16th Annual Executive Summit on Emerging Strategic and Financial Issues in the Pharmaceutical Industry

October 28, 2020
Virtual Conference from 1 pm EST to 4 pm EST

1:00 p.m. **Welcoming Comments**
- **Peter Young**, CEO and President, *Young & Partners*

1:10 p.m. **Keynote Speaker**

Perspectives on the Development of Vaccines and Gene Therapies
- **Peter Marks**, M.D., Ph.D., Director, Center for Biologics Evaluation and Research, *U.S. Food and Drug Administration*

1:30 p.m. **Fireside Chat – The Impact of the Pandemic**
- Adjusting the FDA Operations to the Pandemic
- Biopharma Industry Challenges Created by the Pandemic

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

3:30 p.m. **Challenges Facing the BioPharma Industry**
- **Lisa Henderson**, Editor-in-Chief, *Pharmaceutical Executive*
- **Dr. Stephen P. Spielberg**, MD PhD, Senior Adviser, *Young & Partner;* former Deputy Commissioner for Medical Products and Tobacco, *FDA*

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

4:00 p.m. **Virtual Networking Hour**

Perspectives on the Development of Vaccines and Gene Therapies

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

The FDA's role in the development of vaccines involves strain selection and reference standard population, lot release, evaluation of safety and efficacy, post-market surveillance, advancing vaccine technology and helping to ensure public confidence.

The importance of public confidence in the safety of vaccines is illustrated in the stark difference between the incidence of deaths and other adverse events in people who are vaccinated with a Measles, mumps, rubella ("MMR") vaccine (3.435 per 10,000) vs those who contract measles (>3000 per 10,000). A similar difference in incidence exists with influenza and flu vaccines.

Most of the SARS-CoV-2 vaccines are targeting the spike protein (S). Some are developing vaccine candidates that target the nucleoprotein (N). Others are targeting both or the whole viral particle. Approaches include DNA, RNA, Protein Subunit, Inactivated Virus, Non-Replicating Viral Vector, Replicating Viral Vector and Virus-like Particles.

At FDA our priorities for the development of SARS-CoV-2 vaccine are manufacturing quality, safety, efficacy and post-market surveillance. In June, we put out guidance for the development of licensure of vaccines to prevent COVID-19. It became clear to us that the first wave of vaccines might be eligible for emergency use authorization so we issued guidance on that in October.

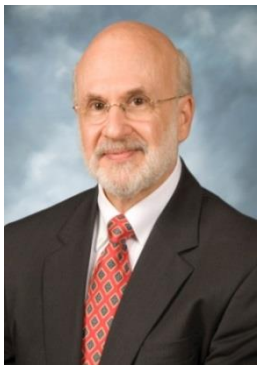
FDA encourages enrollment of diverse populations is all phases of vaccine clinical development including racial and ethnic minorities. Enrollment should include populations of elderly individuals, pregnant women and women of childbearing potential and children. We were specific in our guidance about targeting a 50% efficacy endpoint with a lower limit of a 95% confidence interval of 30%. There has to be a robust safety evaluation and subject follow up should be long enough to evaluate duration of immune response. Accelerated approval may be considered in the future if an applicant can establish a surrogate endpoint that is reasonably likely to predict clinical benefit. Emergency Use Authorization may be appropriate once studies have demonstrated the safety and effectiveness of the vaccine but before the manufacturer has submitted and/or FDA has completed its formal review.

There are 192-194 SARS-CoV-2 vaccines in development globally. FDA has been highly responsive to sponsors regarding vaccine development plans. We are working with our regulatory counterparts and other stakeholders, including WHO, to promote convergence.

There are 5 approved gene therapies in the United States. The number of Initial New Drug ("IND") applications to FDA is increasing noticeably with over 1,000 active IND's. MIT NEWDIS estimates that there will be 40-60 new gene therapy product launches by 2030. Availability of high quality manufacturing capacity is currently limiting the development of gene therapy. FDA is collaborating with a variety of stakeholders to develop more streamlined pathways that facilitate the manufacturing of advanced therapies.

Unfortunately, current manufacturing platforms are only commercially viable at patient populations of 100 or more. Animal models may be less than that ideal for modeling individualized therapies outside of the clinical setting. New model systems include organoids and humanized mice. We are exploring how to generate efficacy data in very small populations. Bayesian clinical trial designs might be part of the solution. Public-private partnerships to enable product access to diverse populations through streamlined production may improve product access.

Fireside Chat – The Impact of the Pandemic



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

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

Spielberg: What lessons have you at the FDA learned as a result of the pandemic?

Marks: Our previous process for developing guidance would take us months to years. What we've learned is that you can systematize this process and make it much more expedient by having an owner draft the guidance then follow up with a limited number of discussion sessions. If you need to revise guidance after publishing, you do so. Perfect is the enemy of good.

Trials that relied on wearables or remote-monitoring as opposed to those that required in-hospital visits have been doing much better during the pandemic. If we can reduce the burden on patients of participating in clinical trials, we should.

