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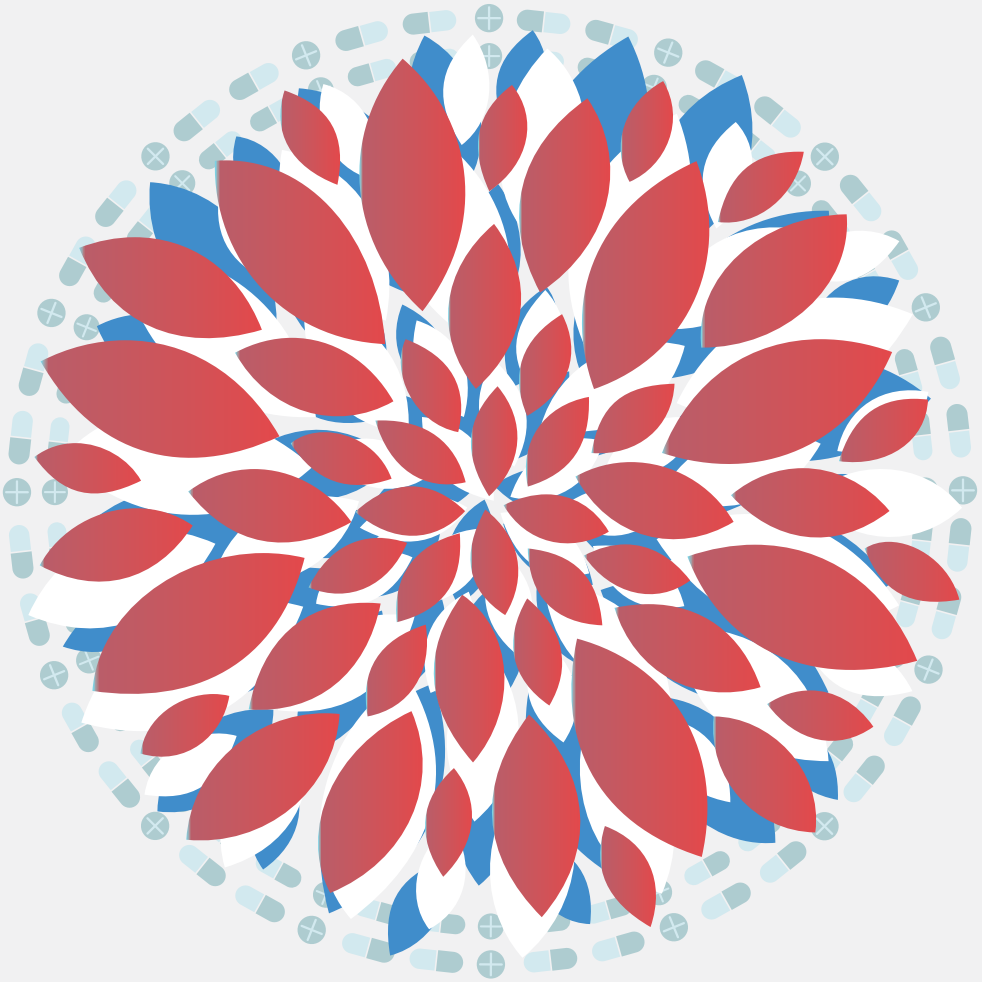

UNITED STATES BIOPHARMACEUTICALS

2017

Innovation – Hubs - Manufacturing
Contract Services – Logistics & Distribution

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Dear Reader,

Welcome to the 2017 edition of the United States Biopharmaceutical Industry Report, a joint CPhI-GBR analysis launched at the first ever CPhI North America in the historic town of Philadelphia. It is two years hence since CPhI and GBR last reported on the U.S. pharmaceutical industry and a swath of developments and potential changes have passed over the industry – most notably the new administration in Washington. The full implications of which are still unclear, but may well precipitate increased domestic manufacturing, tax incentives to repatriate revenues from overseas, a new surge in M&As and the ongoing reform and potential repeal of the Affordable Care Act.

