Agenda and Summary of Speeches

14th Annual Young & Partners Pharmaceutical Executive Summit

Emerging Strategic and Financial Issues in the Pharmaceutical Industry

October 24, 2018
The Yale Club at 50 Vanderbilt Avenue - New York City

11:30 a.m. **Registration**

12:00 p.m. **Luncheon and Welcoming Comments**
Peter Young, President and Managing Director, *Young & Partners*

12:15 p.m. **Luncheon Speaker**

The Pharmaceutical Market: Trends, Issues and Outlook
Doug Long, Vice President, *IQVIA*

1:00 p.m. **Drug Discovery: A Profile of Innovations**
Dr. Stephen P. Spielberg, MD PhD, Senior Adviser, *Young & Partners;*
former Deputy Commissioner for Medical Products and Tobacco, *FDA*

1:30 p.m. **The Pharma and Biotech M&A and Financing Landscape**
Peter Young, President and Managing Director, *Young & Partners*

2:00 p.m. **Successfully Navigating the Current FDA Approval Process**
Evan Loh, MD, President, Chief Operating Officer and Chief Medical Officer, *Paratek Pharmaceuticals, Inc.*
Dr. Stephen P. Spielberg, MD PhD, Senior Adviser, *Young & Partners;*
former Deputy Commissioner for Medical Products and Tobacco, *FDA*

2:45 p.m. **Coffee Break**

3:15 p.m. **Deal Makers Intentions: Where Are We Heading?**
Neel Patel, Managing Director, *Syneos Health Consulting (formerly Campbell Alliance)*

4:00 p.m. **The Rise of BioPharma in China**
Xiaoqiang Yan, PhD, CEO and CSO, *Generon (Shanghai) Corporation Ltd.*
Peter Young, President and Managing Director, *Young & Partners*

4:30 p.m. **The Intersection of Policy and the BioPharma Industry**
Lisa Henderson, Editor-in-Chief, *Pharmaceutical Executive*
Peter Young, President and Managing Director, *Young & Partners*

5:00 p.m. **Speaker Roundtable**
Moderator: Peter Young, President and Managing Director, *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**

The Pharmaceutical Market: Trends, Issues and Outlook

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

There have been a number of significant changes since the Pharmaceutical Executive Summit last year. The current mid-single digit market growth rate has improved over what it was last year. A number of non-pharmaceutical companies are in the midst of integrating vertically. More people have drug deductibles now and, as such, are changing their behavior during their deductible period. There were a record number of generic approvals last year, but many of those drugs never launched due to deteriorating economics.

Total market growth, although rebounding, is significantly down from the Hepatitis C boom in 2014/2015. For example, $10 billion dollars of viral hepatitis drug sales have been lost since the 2015 peak and narcotic analgesics have seen ~$3 billion dollars of lost sales since the 2015 peak. The therapy areas that have demonstrated the most growth over the last year have been treatments in oncology, autoimmune, and HIV.

There were 5.8 billion dispensed prescriptions in 2017, up 1.5% when adjusted for prescription length. Prescription growth has been driven mainly by the aging population. Hypertension, Mental Health and Diabetes accounted for 55% of prescription growth over five years, while pain medicines declined.

Market Access teams are currently facing 6 key issues: 1) tighter, more consolidated payer management, 2) higher payer out-of-pocket payments, 3) amplified public pressure and demand for price transparency, 4) more stringent medical benefit management, 5) increase in value based models, and 6) an evolving payer landscape.

Generics companies have realized that “me-too” type products are unlikely to be financially viable. In the first quarter of 2018 only 10 out of 117 approved generics were launched. Three generic purchasers have 90% share of generic purchases which is pushing prices down.