Spielberg: How is the agency monitoring the global supply chain for API, excipients, etc.? Is the FDA exploring the use of technology to acquire audit information?

Marks: We're trying to not send our people into harm's way. We are trying to leverage information from paper, local inspectors, and inspectional histories as best we can. For COVID-19 vaccines we feel obligated to make site visits. The problem with implementing technology is the subject of the audit has control of what our auditors can or cannot examine. There is no substitute for a person walking around a facility and making observations.

Spielberg: How is the agency approaching the issues of cybersecurity as it pertains to the "hackability" of wearables?

Marks: The Center for Devices and Radiologic Health has a group committed to dealing with the issue. The concern is not so much for wearables like watches as much for implants like implantable cardioverter-defibrillator or pacemakers.

Spielberg: What has the reaction from sponsors been with regard to their ability to execute clinical trials at clinical trial sites?

Marks: You don't really know what the effects of a hurricane were until the winds die down and the skies are clear. Unfortunately, I think the COVID-19 impact on clinical trials will only be elucidated once we have gotten through this very difficult time. CBER will probably implement an evaluation process to help sponsors determine what they can salvage.

The Pharma and Biotech M&A and Financing Landscape

PETER YOUNG
CEO & PRESIDENT
YOUNG & PARTNERS

The current business and financial environment is both positive and negative for the pharma and biotech industry. The high degree of successful innovation by both pharma and biotech 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 the industry's success. 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 are putting negative pressure on the industry.
The biopharma industry's efforts related to the pandemic have been a positive in terms of public perceptions.

Pharma & Biotech M&A

Although the number of deals has increased, the dollar volume and the average deal size has fallen considerably. In the first three quarters of 2020, 20 deals were completed worth $69.5 billion versus 21 deals completed worth $172.9 billion in 2019. The acquisition of Allergan plc by AbbVie Inc. accounted for $62.3 billion, so the remaining 19 deals had a value of $7.2 billion. The pipeline of deals appears to be very modest as well. As of September 30, 2020, the dollar volume of deals announced but not closed totaled $437.3 million (4 deals).

Biotech M&A activity has been modest historically, with small spurts of activity from time to time. Thus far in 2020, the number of deals is lower on an annualized basis, but the dollar volume is on track for a record year. In the first three quarters of 2020, 20 deals worth $34.3 billion were completed versus 34 deals worth $19.0 billion completed in all of 2019. The dollar volume of the pipeline of deals as of September 30, 2020 was $30.3 billion (11 deals) with the largest being Gilead's $20.9 billion acquisition of Immunomedics.

Biotech Equity Financing

Biotechnology has fallen in and out of favor with the equity issuance market over the years. Volume in the first three quarters of 2020 puts the year at a record pace. In terms of the dollar volume of equity financings, the first three quarters of 2020 has already exceeded previous yearly records. IPO volume in terms of number of IPOs in the first three quarters of 2020 puts the year on track to exceed previous record levels. IPO dollar volume in the first three quarters of 2020 has already exceeded previous annual records.

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. The industry's drug development innovation and productivity has been moderate. However, combined with indirect development through the biotech industry, overall development activity has been strong and will continue to be strong. There has been a shift in emphasis towards orphan drugs, oncology therapies, new innovations such as gene therapy, immune-therapy, 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 the negative pressures on the industry continue, in spite of a mixture of 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 2020 to be strong in dollar

terms because of the completion or announcement of a small number of large mega deals, but well below the record $200+ billion years. Mega deals that merge existing mature biopharma companies are, with only a few exceptions (the recent AbbVie/Allergan deal, for example), are no longer being pursued as CEOs and boards recognized that cost synergies alone are not long term creators of value. But there are large and medium sized deals with a strategic rationale or a theme around adding new and growing technologies and products that are being pursued. 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. Debt financing will be driven by the M&A transactions that will have to be financed. Companies will continue to rebalance their balance sheets post larger M&A transactions. Equity issuance will continue at its current solid, but modest pace.

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. M&A volume has been solid and will continue to be through 2020. The pipeline of deals announced but not closed is consistent with the biotech M&A activity thus far this year. Big Pharma will continue to dominate the larger biotech M&A deals for the obvious reasons. 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 pursue the equity markets, partnering, licensing and royalty monetization for funding and for shareholder liquidity. Secondary equity offerings and IPOs will continue at the current record rates as long as the market continues to favor biotech companies as it has been.

The Pharmaceutical Market: Trends, Issues and Outlook

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

The pandemic created unprecedented change in the healthcare systems. It served as a catalyst for long overdue adoption of digital solutions. At the same time, it impacted patient care dynamics, the outcomes of which we may not understand for years to come.

Environmental changes included adaptation of the system in terms of improved access to medicine, expanded telehealth, expanded system capacity and improved access to healthcare. R&D adaptations included protocol simplification, remote site monitoring/source data verification & remote visits, novel trial design, digitization of study procedures and digital patient engagement. Providers and patients quickly adapted by adopting telehealth at unprecedented levels.

