p.m. **Challenges Facing the BioPharma Industry**
Lisa Henderson, Editor-in-Chief, *Pharmaceutical Executive*
Dr. Stephen P. Spielberg, MD PhD, Senior Adviser, *Young & Partners;*

former Deputy Commissioner for Medical Products and Tobacco, *FDA*
Peter Young, CEO and President, *Young & Partners*

5:00 p.m. **Speaker Roundtable**
Moderator: Peter Young, CEO and President, *Young & Partners*
Selected Topics: Alternative Pharma and Biotech Strategies; What to do about Pricing?; Innovative Approaches to R&D; Macro Trends Affecting Biopharma

5:30 p.m. **Networking Cocktail Reception**

7:00 p.m. **Conference Ends**

Making Individualized Gene Therapy a Reality

DR. PETER MARKS
DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION

PETER YOUNG
CEO AND PRESIDENT
YOUNG & PARTNERS

Young: Could you tell us about your career path?

Marks: I was on a traditional clinician investigator track at Brigham and Women's Hospital where I had done my internship, residency and fellowship. After I had my kids, I was recruited by a close mentor to Genzyme Pharmaceuticals to do clinical drug development. I then went back to academic medicine and worked at the Yale Cancer Center. I joined the FDA in 2011 as the Deputy Director of the Center for Biologics Evaluation & Research ("CBER") and then took over as Director in 2016.

Young: What was the attraction of the FDA?

Marks: The management and leadership skills I had developed during my time in industry were not being utilized at the Yale Cancer Center. I felt the role at the CBER would allow me to combine the skills I had honed in my previous roles.

Young: How have your prior experiences affected your approach in your current role?

Marks: A lot of innovation comes out of academic medicine but it reaches patients via industry. Having been in both worlds I can appreciate the challenges academics face when trying to develop products to a point that piques the interest of industry participants. One of the programs we have developed at the FDA is the INTERACT program which helps academic investigators turn ideas into Phase 1 studies that they can leverage for potential partnerships with industry.

Young: Were there any big surprises when you joined the FDA?

Marks: Because of the government contracting system, the IT systems at FDA are about 15 years out of date, which was a disappointment. On the upside, I was worried that the rank-and-file would not be particularly motivated, but have been astounded at the level of the commitment demonstrated by the public servants at the FDA.

Young: What are the biggest challenges in the areas you are responsible for at CBER?

Marks: CBER is responsible for complex biologic products, which include vaccines, blood products, cellular therapies, gene therapies, allergenic products, etc. We regulate very high tech, cutting edge products including genetically modified CAR-T cells. However, we also regulate stem cell therapies which are total quackery and which bad actors are trying to purvey by skirting our oversight. The challenge for us is balancing our desire to encourage innovation with our mandate to ensure safety and efficacy for patients.

Young: Could you discuss the landscape around genetically modified cell therapies?

Marks: We have two marketed CAR-T cell products in the United States. Both of them are really remarkable in that they have helped people who otherwise have no available treatment. In the area of liquid malignancies, there are similar products targeting BCMA in multiple myeloma that have shown real promise. There is a whole host of products being developed to treat solid tumors.

Young: Why do you think there has been such acceleration in the gene therapy area?

Marks: At the same time as advances were made in cellular therapies, there were other major scientific advances in the development of gene editing technology. The CRISPR-Cas9 genome editing system is akin to Microsoft Word with regard to ease-of-use. CRISPR-Cas9 has allowed for cell modifications that can create "off-the-shelf" cell therapies which would drastically reduce the cost of treatments from the current generation of autologous products.

Young: What are some of the other challenges gene therapies are facing?

Marks: There is a dilemma between centralized versus localized manufacturing of individual treatments. The next generation of products are likely to be allogeneic rather than autologous, so it is not clear to me that investing large amounts in manufacturing infrastructure makes sense. These therapies will eventually be able to help more people (and make more money) if they are able to be used in greater populations of patients than they are now. They are so expensive that they are only being studied in very specific populations. If the costs of therapies were reduced to a level comparable to adjuvant chemotherapies, you could see them being used to treat small amounts of residual disease in more common cancers like lung or pancreatic, bringing benefits to many more people.

Young: Do you have any comments on the ongoing pricing debate about the currently marketed therapies?

Marks: Zolgensma is a remarkable therapy. Children with spinal muscular atrophy do not usually make it past 1.5 years. After four to five years, the children in the clinical trial for this therapy were still alive. Priced at $2.175 million, there is significant concern among insurers that they will get stuck "holding the bag" as most people in the United States change insurance plans every 3 years. So there is a problem.