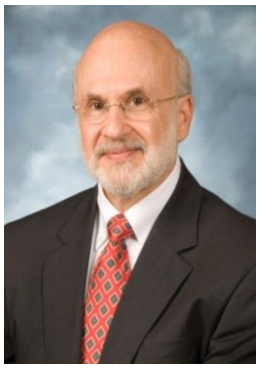
Opioid overdoses was a key driver of the 59,000 to 65,000 overdose deaths in the United States in 2016 with more that 40% of those deaths involving prescription opioids. Despite increasing overdoses, opioid prescriptions have been declining rapidly since 2011.

There were 42 New Active Substances launched in the United States in 2017, up from 19 in 2016. Of therapies launched in 2017, Ocrevus, a Genentech therapy for multiple sclerosis, leads sales dollar performance through June 2018. The 2017 late phase R&D pipeline remains robust with a focus on cancer and nervous system disorders.

We are projecting net total spending growth will average 2-5% over the next five years. Growth will continue to be driven by innovation, but offset by slower price growth and the increasing impact of patent expiries. The future outlook is very uncertain. It is becoming harder to predict the revenue that will be achieved by new products, what will happen to existing products with patent expirations and biosimilar penetration, and the impact various structural changes will have on the biopharma system.

Drug Discovery: A Profile of Innovations

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



For the majority of therapeutic development history new therapies were created via a combination of observation, trial and error, and belief systems. It was not until the end of the 19th century that chemistry started to play a role. This fundamental approach via chemistry eventually evolved into target elucidation (via high throughput screening) and eventually proteomics. The goals of therapeutic development are to increase target specificity, decrease "spill over" and optimize pharmacokinetics all with the aim of improved efficacy, decreased side effects and enhanced risk/benefit profile.

The levels of molecular interventions that I will cover include gene replacement, RNA, gene modification and cell therapy.

Challenges associated with gene replacement therapies include targeting the right cells/organs and "insertion" into the right place with regard to expression.

Jesse Gelsinger, a patient participating in an early clinical trial treating ornithine transcarbamylase deficiency, died because clinicians did not understand how to precisely target.

Fast forward to a recent example, retinal dystrophy due to RPE65 gene deficiency therapy that works via intra-ocular, sub-retinal injection of a gene into the adeno-associated virus vector. Another example is therapy for Hereditary Amyloidosis due to abnormal TTR protein seeks to block production of the protein using small, interfering RNA to block mRNA. It is delivered in a lipid emulsion designed to target distribution heavily to the liver. The treatment is required every three weeks as to continually block newly synthesized mRNA. There remain residual questions regarding different mRNA kinetics and thus the need to modify administration.

CRISPR is a very promising development. It was discovered and adapted from bacteria, which utilize the technique to defend against viruses by cutting viral genomes. Some challenges include "off-target" effects, errors and potential toxicities in the repair processes post-cutting DNA and expanding "effectors" for different tasks.

CAR-T is being applied in treatments for ALL and large B-cell lymphoma. Patient's own T cells are harvested, modified to target CD19 on surface of tumor cells and to kill the cells. Labeling now restricts treatment to certified clinical centers, but the potential is enormous. This is part of an explosion of the use of multiple different pathways to harness immune responses against cancers.

In summary, we are actively developing new drugs and methods of treatment that were unimaginable even a few years ago. Our understanding of the human genome and how it can be used as a foundation for cures is expanding rapidly. The opportunity to treat heretofore untreatable patients is incredible. It does carry with it some ancillary challenges with the information growing faster than we can integrate – a huge informatics challenge.

The Pharma and Biotech M&A and Financing Landscape

PETER YOUNG
PRESIDENT AND MANAGING DIRECTOR
YOUNG & PARTNERS

Overall Environment - Pharmaceuticals

There are a number of positive business trends including aging populations in developed countries, growth in demand in many parts of Asia, ageing related drug therapies showing tremendous growth potential, escalation in the development of orphan drugs, R&D productivity, new drugs and drug candidates. Pharmaceutical companies are successfully using acquisitions, partnering arrangements and in-licensing to stimulate innovation. The FDA has endeavored to speed up its approval process, which has resulted in an increase in the number of drug approvals. There were 46 drugs approved in 2017 a significant increase from the 22 drugs approved in 2016. The European Medicines Agency recommended 92 medicines for marketing authorization in 2017, 35 of which had a new active substance never authorized in the European Union before.