It is in these evolving times that gaining access to the latest news, developments and insights is so critical. At CPhI we have committed to keeping the industry informed though our partnerships and reports that we undertake at each event – combining on-the-ground research with analysis by leading executives and consultants. Our events are a crucial barometer of the industry's overall health and the launch of CPhI North America is testament to the strength and underlying conditions of growth in the region. But beyond the exhibition, conference sessions and networking opportunities, thought-leadership is an essential tenet of why CPhI is so fundamental to helping fulfill the industry's future development.

This report includes interviews conducted from over 80 of the biopharmaceutical industry's most insightful and authoritative industry associations, academic institutions, research organizations, consultants and analysts. Collectively, they evaluate and condense the key biopharma trends and recent achievements into a unique 360-degree view of the world's preeminent pharma market.

As you peruse through the report, the themes examine:

- The regulatory framework: speeding up the country's approval process while maintaining the gold quality standard
- The U.S. four major life science hubs, New Jersey, Pennsylvania, Massachusetts and California; four uniquely nurtured ecosystems
- R&D and innovation; biotech startups pushing the boundaries of innovation through cross collaboration
- Outsourcing from innovation to marketing; the indispensable partner
- Distribution and logistics; an increasingly consolidated market

Despite the veil of confusion and uncertainty that accompany most times of change, the U.S. biopharmaceutical industry continues to boldly move ahead – with $50 billion R&D investment, 550 new drugs approved by the FDA between 2000 and 2015, and over half of all global innovation. Meanwhile, the push for increased manufacturing at home has not gone unnoticed, with international companies looking to spread stronger roots in the U.S., and an even more robust M&A climate – up by over $100 billion from the decade prior.

Moreover, the rise in niche biotechnology companies – often the offspring of university incubators – is meeting a need for personalized solutions in areas such as oncology, enhanced immune class, diabetes/obesity, CNS, anti-viral, mental health, and pain management.

But these new extremely specialized biopharmaceuticals often come in small batches and are expensive to develop and manufacture, requiring temperature regulation and customized packaging – all at a time when there is public consternation at drug pricing. However, the end results of the billions of dollars that the U.S. pharmaceutical industry spends on researching new cures are of indisputable benefit to the entire globe – it fundamentally drives pharmaceutical advancement.

Our aim is to bring the incredibly dynamic innovations and manufacturing practices, regulations, crucial supply chain partners and regional associations' perspectives into one report. Ultimately, to help you make better informed decisions this week and improve your new partnerships and collaborations.

A very warm thank you goes to our partners at BioNJ, HINJ and LSPA for your continued support, as well as to all the executives and researchers who shared their valuable insights.

Rutger Oudejans
Brand Director
CPhI

Katya Koryakovtseva
General Manager
Global Business Reports

Exclusive interviews

Industry executives from various types of companies, associations and government discuss market trends and opportunities.

10, 16, 31, 32, 49 and many more

Editorial content

Global Business Reports' journalists provide unique insights into all aspects of biopharmaceutical industry by working on the ground and meeting with key industry leaders.

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Quantitative data and maps

Quantitative data and maps highlight many of the underlying trends across all levels of the value chain in the US Biopharmaceutical industry.