Young: Do you have any comments on the data integrity issues concerning Zolgensma?

Marks: The product is still on the market because it is safe and effective. The data that was compromised would not have hindered the product's approval given the overwhelming efficacy of the treatment. When I was at Novartis, I worked on the development of an oral iron chelator that missed the primary endpoint in its clinical trial, but hit all the secondary endpoints. We realized that the dosing for the trial had been miscalculated. I suggested that we be transparent with the FDA about the mistake and work to make them understand that the product had worked as it was supposed to. That suggestion was not received well. It took several months to convince management to proceed with my recommendation. We went to the FDA with a number of experts and a very cogent explanation of the mistake and the product was ultimately approved.

Young: What in the gene therapy field looks most promising?

Marks: I am confident we will see gene therapies for the two major types of hemophilia. A gene therapy for beta thalassemia is already approved in Europe. There are a variety of gene therapies in the pipeline for some of the more prevalent rare diseases. In the future, I believe manufacturing scale limitations will be overcome such that gene therapies can be developed and feasibly commercialized in larger indications such as cardiovascular diseases. On the opposite end of the spectrum, the unique genetic composition of many diseases can be a function of many different mutations. In using gene editing to develop treatments, each of those mutations must be addressed. As such, it is very difficult to manufacture such individualized treatments efficiently. If the United States wants to keep its lead in biotechnology, we need to be thinking about ways to make these treatments less expensively. China is developing the largest number of CAR-T products and they are hoping to ultimately have an export market in gene therapy.

Young: Do you have any comment on any of the other areas under your purview?

Marks: Vaccines are comparatively low margin products, but they are a very cost effective public health measure. We worry that there is not enough financial incentive to encourage development of better vaccines. I am also increasingly worried about anti-vaccination sentiment and the part social media plays in promoting such sentiment.

That anti-vaccination sentiment is derivative of broader anti-science sentiment that encourages suspicion of advanced innovations like gene therapies. I hope that by gentle education this sentiment will ultimately be eradicated because the incredible benefits of gene therapies will only be realized if they are accepted into the mainstream of medicine.

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

Total pharmaceutical market growth is slowing to a CAGR of 4-5%. China growth has been declining and is no longer seeing double digit growth. Growth in Europe has been declining and Japan has been shrinking because of price cuts. The most stable market is the US.

While pharmaceutical list prices were up 5.5% in 2018, net prices were only up 0.3% which is less than the 1.9% that the Consumer Price Index grew.

Patient out-of-pocket costs for Brands and Generics in total have decreased since 2014. As more innovative products are entering the market, their high prices have come under increased scrutiny. Spending is growing fastest for oncologics among specialty prescriptions and anti-diabetics among traditional prescriptions.

A record number of innovative medicines were launched in 2018, bringing 59 new treatment options to patients. R&D expense grew at a ~5.0% CAGR from 2010-2018, outpacing revenue growth. Clinical development productivity has declined in the past 5 years primarily due to increasing trial complexity. In 2011, Big Pharma originated 52% and commercialized 62% of new approvals. In 2018, Big Pharma originated 19% and commercialized 32% of new approvals. Big Pharma is losing it's share of drug innovation and is facing steep decline in the commercialization of new molecules.

There have been 23 biosimilars approved and 9 of them have launched. The lack of biosimilars in the marketplace is a commercial issue, not a regulatory issue. Litigation between biosimilar manufacturers and the reference biologic manufacturers has delayed the launch of a number of approved biosimilars.

Prescription opioid volume is declining significantly. Drug overdose deaths in the United States declined for the first time since 1990, primarily due to a dip in deaths from prescription opioid painkillers.

Consumerization is altering the pharmacy landscape in four primary ways: 1) expanded care included counseling, medication therapy management and expanded clinical reach, 2) finding the time through pharmacy automation and medication disbursement synchronization, 3) convenience including medication delivery and telepharmacy, and 4) considering cost, including prescription discount cards.

Non-adherence is the largest avoidable cost and has value proposition to patients, hospital, insurers, pharmacies physicians and CMS and taxpayers alike. Adherence is not uniform regionally and varies by different factors such as method of payment. Medication adherence performance measures need to be adjusted for sociodemographics in addition to clinical complexities.

We are projecting net total spending growth to average 3-6% over the next five years. Rising cost of care and increasing scrutiny around value will require a structural re-appraisal of the payer role and new sustainable models.