Negative trends include serious challenges and negative publicity related to the pricing of drugs, growth in Europe has been weak, the cost and time to successfully commercialize a drug continues to go up dramatically.
In spite of efforts to improve, the U.S. FDA and sister organizations in Europe and elsewhere continue to have approval processes that are expensive and lengthy. New competitors are emerging from India and China who are aspiring to evolve from generics and API production to being fully integrated pharmaceutical and biotech companies. Drug safety issues have plagued many already established drugs.

Overall Environment - Biotechnology

A large number of biotech companies have demonstrated their ability to invent new drugs and create shareholder value. There has been an emergence of a number of significant breakthrough technologies such as CRISPR, CAR-T, etc. Biotechnology innovation has been very successful and has continued to exceed the pace of the pharma companies. Biologics can hold on to their markets longer because production is complicated and expensive for most generic manufacturers and the regulatory pathway for biosimilars is still being clarified. Biologics patent treatment is favorable, with innovator biologics having 12 years of data exclusivity on top of the existing patent lives. Venture capital funding has been readily available, but funding can vary by stage of development, therapeutic area, technology base, etc.

Negative trends include more stringent demands regarding proof of safety for FDA approval. Additionally, standards are shifted towards proof of comparative increases in efficacy.

Pharma M&A

During the first three quarters of 2018, 12 Pharma M&A deals were completed worth $18.0 billion versus 23 deals completed worth $42.1 billion in 2017. On an annualized basis, this is a dramatic decrease in both the number of transactions and the total dollar volume. As of September 30, 2018, the pipeline of deals announced but not closed was also down - a meager $93.9 billion (11 deals) with the Takeda acquisition of Shire dominating, accounting for $81.7 billion of the total.

Biotech M&A

Biotech M&A activity has almost always been modest historically, with small spurts of activity from time to time. However, in the first three quarters of 2018, 24 biotech M&A deals were completed worth $31.4 billion. This was a significant increase on an annualized basis compared to 2017 when 24 deals worth $15.1 billion were completed. This year, the three largest deals in the first three quarters were the acquisitions of Juno Therapeutics for $10.0 billion, Novartis' acquisition of AveXis for $8.1 billion and Sanofi's acquisition of Ablynx for $4.1 billion. The pipeline of deals announced but not closed as of September 30, 2018 was $35.0 billion (6 deals).

The Future

The business outlook for pharma companies is a mixture of positives and negatives. The industry's trajectory in drug development innovation and productivity has been improving both directly and indirectly through the biotech industry. However, there are many industry uncertainties that are evolving with regard to pricing, industry structure, the lower value of pharma's sales and distribution to biotech companies pursuing orphan drugs, and ongoing patent expirations. 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 has been partnering, in-licensing, and acquiring to maintain growth and the strength of their overall business portfolios, but the business models of many of these companies is failing. The need to fill the shrinking drug pipeline will also fuel acquisitions, 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. Although there will be successes and failures by individual companies, biotech companies have demonstrated their ability to develop new drugs at a faster pace than the larger pharma companies. We believe that the biotech M&A market will continue to be strong both in terms of the numbers of deals and the dollar volume for the rest of this year and into next year. We expect the need for new drug candidates and revenues will drive pharma companies to pursue biotech company acquisitions, in spite of the lofty valuations and the easy access to capital that the biotech companies are enjoying currently. However, their interest will be focused on specific targets in favored therapeutic and technology areas and/or 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. Both the secondary equity issuance market and the IPO markets will continue to be favorable for biotech companies as long as the overall stock market performance is strong.

Successfully Navigating the Current FDA Approval Process

EVAN LOH, M.D.
PRESIDENT, CHIEF OPERATING OFFICER AND CHIEF MEDICAL OFFICER
PARATEK PHARMACEUTICALS, INC.