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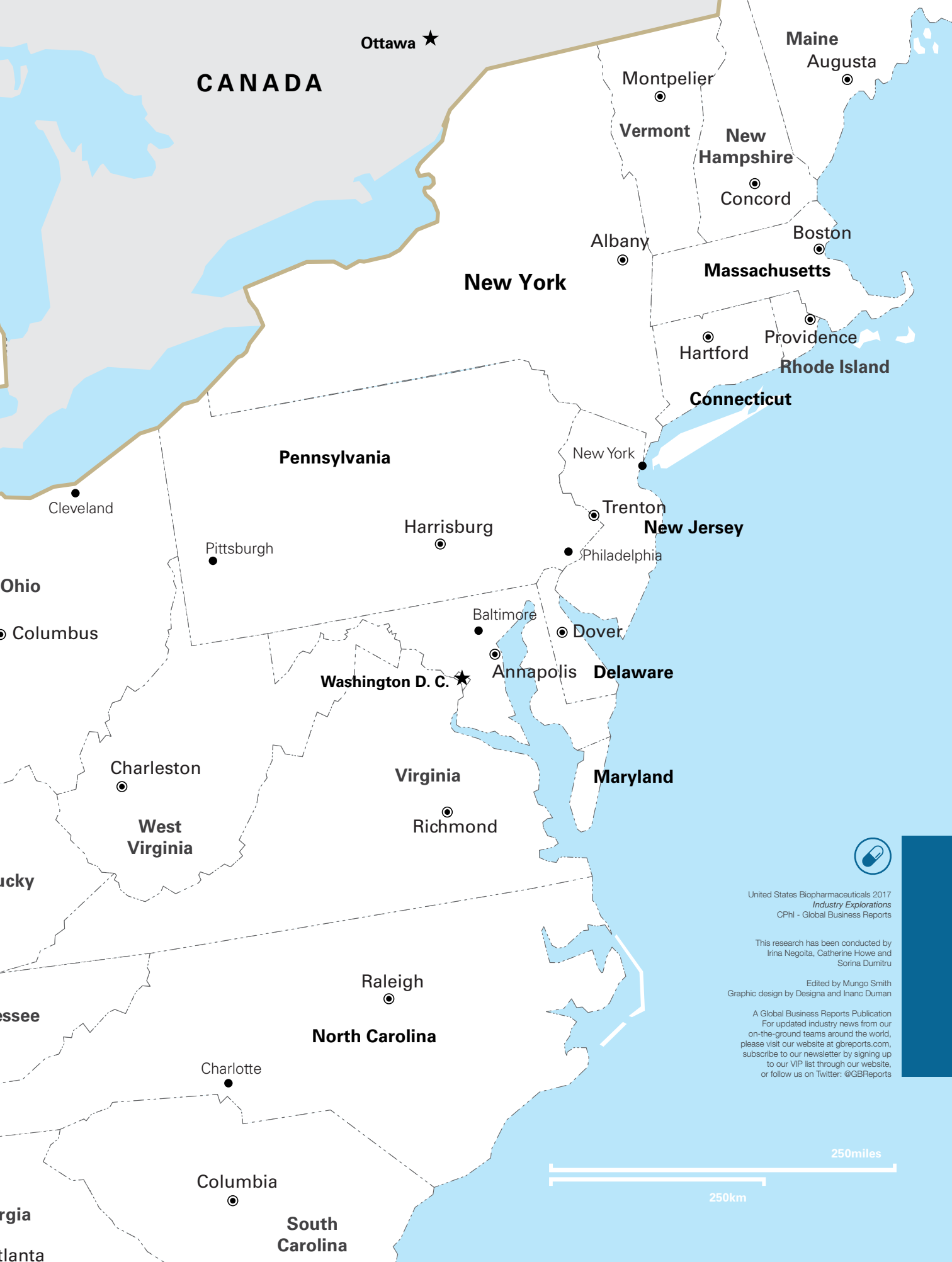

United States Biopharmaceuticals 2017
Industry Explorations
CPhI - Global Business Reports

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Image courtesy of CordenPharma

INTRODUCING THE U.S. BIOPHARMACEUTICAL INDUSTRY

"As U.S. companies wait for clarity on the timing of tax reform, there is a window of opportunity where international companies may be more aggressive in acquiring targets in the United States. The attitude might be that it is better to buy now before the U.S. companies make the acquisitions".

- Andrew Forman,
Life Sciences Global Sector Resident,
Ernst & Young

Introducing the U.S. Biopharmaceutical Industry

Maintaining global leadership amid changing tides

As with other sectors across the United States, the life science industry has entered 2017 amidst a great deal of speculation regarding prospective changes under the new Administration. Having come under fire for high drug pricing during Donald Trump's first news conference as President-elect, many drug companies took a hit on stock prices in early 2017, and pharma giants such as Johnson & Johnson, Novartis, Merck, Eli Lilly, Amgen and Celgene have been further placed in the media spotlight since. However, the global powerhouse's industry outlook remains very positive and the nation is unlikely to relinquish its position as world leader in the foreseeable future.

Global health care expenditure is projected to mount from $7 trillion in 2015 to $8.7 trillion by 2020. An 8% increase in the United States' ageing population is of course a great success in an industry that strives to buy time, but also shakes up current dynamics within life sciences.

