

Conference Summary

**Pharmaceutical Executive Summit: “Emerging Strategic and Financial Issues in the
Pharmaceutical Industry” - December 11, 2013**
The Yale Club of New York City

- 11:30 a.m. **Registration – Trumbull Room**
- 12:00 p.m. **Welcoming Comments**
Peter Young, President and Managing Director, Young & Partners
William Looney, Editor-in-Chief, Pharmaceutical Executive
- 12:15 p.m. **Luncheon Keynote Speaker and Fireside Chat**
- Winning in the New Business Environment**
Fred Hassan, Managing Director, Warburg Pincus and Former CEO of Schering-Plough
- A Fireside Chat with Fred Hassan**
Peter Young, President and Managing Director, Young & Partners
Fred Hassan, Managing Director, Warburg Pincus and Former CEO of Schering-Plough
- 1:15 p.m. **The Pharmaceutical Industry Strategic and M&A Trends**
Peter Young, President and Managing Director, Young & Partners
- 1:45 p.m. **Perspectives on the Future of Orphan Drugs**
Dr. Gayatri Rao, Director, Office of Orphan Products Development, The FDA
- 2:15 p.m. **The Pharmaceutical Market: Trends, Issues and Outlook**
Doug Long, Vice President, IMS Health Inc
- 3:00 p.m. **Biotech Deal Making – M&A, Licensing and Partnering Trends**
Randolph Guggenheimer III, Managing Director, Young & Partners
- 3:30 p.m. **The Impact of Value-based Trends on Pharma**
Peter A. Tollman, Senior Partner and Managing Director, The Boston Consulting Group
- 4:00 p.m. **Patent Issues Affecting Pharma/Biotech**
David K. Barr, Partner, Kaye Scholer
- 4:30 p.m. **Speaker Roundtable**
Moderator: Peter Young, President and Managing Director, Young & Partners
Participants: Executive Summit Speakers
- 5:30 p.m. **Cocktail Reception – Trumbull Room**
- 7:00 p.m. **End of Conference**

Winning in the New Business Environment

FRED HASSAN

Managing Director, Warburg Pincus

Former CEO, Schering-Plough



It is a pleasure to be back here again after 4 years. I was the keynote speaker for this event in December of 2009. At that time I described my successful experience with Schering-Plough and other principles of leadership. Two important things have happened since that time: first, my new book was published (*Reinvent: A Leader's Playbook for Serial Success*) and second, in addition to the six case histories I speak of in my recently published book, there is now a seventh case which is the turnaround and transformation of Bausch & Lomb. In that situation I was not the CEO but the Chairman. My colleague from Schering-Plough, Brent Saunders, was the CEO and he and I utilized the same playbook and principles in leading Bausch & Lomb that we used successfully at Schering-Plough. So, the strategies laid out in the book really do work and in a wide variety of industries, not just in the pharmaceutical industry.

The six takeaways which I speak of in my book and which I hope to convey today include: be authentic, be purposeful, be connected, keep leading, role model your expectations, and keep winning. However, before I get into these takeaways I want to take a moment to briefly look with you at the industry ecosystem. The biggest tailwind for the industry is the fact that there are numerous currently unmet needs. I cannot think of any other industry today where so much can be done for so many people. The second most prominent tailwind for the industry is the aging of the baby boomer generation. New sciences and technologies being discovered recently are also a large tailwind for the industry. In fact, very recently we have seen some breakthroughs and products approved for treatment of difficult to treat diseases such as Hepatitis-C. The final tailwind I see for the industry is the demand for pharmaceutical products coming from emerging markets.

The pharmaceutical industry is also facing several headwinds. The most significant of those headwinds is the current regulatory environment. Regulatory science and strategy has not been able to keep up with advances in the science of medicine. The heavy regulatory burden and the variability of regulations imposed on pharmaceutical companies has made creating drugs and getting them approved extremely difficult. The industry also faces the headwind of payer hurdles. Health budgets everywhere are dealing with deficits and this issue is exacerbated by the emergence of a huge population of people turning 65 or older. The final headwind pharmaceutical firms are facing is R&D success rates. In the mid 1980's the FDA commissioner finished a study that showed that 75% of molecules entering Phase 3 clinical trials ended up going to market. About half of molecules entering Phase 3 trials today go to market. This is an alarming trend. As I wrote in my book, the industry needs to reinvent the product portfolio by 70% every 10 years in order to keep up with product exclusivity expirations. Since about 2006, the industry has slipped from that level to a very concerning level today of only 46%. These tailwinds and, more importantly, the headwinds facing the pharmaceutical industry today necessitate an attitude of reinvention and a leadership style which is focused, in my opinion, on the six takeaways which I mentioned earlier.

The first takeaway for leaders in the industry is to be authentic. Authentic leadership starts with being authentic with oneself. You must know who you are, and more importantly who you are not. Similarly, you must know what your company is good at and what it is not good at. You must understand your company's strengths, weaknesses, opportunities, and threats and work to constantly pressure test the firm in the context of those attributes. I learned this lesson first hand while with Wyeth in 1991. At the time I was the head of Wyeth's domestic business and Wyeth R&D. At one point we had made a decision to remove our current head of R&D and were looking for a successor. Bob Essner asked me a question that forced me to be much more authentic with myself and that question was, "Fred, are you an R&D guy?" This was all he had to say for me to

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realize that I needed to bring in a true R&D champion, such as Bob Levy, who ended up turning Wyeth into a very strong R&D machine.