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

Spielberg: How was Paratek able to successfully navigate the complexities of the FDA NDA approval process?

Loh: In the mid to late 2000's, the FDA shifted their focus from "test-of-cure" (as an endpoint to measure antibiotic efficacy) to a clinical endpoint that would not conflate therapeutic benefit with the ability of the human body to heal itself. They eventually settled on early clinical response endpoints which assessed therapeutic benefit in the first 24 to 48 hours after administration. The Generate Antibiotics Incentives Now ("GAIN") Act passed in 2012 created Qualified Infectious Disease Product ("QIDP") status which comes with an expedited review process. When dealing with the FDA, we have seen two main places where things can go wrong. First, you need to listen very carefully to both what the FDA is saying in conversation with you and what they are not saying. Secondly, you need to pay enough attention to Chemistry, Manufacturing and Controls. It's a fool's errand for a small biotech company to think that they are going to be smarter than the FDA and come up with creative pathway with a set of outputs that the FDA has not agreed to. We did not have any issues understanding efficacy but there is a bias at the FDA that randomization protects against imbalance with regard to safety outcomes. Randomization does not protect against low frequency adverse events. We are a biotech company that prioritize patient safety as much as the FDA does, but the discussions around data monitoring for low frequency outcomes were very difficult to have. No biotech company has the capability to run 10,000 person trials to understand a difference in outcomes of 1%.

Spielberg: One of the challenges is that there is no unimodal FDA and many of the internal review divisions cannot agree to new statutory requirements. From the point of view of the reviewer, there is significant downside to approving a drug that may than have a new side effect that emerges as opposed to holding up the process. The scientific reality is that some side effects cannot be picked up outside of post-market surveillance, which is why we have it. There are legal requirements on the agency to implement the will of Congress. As such, lobbying agencies can affect real change with regard to the review process. The change to open hearings has given patient advocacy groups the opportunity to effectively present their case for speeding up the process. This has been particularly true in the rare disease space. All 46 of the compounds approved last year met PDUFA date goals. The agency really encourages communication to facilitate alignment with regard to required clinical outcomes. The agency must abide by the will of the people as implemented through statute and regulation.

Loh: I'd like to emphasize how important it is to have a dialogue with the agency. They do not like surprises, especially during an expedited review process. During the labeling discussion, we tried to rely on historical precedent with regard to how the agency had labeled past antibiotics. They were relatively deaf and blind to observations on the comparator arm, where the comparator is already approved and labeled. It's important to not get frustrated in this regard.

Spielberg: The ability of the reviewer to move forward effectively and expediently all comes down to confidence. There needs to be a level of respect for the difficulty of the job that they have to do. The public health has to be protected and both the agency and the developer play roles towards that end.

Dealmakers' Intentions 2018 Where are We Heading?

NEEL PATEL
MANAGING DIRECTOR, COMMERCIAL STRATEGY & PLANNING
SYNEOS HEALTH, INC.

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

2018 deal-making volume will be the second strongest year in the past decade. The landscape is shifting from a seller's market to a buyer's market in Oncology where there is now a significant supply surplus as sellers are looking to capitalize on the high valuations of the last few years. Despite high deal volume, there is an increased aversion to risk as buyers are becoming more selective with regard to their deal making and are structuring deals so that the sellers retain more of the future risk.

There has been an unprecedented amount of financing that has been available to life sciences companies in the past four years. The dollar volume of IPOs this year is likely to eclipse the previous record. Venture financing in particular have increased aggressively since 2009. In addition, the average size of venture deals has more than doubled in the past five years. A surge in Series A financing dollars suggests a healthy investor appetite to fuel new company formation.

Internal factors are a greater driver of deal-making than external factors these days. Surprisingly, pricing is expected to have a relatively limited impact on deal-making. Factors strongly projected to affect deal making revolve around financing, i.e. Repatriation of Overseas Cash, Favorable U.S. Corporate Tax Code, etc.