PETER YOUNG
CEO & PRESIDENT
YOUNG & PARTNERS

There are both positives and negatives to the current business and financial environment for the pharma and biotech industry. The high degree of successful innovation by biopharma companies, the higher number of FDA drug approvals, the regulatory changes that have been favorable to the industry, and success of orphan drug efforts have all contributed to success in both industries. However, there are a number of negative factors such as pressure on pricing, the stubbornly high cost of drug development, periodic safety and manufacturing issues, and international pricing discrepancy that are putting negative pressure on the industry. These factors all contribute to changes in the stock market, M&A and equity financing activity of the industry.

Pharma & Biotech M&A

The Pharma M&A market increased significantly in dollar terms in the first three quarters. The number of deals is at about the same pace as last year. In the first three quarters of 2019, 13 deals were completed worth $80.4 billion versus 15 deals completed worth $18.6 billion in the first three quarters of 2018 and 25 deals worth $26.4 billion completed in all of 2018. However, Takeda's acquisition of Shire accounts for $62.0 billion of the amount this year, so the rest of the market is only $18.4 billion. The pipeline of deals, however, appears to be very strong. As of September 30, 2019, the deals announced but not closed totaled $203.8 billion (5 deals), with the Bristol-Myers Squibb acquisition of Celgene accounting for $99.6 billion and the AbbVie acquisition of Allergan accounting for $86.0 billion of the total. The market appears to be made up of a solid, but not record number of small to medium sized deals, with one or two larger deals mixed in. The large deals all appear to be strategic in nature where the buyer is either making a significant move into new areas or defensive in nature because the acquirer's base of business is too narrow geographically or otherwise.

Biotech M&A activity has been modest historically, with small spurts of activity from time to time. In the first three quarters of 2019, volume declined relative to last year. 22 deals worth $14.3 billion were completed versus 27 deals worth $42.4 billion completed in the first three quarters of 2018. Even then, one deal, the acquisition of Loxo Oncology by Lilly for $7.2 billion accounts for half of the total in the first three quarters of this year. This is also a decrease on an annualized basis compared to all of 2018 when 35 deals worth $45.5 billion were completed.
The dollar value of the pipeline of deals as of September 30, 2019 was also very modest at $5.6 billion (9 deals), further evidence of a weakening M&A market. M&A volume has been strong in the U.S., but has fallen off in Europe.

Biotech Equity Financing

Biotechnology has fallen in and out of favor with the equity issuance market over the years. Equity issuance (secondary and IPO) in the first three quarters of 2019 totaled 148 offerings worth $15.6 billion versus 200 offerings worth $21.7 billion in the first three quarters of 2018 and 250 offerings worth $26.6 billion completed for all of 2018. In the first three quarters of 2019 38 IPOs were completed worth $4.3 billion. This compares to 50 IPOs worth $4.9 billion in the first three quarters of 2018 and 68 IPOs worth $7.4 billion in all of 2018.

Pharma & Biotech Future Outlook

The business outlook for pharma companies will continue to be positive with regard to drug development, with promising drugs in the pipeline. There has been a shift in emphasis towards orphan drugs, oncology therapies, new innovations such as gene therapy, Car-T, immune system solutions, CRISPR, etc. Generic pharma companies are under severe profit pressures and will continue to consolidate, cut costs, and try to push selectively into higher value and more protected product areas. They are under intense pricing and competitive pressure. Specialty pharma were

partnering, in-licensing, and acquiring to maintain growth and the strength of their overall business portfolios, but the business models of many have been failing.

The stock market prices and valuations of the Ethical Pharma industry companies have weakened as negative pressures on the industry continue despite R&D and commercial successes. It is our expectation that the negative news will continue to counterbalance the positive news for the biopharma industry. Specialty and Generic Pharma company share prices will continue to suffer as these companies deal with serious business issues/pressures.

Young & Partners expects M&A activity in 2019 to be strong in dollar terms because of the completion or announcement of a small number of mega deals, but well below the record $200 billion. Separately, pharma companies are focused on acquiring biotech which is affecting the biotech M&A volume. But pharma is also heavily pursuing in-licensing arrangements, partnerships and joint ventures with biotech companies and other pharma companies.

The development capabilities of biotech companies have been and will continue to be positive overall. Biotech companies have demonstrated their ability to develop new drugs at a faster pace than larger pharma companies.