Fostering the Ecosystem

The U.S. biopharmaceutical ecosystem is diverse; from the large, vertically integrated companies, to the rising number of biotech startups that are yet to reach commercialization. Whilst on the one hand companies are expanding capabilities both through organic and inorganic growth, outsourcing trends are also on the rise, as companies increasingly seek to streamline development timelines. The industry's first priority, the advancement of medicine, is reflected in increasing cross-collaboration, technology transfer and strategic partnerships. Equally important as a driving force is the representation by associations seeking to align priorities, promote collaboration and advocate on behalf of their members.

Industry Dynamics: M&A Drivers

The U.S. landscape is continuously shifting, with M&A activity rising to over $200 billion in biotherapeutics over the last three years, up from an average of less than $100 billion over the decade prior. A primary driver has been the growth gap created by patent cliffs which, combined with a dearth of FDA approvals, caused a period in which drug companies did not grow. Commenting on the high level of activity in recent years, Andrew Forman, life sciences global sector resident at Ernst & Young, stated: "We call this shift the New Normal… Per IMS, the global pharma industry was growing at about 4%, so over the past five years, big pharma in aggregate had about a $100 billion growth gap, and as a result there was a need for them to catch up. This started to happen over the last three years, and big pharmas' M&A activity in 2016 as a percentage was the largest it has been in about five years and we expect this to continue over the next several years."

Patent cliffs still in play for some major products are also driving activity as com-

"There is a lot of potential for regulatory reform and corporate tax reform – we have one of the highest corporate tax rates in the world among the developed nations. The Mercatus Center at George Mason University has looked at the deadweight loss due to regulations within the U.S. economy and found that if the level of regulation had been frozen at 1980 levels, our GDP would be roughly 25% higher than it is now. Regulatory reform and corporate tax reform would encourage investment in this country."

- Kevin Swift,
Chief Economist,
American Chemistry Council (ACC)

ECONOMIC IMPACTS OF THE U.S. BIOPHARMACEUTICAL INDUSTRY, 2014 ($ IN MILLIONS)

Source: TEConomy Partners data, calculations and analysis; IMPLAN 2014 U.S. model.

IMPACT TYPE	Employment	Labor Income	Value Added	Output	State/Local Personal Tax Revenue	Federal Personal Tax Revenue
Direct Effect	853,818	$105,111.7	$247,918.4	$558,372.1	$3,190.7	$20,400.7
Indirect Effect	1,710,333	$112,847.3	$184,319.8	$363,617.8	$3,097.2	$20,711.0
Induced Effect	1,882,213	$92,684.3	$161,925.5	$295,551.1	$2,558.0	$17,164.9
Total Impacts	**4,446,365**	**$310,643.2**	**$594,163.7**	**$1,217,541.0**	**$8,845.9**	**$58,276.6**
Multiplier	**5.21**	**2.96**	**2.40**	**2.18**		

> Companies are also looking to bolster their product pipelines through later-stage M&A assets which will help them to continue to grow in the future as they launch new products. Many pharmaceutical and larger biotech companies have strong balance sheets, which they can leverage for M&A. There is a keen interest in biotech assets and newer technologies which may command additional higher pricing and more specification in the market.
>
> - Andrew Getz, Partner, Deal Advisory, KPMG

panies face additional competition. Equally, some companies have chosen to narrow their focus through divestitures, arising from portfolio rationalization. "In the last several years, about 25% of M&A has come from portfolio divestitures involving adjacent businesses such as consumer, animal health, vaccines and medical devices among other assets," commented Forman.

Citing a focus on therapeutic specialization leading to acquisitions primarily of rapidly growing biotech companies and divestitures, he continued: "These therapeutic battlefields have been intensifying, driven by a wave of innovation – record FDA approvals in the past several years and most recently rising payer pressure to address rising costs and now a central focus in Washington."

As competition increases and the focus shifts from blockbuster drugs to more specialized treatments and cures, business models are also shifting, embracing M&A and collaboration to target more specific therapeutic areas, reflected in more targeted pipelines. The rising number of biotechnology companies also provides opportunities for big pharma companies and reciprocal benefits in the form of additional funding and commercial expertise.