The second takeaway is be purposeful. You must as a leader know what you want and how you are going to get it. It is important to create a vision, mission statement, and values statement for your firm and to clarify and communicate expectations to all of your employees. You should strive to create a sense of bigger meaning for your people. At Bausch & Lomb we focused on this and created a core document called, "the Bausch & Lomb Way". Our motto did not include achieving things like 15% growth in EPS. People knew we were running the business to achieve financial results, but we focused on describing our business and our goals in terms of helping people see better and people felt really good about this mission.

The third takeaway is be connected. Connect with yourself first and then connect with those around you including stakeholder communities that are important to the enterprise. Many good CEOs go by the wayside because they do not remain connected either with themselves or their communities. You must build active listening and learning skills for yourself and for your entire organization and utilize these skills in interacting with regulatory bodies such as the FDA and other outside organizations. Most importantly, you must connect with your customers. In order to connect with your customers you must build trusting relationships. In building these relationships it is not enough to simply sell lots of good products.

The fourth takeaway is to keep leading. Keep leading means once you have a company, a machine in place, you need to build an inspirational leadership team to manage the business. An inspirational leadership team is important because you must get the broader employee population excited about managing the business. Building strong resonance with front line management is extremely important. Front line managers are the first tier managers who can truly influence the people at the forefront of the business and thus it is extremely important to have a strong relationship with and the respect of this group. It is also extremely important in this industry to choose the best possible head of R&D and to partner with this person and remain close to this process so that the firm can become excellent in R&D. You must also be bold on R&D portfolio decisions and project management. You must continuously prune the business and focus where you can win. You must then drive the winning projects to their goals.

I maintain that people plus culture plus execution drives success in a firm and the fifth takeaway is to role model your expectations which is important to keep this equation in balance. You must focus on picking the absolute best team at the top and ensure that each of these people is excellent in his or her area, an inspirational leader of people, and is 100% committed to rooting for their colleagues. At Bausch & Lomb and other companies I was involved in we took this seriously and were successful because of it.

The last takeaway I bring to you today is to keep winning and reinvent yourself and your environment. Success can cause complacency. When a company becomes arrogant, that is the beginning of their decline as far as I am concerned. In closing, these six takeaways I have talked about today have worked for me in this industry and I'm certain they can work for other leaders. I am very optimistic about the future of the pharmaceutical industry in terms of growth and the opportunities to have a big impact on the health and well-being of the global population.

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Fireside Chat with Fred Hassan - Selected Comments

PETER YOUNG,
President and Managing Director, Young & Partners

FRED HASSAN
Managing Director, Warburg Pincus
Former CEO, Schering-Plough

Peter Young: What advice would you give to the big pharma and biotech executives with regard to strategy and execution approaches going forward?

Fred Hassan: I still believe that portfolio decisions and project decisions are extremely important and that these decisions should not only be made by the R&D head in his or her respective division, but should be openly discussed with the CEO and production managers. These are important decisions and those companies that decide wisely on their portfolio and on the allocation of R&D assets will outperform those that do not go about making these decisions in the right manner. For example, if one has made a great breakthrough in oncology, why not spend a lot of money up front on 10 different indications in Phase 1 clinical trials to see where the technology might work, and then go after those indications, instead of following the classical route of Phase 1, Phase 2, Phase 3 trials. This kind of thinking is possible if the head of R&D has input from multiple senior people in the firm.

Peter Young: Speaking further on that topic, I feel that one of the factors which led to your success at Pharmacia and Schering-Plough was the way you managed R&D. Could you focus for a moment on the critical balancing act that one has to perform around the management of R&D and its priorities?

Fred Hassan: I showed the slide earlier which shows pharma companies are supposed to reinvent 70% of their portfolios every 10 years and that we are now at about 46% which is a huge reason why we have lost 300,000 jobs in the industry over the last 10 years. Those statistics show how important it is to manage R&D well. CEOs, even those without a life science background, should be involved in R&D management. You should, as a leader, always be asking yourself and the R&D group, "When will we see results and if we do not see results what is our plan then?" You must be prepared to kill those projects which are not getting results. Having early kills is important to an efficient and effective R&D process. You must also include the commercial people in the R&D process and always have a medical voice in the decision making process. This creates a balanced approach when making these difficult R&D decisions.

Peter Young: How have you found the transition from CEO to being a private equity professional and a chairman of various companies?

Fred Hassan: As CEOs we tend to focus on our people so that they can focus on the business and we take pride in the success of our people, so as CEOs many of us are very well prepared to make the transition to a different role where we are not in a direct command control situation. I recently made this transition myself and have become a private equity professional. In private equity there are really two primary roles. You are either a deal guy or an operator. I was brought in as an operator and have adjusted to that role. As I look at my firm's portfolio of companies, I am able to assist the CEOs in running those businesses. Also, when assessing potential acquisitions the role is not really too much different than a business development role one might have with an operating company. So in many ways I am doing a lot of the same things I was doing before.