In terms of market impacts, patients stockpiled medications in anticipation of extended restrictions. Ordinary healthcare trends (patient interactions, prescriptions, 90 Day Retail Fills, NBRx) have all been shocked by COVID and none have fully normalized. In Oncology, early guidance shaped the market as patient treatments continued with practices designed to protect patients.

The pharmaceutical industry has responded by accelerating new digital options like telehealth, remote detailing, digital therapeutics, remote patient monitoring and remote clinical site monitoring. While approvals have not slowed, the pandemic has changed the launch environment with many delays due to diagnostic/administration requirements incompatible with the limitations of the pandemic. In-person engagement and scientific meetings were disrupted and digital channels have been leveraged to re-engage.

Enduring changes like patient backlog due to missed or delayed interactions will impact outcomes. Furthermore, current market dynamics introduce new complexities to product uptake and success that has given rise to new commercial models. High unemployment will have lasting effects on payer mix, patient affordability and gross-to-net.

Total Market (Retail, Non-Retail and Mail) sales grew 5.7% in 2019 and have grown 3.7% YTD August 2020. Branded products sales growth has weakened but is still growing while unbranded generics sales are recovering. Immunology, Oncology and Antidiabetics are responsible for over 60% of positive absolute growth in the US and 40% of recent launches. Adjusted prescriptions grew by 3.2% in 2019 and have grown 2.5% YTD August 2020. 88.5% of prescriptions are dispensed as unbranded generics for 2020.

Pharmaceutical companies continue to bring new products to market despite the uncertainty introduced by the COVID-19 pandemic. There have been 52 launches through September 2020. Oncology has accounted for 40% of 2020 launches. Allergan's Ubrelvy for acute migraine leads 2020's launches in sales.

Challenges Facing the BioPharma Industry

LISA HENDERSON
GROUP CONTENT DIRECTOR, APPLIED CLINICAL TRIALS AND PHARMACEUTICAL EXECUTIVE
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DR. STEPHEN P. SPIELBERG
SENIOR ADVISOR, YOUNG & PARTNERS
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PETER YOUNG
CEO & PRESIDENT
YOUNG & PARTNERS

Young: Could you comment on the likelihood of real-world evidence being evaluated in the drug approval process?

Henderson: The pandemic has certainly accelerated the movement towards real-world evidence as it relates to the development of a COVID-19 vaccine. There are a number of pharmaceutical companies that have incorporated real-world evidence into their FDA filings.

Spielberg: The pandemic has increased incidence of depression, anxiety and insomnia. Management of these indications has shifted from pharmacological treatments to Cognitive Behavioral Therapy or Mindful Meditation. This shift may have implications on the economics of new pharmaceuticals for these indications. If you don't superimpose real-world data and rely on a study conducted in a small number of people, the data could be very misleading.

Young: How is the relationship between pharmaceutical companies, physicians and patients changing?

Henderson: Trials are shifting towards a more patient-centric approach where they incorporate patient views and feedback into the design and execution. With the rise of telehealth, it has become apparent that physicians are reluctant to switch medications while unable to see patients in person. This dynamic has impacted commercial models for many companies.

Spielberg: There is a therapeutic relationship between patient and physician that is reliant on trust. We live in an age where there is an excess of disinformation which leaves many patients struggling with how to put medicine into the context of their lives. It astonishes me that there are people who deny the prophylactic benefit of vaccination. Past misadventures like the Tuskegee Syphilis Study have destroyed trust and eroded confidence that physicians act in the best interests of patients. We have to reestablish trust and a belief in science and data. Most of this work will come from patient advocacy.

Young: How will the healthcare ecosystem be impacted by the explosion of scientific innovation that has occurred over the past decade?

Henderson: The challenge with individualized therapies is that they are often applied to small populations. These are populations that are difficult to access for clinical trial purposes. Manufacturing, supply chain and delivery are major concerns for the companies developing and commercializing these novel therapies. Pricing for these therapies is astronomical but the benefit that they provide is unquestioned.

Spielberg: There are questions around how to get these remarkably complex molecules into a formulation suitable for small volume delivery. Some of these therapies are legitimate miracles and we have not been able to effectively

communicate the value of these new compounds in terms of human life. The science has evolved more rapidly than that the pragmatic aspects of pharmacological therapy.

Young: How can the pharmaceutical industry more effectively communicate the benefit of their products in terms of costs to the healthcare system?

Henderson: The actions of the pharmaceutical companies during the pandemic have the potential to have a very positive impact on their public image. Pharmaceutical companies tend not to point fingers with regard to the lack of transparency in the healthcare system and this might change in future.

Spielberg: We need a new playbook on communicating the unprecedented conversion of basic science into drugs that benefit people. If we do not develop one, we throw out the greatest opportunity humankind has ever had to relieve suffering and improve the quality of life.