M&A volume will be solid, but less than last year. The pipeline of deals announced but not closed at the end of the third quarter was relatively modest and consistent with a moderate volume of biotech M&A activity this year. However, buyer interest will be focused on specific targets in favored therapeutic and technology areas and on biotech companies that have made significant clinical progress.

Biotech companies will continue to tap the equity markets, partnering, licensing and royalty monetization for funding and for shareholder liquidity. Secondary equity offerings have been strong and will continue to be strong, but IPO volume will remain middle of the road in terms of volume and strength with increased uncertainties facing the industry.

BILL SHEW
MANAGING DIRECTOR, COMMERCIAL ADVISORY GROUP
SYNEOS HEALTH, INC.

Syneos Health has been doing a survey for the last eleven years specifically around deal making. It is a forward looking study that focuses on the expectations of pharmaceutical executives regarding licensing and acquisition deals over the upcoming year.

2019 has been marked by high-value, low-volume deal-making activity. There is still a significant supply of Oncology and Neurology assets available but Hepatic, Inflammation and Hematology are areas where buyer interest has increased. There is also an increased appetite for early-stage technologies.

Key factors that will continue to drive deal-making are the easy access to capital for small companies for financings, a favorable US tax code and an accelerated approval rate for NDAs. Buyers are more optimistic than sellers about there being an increase in deals whether licensing/partnerships or M&A. We have not seen that confidence manifest itself in terms of deal volume.

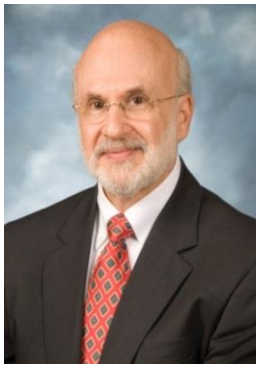
IPO's are expected to cool as the public markets experience further volatility, but expectations are still bullish overall.

Demand has shifted for preclinical candidates, suggesting that many attractive late-stage targets are too expensive, despite robust demand for NDA stage and Marketed assets, and that buyers are looking to fill early pipeline. Oncology, Dermatology and CNS are experiencing a significant supply surplus. Hematology, Hepatic and Inflammation are experiencing a demand surplus. Interest in Hepatic has spiked significantly since 2016. More than three-quarters of companies are either aggressively or opportunistically assessing orphan drugs as part of their Business Development strategy. Immuno-oncology, CAR-T cell therapy and CRISPR/Cas9 continue to be among the "hottest" areas for licensing but interest in other next generation gene editing and stem cell therapies is emerging.

Market exclusivity is the most important factor after the assessed probability of regulatory and technical success when evaluating assets. The increase in the cost of capital over the years is likely due to the general availability of funding resulting in a higher proportion of early-stage companies which demand a higher expectation of return. Differing opinions of commercial potential are cited as the primary reason why deals fail. 38% of buyers highlighted a need to improve bandwidth within their teams to review deals.

Respondents report an average cumulative conversion rate close to 3.6%. The average number of deals evaluated dropped to about half the amount as reported in 2017, suggesting that companies may be taking a more selective approach to deal evaluation.

Fireside Chat: The Voice of the Patient



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

PETER YOUNG
CEO & PRESIDENT
YOUNG & PARTNERS

Young: How are patients influencing the drug development landscape?

Spielberg: When I started seeing patients in 1966, I was taught to find and respect the human being in every patient that I saw. As scientific medicine has come into practice, we have seen a dynamic tension between meta analysis of questionable clinical trials and taking care of each individual patient. Shared decision-making has emerged as a method of relieving this tension by re-establishing the balance of ownership of illness between patient and doctor. Doctors are encouraged to give the patient the information they need to make rational choices. The perception of value proposition of any given therapy is not homogenous in a patient population, patients make individual assessments. These assessments influence not only economics, but patient adherence to prescribed therapies.

Patients are forming advocacy groups, some of which, like the Cystic Fibrosis Foundation, have been responsible for the successful development of new medicines. The advocacy groups have been successful working with patients, doctors, industry and the FDA. In the early 2010's, advocacy groups pushed for the FDA to create forums for discourse on a wide variety of topics. These forums were filled with advocates, doctors, pharmaceutical companies, FDA employees, NIH employees and reporters. These forums allowed patients to define what mattered to them as well as influence the new drug application ("NDA") review process. While it has become easier to study molecular targets and demonstrate specific, validated endpoints and outcomes based on surrogate markers and clinical outcomes, it is very difficult to develop data that can support an NDA based on patient-centric outcomes. However, if this challenge could be overcome it could increase adherence and even open up the opportunity for dialogue about economics.