The Pharmaceutical Industry Strategic and M&A Trends

PETER YOUNG

President and Managing Director, Young & Partners



This is both an exciting and challenging time for the pharma industry and its sister industry, biotech. The most important overall pharma industry observation is that the ethical pharmaceutical industry business model that has worked for many decades continues to be under siege and that generic pharmaceutical companies are facing their own unique growth challenges.

Despite advances in drug development technologies, the cost of drug development has soared for numerous reasons to \$1.1 billion per drug and the time to commercialization has increased to over 12 years. Further, the drug discovery success rate of the major pharmaceutical companies has faltered. This has been driven by a number of factors, including stricter regulatory approval processes.

There have been other changes in the global markets as pricing pressure has increased from governments around the world, costly advertising has become a common practice, sales force practices have become more restrictive in the U.S., and patents are being circumvented by governments in certain countries.

Finding the right replacement of the failing historic business model of the pharma industry has been difficult for companies. Both big and small pharmaceutical companies have been revamping and adjusting their strategies to survive in this new business environment.

Current strategies range from diversification, sale of non-core businesses, large scale mergers, exiting the pharma industry, geographic expansion, regional consolidation, pursuit of biologics, expansion of generics, movement into vaccines, pursuit of orphan and niche drugs, movement away from primary care indications to specialized areas, etc. However, no clear picture has emerged with regard to who the winners and losers will be.

On the M&A front, 29 deals were completed worth \$11.6 billion in the first three quarters of 2013 versus 38 deals completed worth \$30.9 billion during all of 2012. This represents a significant slowdown in dollar activity, but a similar pace in terms of the numbers of deals completed, bolstered by a surge in Asia. The one deal above \$1 billion in value was the acquisition of Bausch & Lomb by Valeant.

The slower dollar pace is driven by a number of factors. Pharma companies have been tentative with regard to larger acquisitions given the host of business uncertainties they are facing and global economic and financial conditions. In addition, the valuations of public pharma companies have also gone up considerably, driving up the cost of acquiring public companies.

However, there are signs that the pace is picking up. As of September 30, 2013, the value of the deals announced but not closed was \$29.9 billion (17 deals), the largest of which was Amgen's pending acquisition of Onyx.

Biotech acquisitions, licensing and partnering deals, which have been very active, are a different category that we compile and present separately.

Finally, what is the future outlook like for the pharma industry? The business outlook for pharma companies will continue to be a mixture of positives and negatives.

There has been an improvement in the stock price valuations of pharma companies recently driven by the strong overall market performance and an improving image of pharma companies. This improvement will continue as the ethical pharma industry works its way through the industry and solutions are being implemented.

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Generics did well in the past as long as they achieved growth. With the clear slowdown in patent expirations, there is considerable concern on the part of investors about the growth of generic pharma companies.

It is clear that the final full year 2013 M&A dollar volume will be less than the 2012 total. We expect the number of deals completed in 2014 to be strong and the dollar volume to increase, subject to global financial conditions. Partial evidence of our prediction is that the current announced pipeline of deals is strong at \$29.9 billion (17 deals) as of the end of the third quarter.

The pick-up in 2014 will be driven by strategic needs and a partial resolution of the current economic and public policy uncertainties. Pharma companies will continue to merge or acquire to achieve scale and enhance their product pipelines. M&A activity in emerging markets will grow as companies look to these markets for growth. The need to fill the shrinking drug pipeline will continue to fuel mergers and acquisitions, in-licensing arrangements, and the formation of partnerships and joint ventures. We will also see companies continue to sell non-core businesses and products to others as they restructure their companies and product portfolios.

Perspectives on the Future of Orphan Drugs

GAYATRI R. RAO, M.D., J.D.

DIRECTOR, OFFICE OF ORPHAN PRODUCTS DEVELOPMENT,
FOOD AND DRUG ADMINISTRATION



Today I hope to provide the you with a brief historical perspective about the Orphan Drug Act, what impact the Act has on drug development in terms of available incentives, some of the trends and statistics in this arena, and finally some of the current hot topics in orphan drugs.

The legislative history surrounding the Orphan Drug Act is quite fascinating. In the decade prior to the passage of the Orphan Drug Act, there were only about ten drugs developed by private industry for rare diseases. Further, only a few more drugs for rare diseases had been developed by academic institutions. So there was a desperate need for development of Orphan Drugs. There were a few notable politicians, famous figures, and even simply parents of children with rare diseases at the time who teamed up with each other and a few patient advocacy groups to bring this issue to the national stage. Through their work and the leadership of various advocates who held congressional seats, the Orphan Drug Act was passed into law in 1983.

The Orphan Drug act created a number of financial incentives for the creation of drugs for rare diseases. When a drug target is designated as targeting a rare disease, the costs associated with the clinical trials performed while developing the drug are eligible for tax credits. The second incentive provided by the act includes a waiver of the standard marketing application user fee which can be quite substantial. The final incentive for developing a drug to treat a rare disease is the 7 year marketing exclusivity which is granted upon approval of the drug.