Buyers are more optimistic than sellers about whether there will be an increase in traditional licensing/partnership deals.

Buyers and sellers share similar interests in what they consider to be key therapeutic areas with the greatest deal potential. However, there are certain areas where there is a mismatch between supply and demand. Oncology is experiencing a significant supply surplus. Hematology, Respiratory/Pulmonology and Renal are experiencing a demand surplus.

CAR-T cell therapy and CRISPR/Cas9 continue to be among the "hottest" areas for licensing, but interest in Immuno-oncology and Microbiomes has increased considerably since 2017.

Respondents report an average cumulative conversion rate close to 1.8%. A surprising 23% of buyers believe that improved bandwidth to evaluate assets would most strongly improve the buying process.

The Rise of Biopharma in China

XIAOQIANG YAN, PH.D.
CEO & CSO
GENERON (SHANGHAI) CORPORATION LTD.

After I finished my PhD, I worked as a research scientist for Amgen for 10 years. When I went back to China to work for Hutchison China Meditech ("HCM"), I realized how far behind China was in the biotechnology industry and figured that there must be opportunities. HCM had me doing research on small molecules only, so I founded Generon in 2004 to focus on large molecules.

There is demand for innovative therapies in China. An increase in discretionary income, broad regulatory reforms aimed at high quality therapies and an improved single-payer system are driving increased use of innovative and biologic therapies.

Growth in biotech has attracted significant private investment, with $6.4 billion of dollars of biotech private investments in 2016, up from $1.4 billion dollars in 2014. The equity markets are also more accepting with 225 pharma investment exits in 2017, up from 54 in 2013.

There has been a transition among Chinese pharmaceutical companies from focusing on small molecule generics to biosimilars to fast followers (companies in-licensing products with existing global Point-of-Care data) to true innovators (companies targeting novel Mechanisms of Action). It will be paramount for Chinese companies continue to focus on innovation.

The development of the Zhangjian Hi-Tech Park in Shanghai from 25 km^2 of farmland to 94 km^2 of a complete bio-pharma ecosystem is an excellent case study of the difference between the early 2000s and today. There are dozens of returnees (Chinese nationals educated abroad) at 50+ companies. Regulations are shifting towards global standards i.e. FDA, EMA, GLP, GCP, GMP, GSP.

We see the current trade war with the U.S. having the greatest impact on investor confidence than on the GDP of China. This will have some impact on the capital needs and shareholder liquidity paths for Chinese biopharma companies.

PETER YOUNG
PRESIDENT AND MANAGING DIRECTOR
YOUNG & PARTNERS

It was not long ago that China was principally a low cost, low quality producer of pharmaceutical intermediates and fine chemicals, along with many companies from India. Subsequently, there was a forced clean-up of manufacturing practices that significantly improved the reputation of Chinese sourced APIs and fine chemicals. The Chinese pharma companies have also been producers of traditional Chinese medicines and many generic pharmaceuticals for local and international consumption. More recently, the Chinese have moved up to be more global producers of generic drugs and are beginning to manufacture and even develop more sophisticated drugs, some of which are proprietary to the Chinese biotech or pharmaceutical companies. There are even increasing numbers of Chinese biotech and pharma companies that are conducting clinical trials for drug candidates in China, Europe and the U.S. simultaneously.

On the regulatory front, it has been a bumpy road for the Chinese FDA as they struggled to develop and implement standards and approval procedures that were appropriate for the Chinese market and increasingly in line with the U.S. FDA and EMA. It has been a struggle which was not helped by the recent vaccine scandal in China. Also, as is

the case for the U.S. FDA, the Chinese FDA is trying to streamline its approval process without compromising science and public safety.

In terms of the Chinese health care market, the attraction of a very large population has always drawn a great deal of interest on the part of both Chinese and Western providers of drugs. China has gone from a system with no healthcare insurance and a hospital centric drug dispensing healthcare system to the introduction of healthcare insurance and a more diversified, modern system of providing patient care. Rising incomes have also contributed to the expansion of healthcare spending.