Young: Can you discuss some of the tangible outcomes of these forums?

Spielberg: There was a concerted effort to identify which facets of Autism parents were most concerned about. In dialogues with sponsors, the FDA has an outcomes group that collaborates with the sponsor to identify validated tools to study those identified facets. This has also prompted academics to develop new scales that can be used in clinical trials that reflect different aspects of patient-centric need. In May 2018, the Right to Try Act allowed eligible patients to have access to eligible investigational drugs and was a manifestation of shared decision-making.

Young: Do you think the Right to Try Act is going to accomplish what it was intended to?

Spielberg: The Right to Try Act took the FDA out of the loop and led to sponsor and patient direct contact. This has been an impediment to data collection. Additionally, sponsors have a hard enough time ensuring supply for their clinical trials let alone meeting the demands of Right to Try patients. However, it has only been a year and sufficient data has not been collected to allow us to evaluate the success of the Act.

Challenges Facing the BioPharma Industry

LISA HENDERSON
GROUP CONTENT DIRECTOR, APPLIED CLINICAL TRIALS AND PHARMACEUTICAL EXECUTIVE
UBM LIFE SCIENCES

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

PETER YOUNG
CEO & PRESIDENT
YOUNG & PARTNERS

Young: Could you comment on what the challenge is with pricing today?

Henderson: There is a lack of transparency in the pharmaceutical supply chain. Patients are only privy to significant out-of-pocket costs and that creates negative sentiment that is directed towards pharmaceuticals manufacturers.

Spielberg: The industry has to figure out a way to solve the transparency problem. They need to communicate to everyday people who are spending significant amounts of money on their products.

Young: There is a significant portion of that out-of-pocket cost that does not go to the manufacturer. There are those that feel that tt is unclear that every party in between the manufacturer and the patient is really adding value.

Henderson: The pricing debate has resulted in more value-based pricing discussions between insurers and manufacturers. Eventually, there will be enough real-world evidence of each therapies' value proposition even if it is not a cure.

Spielberg: The price issue has affected me personally. A close family member is a purchaser of a $30,000 per year oncology therapeutic. The drug is effective and we are grateful for the science, the sponsor and the Agency. It is provided by a single-source, specialty oncologic pharmacy in North Carolina. Three months ago, the pharmacy was bought by McKesson. The price went up 40% and service plummeted. I spend half my time on the phone trying to make sure I get the drug delivered on time.

Young: Are there any innovative approaches to drug development that excite or concern you?

Henderson: The science is absolutely incredible, but there is not much attention paid to the lack of manufacturing infrastructure to support the scaled production of these therapies. Manufacturing is not traditionally a major differentiator in pharmaceuticals, but it is such a critical component for the success of these innovative therapies that it is becoming a differentiator.

Spielberg: Senior management of pharmaceutical companies do not usually have manufacturing backgrounds. The paradigm has always been: discover, develop, market. Manufacturing issues are not insignificant and they are recurring. This is contributing to the problem.

Young: The advent of biologics has also rendered traditional competencies in small molecule manufacturing irrelevant.

Spielberg: Vincristine, a chemotherapy medication used to treat a number of cancers, is cultivated from common flowering plants. Pfizer is the only manufacturer left and they are struggling to provide supply. We now have shortages of simple things like sodium chloride, glucose, sodium bicarbonate.

Young: Do you have any comments about the recent changes at the FDA?

Spielberg: If I was in charge, I would double the FDA's funding so that they could recruit talent. They have very talented, dedicated people in management, but there is a marketplace for bright, young people. The salaries at FDA have not remained competitive.

Young: To play devil's advocate, the FDA and NIH are two of the few agencies that have not seen significant budget cuts in this administration.

Spielberg: Even so, the level of innovation in the products being submitted for approval demands seasoned talent of a different skill set to effectively evaluate products. This talent is difficult to recruit with constrained resources.

Young: Do you have any comment on the high numbers of new approvals that the FDA has been lauded for despite, apparently, limited access to resources?

Henderson: Dr. Gottlieb's push to focus on real world evidence as a driver for approvals was commendable. They also developed a payor guide for the benefit of industry players in an effort to address pricing issues. The FDA's receptivity to dialogue should not be ignored.

Spielberg: I hope the Agency will get funding for more evaluation of institutional changes. Fast-track designation worked exactly as planned. We should be evaluating how to improve those regulatory paradigms.