These incentives were developed several decades ago and since then have only become, in my opinion, even more relevant to drug manufacturers. Let us take a look first at tax credits for costs associated with clinical trials performed in creating drugs which treat rare diseases. These costs are eligible for up to a 50% tax credit. In analyzing the effect of this incentive we looked at data showing the increasing cost of developing drugs over time and found a study showing the cost of drug development from 1963 through 2009. As you can see, the cost of developing drugs has drastically increased over time. The study shows that in 2009 the average non-capitalized cost of developing a successful drug was \$573 million. The drug developer then has the potential to receive up to \$286.5 million in tax credits which is quite significant. Next, if we look at the waiver of the marketing application user fee incentive, we see another instance of the incentives becoming ever more important since their inception. The first ever user fee charged for a new drug application was \$100,000. Now the cost has increased to about 20 times that amount. In 2013 the cost has been about \$1.96 million and next year the marketing application user fee for a new drug will be about \$2.17 million, so these costs have become quite substantial. The final incentive, the 7 year marketing exclusivity granted to approved designated orphan drugs was originally thought to be the least important or least compelling incentive at the time the Orphan Drug Act came into law. Today the feeling is just the opposite. Today there are many companies vying to create a drug for the same rare disease, and the 7 year exclusivity is now the most significant incentive driving research and development in the space.

I would like to now take a look at some of the orphan drug trends we at the FDA have been observing and studying. The first trend or trends I would like to talk about are related to designations and approvals for orphan drugs. We have aggregated some data on the number of designations and approvals for orphan drugs going back to 1983. The data shows that the number of approved designations for orphan drugs has increased substantially since the Orphan Drug Act was signed into law. Taking a look at 2013 we have already hit a record number of designations at 223 as of the end of November. We will likely also hit a record in approvals for new orphan drugs this year since we have already tied with our record of 26 in one year as of the end of November 2013. The trend in designations for treatment by type of rare disease is not surprising. We see the most approved

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designations in the oncology space, followed by designations in neurology, and hematology. The trend in approval of new orphan drugs is similar. The vast majority of approved new orphan drugs treat conditions in the oncology space.

I am going to spend the rest of my speech talking about some of the current hot topics in the orphan drug space. The topics I have chosen to discuss include targeted therapies, repurposing, "same drug", patient input, and rare pediatric diseases.

There has been a significant increase in the development of targeted therapies and companion diagnostics which will likely result in an increase in orphan designations and approvals, making them eligible for the associated financial incentives.

Repurposing has also become a hot topic in the orphan drug space today. Repurposing is when a currently approved drug is pursuing a new indication or patient population. Why is there a growing interest in this space? It is far less costly to repurpose a drug and the path to market requires less time. Approved drugs repurposed for rare diseases are eligible for orphan designation incentives. These drugs are also eligible for orphan grants.

Another hot topic is the "same drug" issue. As more companies have become interested in the orphan space more and more issues of sameness have occurred. For Orphan Drug designation of what is essentially the same drug as an already existing product, the drug developer must provide a plausible hypothesis of clinical superiority. This can be quite challenging.

Increased patient input is another hot topic in the orphan drug space. Recently a greater emphasis has been placed on incorporating patient perspectives throughout drug development and review. The FDA has engaged in a program recently called Patient-Focused Drug Development which includes conducting 20 meetings each year on different disease areas, many of them rare, to obtain patient perspectives on the condition, the impact on daily life, and available therapies.

The final hot topic I want to briefly touch upon is rare pediatric diseases. Recently there has been an increased legislative focus on these diseases and FDASIA has created the Rare Pediatric Disease Priority Review Voucher Program for which guidance is currently being developed. The program is designed to encourage the development of therapies for rare pediatric diseases and in January the FDA will hold a public meeting to discuss ways to encourage and accelerate this development.

2013 marked the 30th anniversary of the Orphan Drug Act and I really just want to end with a thank you to all of those who helped to create the Orphan Drug Act and all of those who were or are advocates of the mission of the Act.

The Pharmaceutical Market: Trends, Issues, and Outlook

DOUG LONG

Vice President, IMS Health



Let us first talk about global forecasts and emerging markets in the pharmaceutical industry. Our latest forecast shows that total global spending on medicines will reach about \$1.2 trillion dollars in 2017, which is an increase of about \$235 billion from the level of spending we saw in 2012. We project annual spending growth to reach a low point this year because of the severe and recent patent cliff, followed by increased growth, particularly in developed markets. The IMS base case forecast for U.S. spending growth calls for between one and four percent growth between 2013 and 2017. Spending in the top five European markets is expected to be essentially flat over that time frame. Taking a look at Asia, we forecast growth in spending on medicines in Japan to be between two and five percent and in China to be between 14 and 17% between 2013 and 2017. I would maintain that China is no longer an emerging market, but instead a market that has emerged.