The Chinese are trying to create the very delicate ecosystem that exists in selected parts of the world such as the U.S. that is required to attract leading researchers, develop drugs successfully, establish and fund biotech companies, and provide the providers of capital with the liquidity and valuation increases that are critical to the success of biotech and pharma ecosystems in the West. These efforts include massive funding focused on graduating large numbers of university trained Chinese scientists, encouraging the growth of venture capital and private equity funds that can invest in Chinese biotech/drug companies, and the recent designation of biotech as one of the targeted industries that Chinese wants to achieve an independent major position in by 2025. This is under the "Made in China 2025" program that was introduced by China in 2015.

There has been a major flood of Chinese private equity and venture firms that have been investing in Chinese biotech companies, along with the venture arms of investors from the West and other parts of Asia such as Singapore. In addition, the Chinese government changed the rules with regard to IPOs in Hong Kong that allow biotech and technology companies that do not have revenues to go public, subject to certain rules and restrictions, on the Hong Kong exchange. Previously, Chinese companies without revenues could not go public in China on any of the exchanges and the only option was to go public in the U.S. or Europe via an IPO or reverse merger. There was an expectation of a flood of initial and secondary offerings of biotech companies earlier this year. However, with the recent severe drop in the Chinese stock market prices, it is not clear how many Chinese biotech companies will go public or list on the Hong Kong exchange, even though Chinese public market valuations across many industries are still higher than those in the West.

The Intersection of Policy and the BioPharma Industry

LISA HENDERSON
GROUP CONTENT DIRECTOR, APPLIED CLINICAL TRIALS AND PHARMACEUTICAL EXECUTIVE MAGAZINE

PETER YOUNG
PRESIDENT AND MANAGING DIRECTOR
YOUNG & PARTNERS

Young: Do you have any comments about what you think might happen with regard to pricing?

Henderson: Luxturna is priced at $450,000 per eye. The CEO of Spark Therapeutics made a calculated decision by investigating civil litigation concerning plaintiffs who had lost their sight due to an accident and the associated recompense awarded by the court. I think that this was a very thoughtful approach to pricing. Further, Ken Frazier, CEO of Merck, was recently quoted saying, "I don't understand why 50% of the value of pharmaceuticals goes into the supply chain."

Young: I do not think pharmaceutical manufacturers are blameless in the sense that they have been raising prices aggressively as a group. This behavious has created a public image problem, even though we all know that drugs reduce the burden on healthcare expenditures via avoided medical procedures, shorter hospital stays, etc. Pharmaceuticals used to be a very admired industry for decadeds. However, today pharmaceutical companies are painted as villains. They need to find a way to change public opinion.

Young: Lisa, what effect has the current administration had on the way the FDA agency is being run?

Henderson: I know that Scott Gottleib, the Commissioner, is very proactive with regard to his initiatives at the agency. He is trying to accelerate drug approvals prudently and flatten the organization. I think he was a very good choice for Commissioner.

Young: What are your thoughts with regard to the vertical consolidation that is going on between the payers, pharmacies, PBM's,etc.?

Henderson: The vertical integration will have a major impact on many fronts. For example, all of these integrated organizations have a specialty pharmacy. Specialty pharmacies used to fill very specific, high-patient touch needs. They now seem to be relatively undifferentiated. New high touch therapies do not require traditional supply chains. In the case of Luxturna, the drug is sold directly to the payor and delivered to the physician for administration. Our reimbursement system is not designed for the future.

Young: Are there other policy issues that you think are worth mentioning?

Henderson: There seems to be a major shift from a focus on data privacy to controlling data ownership and using data as part of the drug development process. How are drug developers making decisions concerning the management of the data they are collecting from clinical trials? Pfizer is exploring how AI and blockchain technology might be leveraged to watch the progress of patients and to improve pharmacovigilance.