I would like to now take a closer look at the U.S. market specifically. U.S. market sales of medicines are recovering from a downturn in 2012 and the number of dispensed prescriptions is growing. The patent cliff has passed for the most part and so that is why we are seeing an increase in sales. In terms of sales by segment in the U.S. the largest growth in sales has been seen in generics, biologics, and oncologics. As many of you might expect, the segments seeing the most negative growth are branded drugs and primary care driven drugs. On a total sales basis in terms of market share in the U.S. by market segment, oncologics maintain the largest share of sales and we expect the biggest mover segments in terms of growth in sales in the U.S. to be the autoimmune, vaccine, and multiple sclerosis segments. For absolute sales growth by leading therapy classes, we have seen huge growth in sales of diabetes medications. Therapy classes seeing the largest negative growth in U.S. sales include analeptics, osteoclast inhibitors, and heparins. In terms of dispensed prescriptions by segment, anti-depressants and lipid regulators take the top spots.

Let us now briefly discuss the generic vs. branded drug dynamic. For sales of medications, generics are now 83% of total prescriptions and 22% of total dollars. Both percentages are the highest they have ever been. Generic drug prices have been increasing steadily over the past few years and exclusivity periods have been quite profitable for generics. Some predict that generic drugs will eventually make up about 90% of total prescriptions. However, I feel that that figure will likely plateau at about 85-86% and then decrease from there not long after the Crestor patent expiration. I do not see how generic companies will continue to grow after that point unless they are able to make inroads into the biologic or specialty pharmaceutical space.

The specialty pharmaceuticals vs. traditional pharmaceuticals is another interesting industry dynamic worth looking at. The specialty drug market share has increased 6% since 2007 and, in terms of U.S. market share of total sales, specialty drugs now make up over 27% of the pie and are seeing sales growth of 7%. In the meantime, non-specialty drugs are seeing a decline in sales of about 5%. Specialty segments with the most significant growth include autoimmune and multiple sclerosis, both seeing double digit growth on a percentage basis. Top specialty products in terms of sales and growth include Humira, Enbrel, and Remicade.

Industry professionals tend to enjoy the discussion of specific firms in the industry, who is performing well, and who is not performing well, who is growing, and who is shrinking so I have included some information here for that purpose. Johnson & Johnson maintains the top spot in terms of absolute growth in sales, followed by Novo Nordisk, Roche (including Genentech), and Mylan. In terms of pure growth, versus on an absolute sales basis, Onyx Pharma is far and away the leader. The largest companies by sales include Novartis, Pfizer, Merck, AstraZeneca, and Roche (including Genentech). Going forward, we would not be surprised to see Roche/Genentech pushing up toward the top spot in the near future.

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U.S. changes in the healthcare system by 2020 will be substantial. Healthcare reform elements may provide support for positive positioning of medicines and increased usage. Via various new entities set up by the government including ACO, IPAB, HIT etc, the hope is to expand patient access to healthcare, increase diagnoses of asymptomatic conditions, create greater adherence to clinical guidelines, and improve compliance and persistency rates. If you break down the nation's health care spending by segment, the largest amount of money is going toward hospital care followed closely by spending on physicians and clinics. Prescription drugs make up about 10% of healthcare. Spending on healthcare is driving U.S. federal deficits and an expansion of Medicaid will likely only exacerbate this issue. Medicaid consumes 11% of the federal budget and about 24% of state budgets on average.

For a few final notes I want to go over a study we did at IMS on healthcare cost containment opportunities and give a summary with regard to brands and generics. We performed a study which showed we could save \$500 billion worldwide simply by getting people to use medicines more appropriately. Just looking at the U.S., the problems identified which, if solved, could save over \$200 billion included medication nonadherence, delayed evidence-based treatment, antibiotic misuse, medication errors, suboptimal generics use, and mismanaged polypharmacy.

Our research developed five top recommendations based on outcome impact, timing and cost. Those recommendations included supporting a greater role of pharmacists to own medicines management, investing in medical audits targeting elderly patients, implementing mandatory reporting of antibiotic use, encouraging a "no blame" culture towards error reporting, and supporting targeted disease management programs for prevalent noncommunicable diseases.

For a summary on U.S. brands and generics I would like to simply provide a few insights for the near future. For branded drugs, the U.S. market growth is rebounding, generics and specialty drugs will grow faster than the market, and generics will dominate many therapy areas as new therapy starts are likely to be generic. Also, a bad economy has led to fewer patient visits. Innovation is improving in specialty and orphan drugs, but not in some primary care areas. Also, the specialty markets are getting very crowded. I want to highlight the fact that successful launches of products are getting more difficult and that more reimbursement and regulatory challenges lie ahead.

In the generic space, you can expect increased commoditization going forward. You can also expect fewer small molecule opportunities, fewer exclusivity periods, and more reimbursement and regulatory challenges. Generic companies are moving up the value chain and optimizing their portfolios. They are also improving quality of innovation and looking at favorable tax treatment in alternative geographies. The largest opportunities for generic companies going forward include follow-on biologics and biosimilars.

Biotech Deal Making – M&A, Licensing and Partnering Trends

RANDY GUGGENHEIMER III

Managing Director, Young & Partners



The biotech industry has had a very strong year in 2013 in both drug approvals and stock price performance. The industry has grown significantly because of a number of positive trends, including demographics and technological advances. The outlook is positive because of continuing innovation and the relative lack of generic competition for biologics. Pharmaceutical companies need new products and product candidates to replace products whose patents are expiring. This has led to strong stock market performance of biotech companies and an outstanding year for IPOs, until recently. On the negative side, a number of companies have faced drug safety issues such as Ariad with Iclusig and product development times and costs have expanded.

Biotech stock price performance has been excellent and financing activity has been extremely strong in the first 9 months of 2013. This is due to new product approvals and positive clinical data. Individual stocks such as Regeneron Pharmaceuticals and Acadia Pharmaceuticals have soared. This has led to significant biotech equity issuance, including a record number of IPOs in 2013. The IPO volume has slowed since September, and it remains to be seen if the IPO window will reopen.

Biotech M&A activity was relatively strong in the first three quarters of 2013 with 21 M&A deals completed worth \$6 billion. This compares to the 19 deals worth a record \$19.7 billion of deals completed in all of 2012. The 2012 total was driven by the Gilead/Pharmasset deal, a transaction that is still four times larger than any acquisition of a biotech company with no marketed products.

Earnout transactions became very popular following the 2008 financial crisis, growing as high as 67% of biotech M&A transactions in 2010 before falling to 32% of deals in 2012. In the first three quarters of 2013, earnout deals rebounded, accounting for 62% of transactions despite the strong IPO market as an alternative to a sale transaction. This activity level indicates that earnout transactions are here to stay as pharmaceutical companies like the risk-sharing of the deals and sellers are willing to share in the risk for greater upside potential.

Biotech product licensing continues to be significant. Although the number of deals has fallen somewhat over the last couple of years the “BioWorld dollars” have increased, reflecting the level of competition and need for attractive products among pharmaceutical and large biotech companies.

Looking ahead, biotech companies have a bright future as they continue to develop new products, especially for specialty and orphan indications. The equity markets have allowed many companies to fund themselves adequately. Pharma and large biotech companies will continue to try to acquire biotech companies to enhance their pipelines. They are expected to continue use M&A as well as non-M&A methods such as licensing and partnering arrangements.

The Impact of Value-based Trends on Pharma

PETER A. TOLLMAN
Senior Partners and Managing Director
The Boston Consulting Group



A lot has been written about value-based healthcare and its potential to transform the healthcare system and hopefully ensure that some of the negative trends in the system do not turn out to be true. There has been less written about the impact of value-based healthcare on the pharmaceutical industry. If you talk to people in the industry today, they tend to focus on the headwinds pharma companies face including safety concerns, R&D productivity, cost pressures, healthcare reform, the patent cliff, and increased regulation.

One of the primary reasons people in the industry are focused on the headwinds and not on all of the influential tailwinds is that there exists the lack of a true value metric for the industry. By value in this context I mean simply patient outcomes as a function of the cost of achieving those outcomes. This discussion or metric does not really show up when you observe the various players in the healthcare system from afar. When you look at academics, you see them trying to maximize their publications. When you look at industry and corporations they are concerned with maximizing worker productivity. When you observe hospitals and other care providers you see that they are trying to maximize procedures performed. The payers are trying to minimize medical loss ratios, and the pharmaceutical and biotechnology firms are trying to maximize sales. Nowhere to be found is the patient or patient welfare. We believe that a measure of value, if utilized by the players in the industry, could improve the overall economics of the healthcare system.

Creating a value metric that people will use in the industry is not easy. It is not easy to measure patient outcomes broadly. It is easy to measure costs and thus costs are what decision makers tend to focus on. We must change the pharmaceutical game. We believe that developing a drug should be more of a triathlon than what we see currently as a marathon.

Now, how should we be looking at outcomes? I will defer to a study done by an institution called ICHOM which is a partnership between various groups who looked at outcomes using a hierarchical system. The three tiers or patient outcome metrics used include: health status achieved or retained, process of recovery, and sustainability of health. So if you are a producer of drugs you want to be able to have an effect on one or more tiers and be able to measure your drug's effects on those tiers. This can be very difficult if you are producing drugs for which registries do not currently track these tiered outcome metrics such as for oncologics. If you are a pharma company, this could affect how you think about what you should offer in terms of products.

So what are the implications for pharma of what I have discussed here today? The first implication is around data generation. You must generate outcomes data early on to understand the value of a drug in "real life". You must think about value-optimized solutions and strategically pursue value opportunities "beyond the pill". There is a lot of white space or underserved space available with regard to treatment of certain conditions and treating those conditions all along the treatment lifecycle. The final implication of what we have gone over today for a pharma company is related to business model innovation. You must encourage value-creating business model innovation in the current environment in order to be successful long term.

Patent Issues Affecting Pharma/Biotech

DAVID K. BARR
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I would like to focus today on two key issues which I think you will find interesting. One issue is of particular interest to me. I began my career as a patent lawyer in 1983 and that was a very fascinating time to be entering the field because in 1982 the Court of Appeals for the Federal Circuit began hearing cases and in 1984 the Hatch Waxman Act was passed. The confluence of those two things was extremely important for the world of patent litigation.

In 2012 and 2013 the U.S. Supreme Court issued some important decisions that have had a significant effect on patent litigation. The first ruling was in the case *Association for Molecular Pathology v. Myriad Genetics* or “Myriad”. In the Myriad case the judge’s ruling undid about 30 years of patent office precedent in terms of the patentability of isolated gene sequences. The second ruling came in the case *Mayo Collaborative Services v. Prometheus Laboratories* or “Mayo”. The ruling in the Mayo case invalidated a patent because the court held that it was based on a law of nature and, even though the specifics may not be entirely of great importance to our discussion today, it does go to show that the Supreme Court has twice overturned what lower courts have found clearly patentable inventions. The final case I want to speak about today is the *Federal Trade Commission v. Actavis* case or “Actavis”. This case was of particular interest to the pharma industry because one of the ways that branded pharma and generics were resolving ANDA Hatch Waxman cases was through reverse payments. These reverse payments occur when the branded pharma company or the plaintiff who is suing a generics producer ends up paying the generic company to delay its entry into the market beyond the date the generic could have come into the market had they prevailed in the patent case. The judge in this case found that the reverse payment method of settling these cases creates an anticompetitive situation that violates antitrust law. Let us now take a detailed look at each of these cases and the rulings that came out of them.

The Myriad case was extremely important because the case redefined the scope of patentable subject matter. The current basic principles of law in this area state that, “whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.” In addition, the Supreme Court has long held that, “laws of nature, natural phenomena, and abstract ideas are not patentable.” The question in the Myriad case was could a gene sequence be patented. The ruling, which was quite profound, overturned 30 years of precedent when it held that the isolation of naturally occurring DNA sequences was not patentable. The case stemmed from a challenge to patents granted to Myriad based on the discovery of 2 genes. Myriad had developed diagnostic tests based on this discovery and The Court of Appeals for the Federal Circuit had twice held that Myriad’s claims to “isolated” DNA segments were patentable. Myriad was thus granted patents based on the discovery of the BRCA1 and BRCA2 genes and the mutations in these genes, which can substantially increase the risks of breast and ovarian cancer. The Supreme Court addressed two types of patent claims when hearing this case: claims to the DNA sequences of the BRCA1 and BRCA2 genes, and claims to “complementary” or “cDNA” sequences of the BRCA1 and BRCA2 genes; *i.e.*, sequences from which the “introns” have been deleted. The Supreme Court ultimately reversed the Federal Circuit rulings and decided that isolated naturally occurring DNA sequences are not patentable. However the Supreme Court did affirm the Federal Circuit’s ruling that complementary DNA in this case or Non-Naturally Occurring DNA Sequences may be patentable.

In the Mayo case, there was not the question of whether a product of nature, but a law of nature could be patented. In this case the patent under question protected a diagnostic test that directed the calibration of the proper dosage of thiopurine drugs used to treating both gastrointestinal and non-gastrointestinal autoimmune diseases, by measuring blood levels of metabolites of the drugs after administration to patients. The inventors had discovered the metabolite levels that are indicative of either too high or too low a drug dosage of the

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thiopurine drug. The Supreme Court's decision begins with basic premises: "Laws of nature, natural phenomena, and abstract ideas are not patentable" and, "Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work" and "To transform an unpatentable law of nature into a patent-eligible application of such a law, one must do more than simply state the law of nature while adding the words 'apply it.'" The court ultimately held the patent invalid because it covers a law of nature. Potential implications of this ruling include potentially putting at risk the patents that form the foundation for certain biotech and diagnostic companies, licensees under patents may now challenge those patents, and investment in certain areas of research may diminish.

The Actavis case was a bit different than the first two mentioned. The Actavis case involved what is called a "reverse payment" and in 2013, the Supreme Court resolved a split between different Circuit Courts as to whether a "reverse payment" – or payments from the branded company to the generic company in exchange for the generic agreeing not to enter the market until a date later than the generic would have entered had it prevailed in the patent litigation – in settlement of a Hatch-Waxman patent suit can violate the antitrust laws. In ruling on these cases some circuit courts had applied a "scope of the patent" test which said, "absent sham litigation or fraud in obtaining the patent, a reverse payment settlement is immune from antitrust attack so long as its anticompetitive effects fall within the scope of the exclusionary potential of the patent." Other courts had ruled that reverse payments were "presumptively illegal," although the presumption could be rebutted but in order to rebut it had to be shown that the payment was for a purpose other than delayed entry or that the payment offered a procompetitive benefit. The Supreme Court took a different approach in the case and stated that "reverse payments" are to be assessed under full "rule of reason" analysis to determine whether the conduct is anticompetitive and that, "An unexplained large reverse payment itself would normally suggest that the patentee has serious doubts about the patent's survival. And that fact, in turn, suggests that the payment's objective is to maintain supracompetitive prices to be shared among the patentee and the challenger rather than face what might have been a competitive market – the very anticompetitive consequence that underlies the claim of antitrust unlawfulness." As a result of this ruling, Hatch-Waxman cases may be more difficult to settle going forward and settlements involving reverse payments may result in extensive subsequent litigation of antitrust claims.

I would like to make a brief comment about the issue of biologics and biosimilars. The Biologics Price Competition and Innovation Act was passed in 2010 and provides for approval of "biosimilar" applications for versions of previously approved biologic "reference" drug products. In my opinion, the act created a complex mechanism for the branded biologic owner and biosimilar applicant to litigate patent issues. In June 2013, Sandoz sued Amgen to invalidate two patents protecting Enbrel that will not expire until 2028 and 2029. Sandoz was in Phase III clinical trials for a biosimilar version of Enbrel and had not yet filed a biosimilar application. Amgen's motion to dismiss was granted in November 2013 because "a district court lacks statutory authority to consider a patent dispute involving a biosimilar product until after such time as an application for FDA approval of the biosimilar product has been filed." The time for appeal has not yet run. However, we now know that at least one company plans to file a biosimilar application and I believe it will not be the last.

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Speaker Roundtable – A Selection of Questions and Answers

Moderator: Peter Young, President and Managing Director, Young & Partners

Participants: Conference Speakers and Guests

Peter Young (Young & Partners): An obvious question to ask all of you is what do you see happening with regard to the Affordable Care Act (ACA) of 2010 given the troubled roll out since October, 1st? Assuming the website is eventually fixed, is the structure of the ACA sound and what impact will the implementation of the ACA have on the pharma industry?

Randy Guggenheimer (Young & Partners): I think that clearly the intention of the Act was to get more people insured. It looks now though that those responsible for implementation of the act are going to be far behind in terms of expanding the number of people covered and there could be significant issues if the young and healthy do not actually sign up. I do think that the system is likely here to stay at least through the Obama administration, and, while they will struggle mightily and it may take a few rounds of signups, I suspect that the uninsured will eventually sign up for a policy. I think that the impact of the ACA on the pharma industry is probably not going to be all that significant. I think that in terms of the number of patients covered it will be below what people had anticipated for a while.

Peter Tollman (Boston Consulting Group): I actually think that the impact of the ACA on the pharma industry will not be very significant at all. I think that the big trends in the industry are really around the direction of innovation and value. I think the ACA is here to stay but I believe it is a bit of a sideshow with low impact potential when it comes to the pharma industry.

David Barr (Kaye Scholer): The only comment I have is that I agree with some of the other responders in that there is likely to be very little effect on R&D and pharma research because, knowing the clients I work with, they have pipelines of research and they are serious about going after their molecules and biologics. In addition, a lot of this research is coming out of the universities and startups and I really do not think the ACA itself will impact the bulk of this research. I believe that there will still be a search for new drugs.

Doug Long (IMS Health): I am a bit skeptical about the new legislation and, while I think that it will be difficult to repeal, I really wish people had been more forthright when advertising the Act. In terms of the impact on the pharma industry, I do not necessarily agree that the impact of the ACA will be minimal because you hear about the price of insurance a lot but what we are not hearing a lot about is the increase in copays for drugs. Where historically private insurance has done a good job of shielding the patient from the economic impact of expensive drugs, the ACA patients will now see their deductibles and copays increase substantially and this could mean that people decide not to buy particular drugs.

Peter Young (Young & Partners): If you are able to move ten years into the future, what do you think the big pharma, specialty pharma and biotech industries and companies will look like?

Doug Long (IMS Health): We have talked about the end of the generic wave which means that the market in many classes of drugs will become commoditized. I am not sure that I agree with Fred Hassan that we are going to see a big uptick in innovation because it used to be that “me toos” could be approved and now you must show that your product is significantly better than the existing treatment. I think this will have an impact on how much money people are willing to spend on the next cholesterol drug or the next diabetes drug. As a result you are seeing a lot of people move to the orphan drug and specialty drug spaces and I believe in 10 years it will be a lot more crowded in the specialty space. You will see crowding in places like oncology and hepatitis C with companies focusing on more and more narrow indications. The marketplace will be much more competitive and companies will need to show value in their products, as Peter Tollman has mentioned today.

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Peter Tollman (Boston Consulting Group): I agree with much of what Doug said. I also believe there is a lot of overcapacity in the industry. I think the industry will shrink a bit and I think that a smaller more focused industry may create more value for patients in a more rational way. I also believe that the medicalization of the industry is going to continue and that more rational decision making and more evidence based approaches to creating medicine are going to be a byproduct of that trend.

Dr. Rao (The FDA): I agree with Doug Long that the industry will trend more toward the orphan drug space. One of the things I think about is where we are headed in terms of the costs of orphan drugs and how that will affect the interest pharma and biotech companies have in the space. For example, if costs are controlled or pressure is put on the price of these orphan drugs, ten years down the line we may see interest in the space wane.

Peter Young (Young & Partners): What is your view of the emerging market landscape including Asia, Latin America, and Africa for the pharma industry? How will issues such as pricing, intellectual property, and sales and distribution get resolved?

Randy Guggenheimer (Young & Partners): There is no arguing that there is the potential for significant growth in emerging markets, but I think that a lot of these emerging economies are very challenging for pharmaceutical companies. It seems that in China they are using the reports of bribery and scandals in sales of drugs to force lower prices. In India you see a lot of patents being given out to domestic companies and the government vacating the patents of non-domestic firms, making it very challenging to do business in some of these emerging markets. Despite the dramatic growth in the middle class in these emerging geographies, it seems there is also a concerted effort being made by the governments of some of these countries to make sure that drug pricing and drug cost escalation does not mimic what we have seen in the U.S. and so I think it is going to continue to be a challenge for the drug companies.