Reform: Changes to Expect

The main goal of the new Administration was to repeal and replace the Affordable Care Act (ACA), a promise held by the Republican Party for approximately seven years. Even had the push not failed, the process would still have taken years, contrary to the promise for immediate effect and implementation. While Trump's position on the ACA remains unchanged, any replacement or reform would have to provide more effective cover to those still not catered to under the Act. The Republican Bill would have created new limits on Medicaid spending and, more generally, reducing spending in healthcare could remove incentives for insurers to cover those groups.

Although the so-called American Health Care Act did not pass, Trump's remarks on waiting for Obamacare to "explode" indicate that the matter is not yet laid to rest.

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> Regardless of the content in the final tax bill, the drug industry's number one goal is to see repatriation of the cash held overseas. This would provide pharma and biotech companies with over $250 billion dollars in cash, giving them the flexibility to pursue acquisitions. The Republicans claim this is something they want to see happen, so there is no reason for the move to be prevented, assuming that they get a tax bill through Congress, which we predict will take place in the fourth quarter of 2017 or the first quarter of 2018.
>
> - Ira Loss, Executive Vice President, Washington Analysis

Chester "Chip" Davis

President & CEO
THE ASSOCIATION FOR ACCESSIBLE MEDICINES

The AAM is the national association representing manufacturers and distributers of generic pharmaceuticals, biosimilars and bulk pharmaceutical chemicals

Could you provide an introduction to the Association for Accessible Medicines and the motivation behind its rebranding?

Previously the Generic Pharmaceutical Association (GPA), the association rebranded in February 2016 to better communicate its message and work more effectively on behalf of our members and the patients who rely on our products. As the nation's leading industry trade group representing the manufacturers and distributors of generic pharmaceuticals and biosimilars, bulk pharmaceutical chemicals, and suppliers of other goods and services to the generic industry, the new name, The Association for Accessible Medicines (AAM), better captures who we are, what we stand for, and reflects an unprecedented commitment to ensuring an understanding and appreciation of the value proposition our members provide to patients by legislators, regulators and policymakers to a far greater extent than ever before.

How is the new Administration's drive to lower drug costs likely to impact the generics industry?

Unfortunately for the generic industry, when the high cost of prescription medicine is talked about by the President and Members of Congress, there generally is no distinction made between brand drugs and generic drugs and the vastly different economic systems in which they are marketed. Since 2008, while average brand prices have risen 208%, average generic prices have fallen 74%. When policymakers reference escalating drug prices without distinguishing between brands and generics, generics are perceived as equally blamable for the drug cost problem despite incontestable data showing that generics drive savings, not cost. This distortion presents significant danger for the generic industry because pricing policies that might be effective in controlling costs in a brand monopoly market can have the opposite effect in a commodity generic market.

Where should the balance lie in creating an environment that supports affordable access through generics whilst still stimulating innovation?

The 1984 Drug Price Competition and Patent Term Restoration Act, commonly called Hatch-Waxman, established a brilliant balance between stimulating generic competition to lower drug prices and enlarging incentives to increase the development of new brand medicines. By giving generic manufacturers an abbreviated and less costly FDA approval process, the availability of safe and effective generics has increased so that today nine out of 10 prescriptions dispensed in the United States are generic.

R&D spending has increased from about $2 billion annually prior to Hatch-Waxman to approximately $60 billion annually today. Equally, brand drugs companies have been granted more than 1,100 years of patent term extensions under the law's patent term restoration provision. The bottom line is that as generic access and savings have increased, so has spending for new drug innovation and the introduction of new and improved medicines.

What are some of the key developments in the biosimilars space, and what major hurdles must still be overcome from a regulatory perspective?

We are beginning to see the U.S. biosimilars market come to life. There now are four FDA-approved biosimilars, two of which have entered the market, with another 64 enrolled in the FDA's biosimilar products development program. Congressional reauthorization of the biosimilar user fee program later this year, which will boost funding for the biosimilars program through fiscal year 2022, will help hasten the pace of biosimilar approvals.

Nevertheless, there are challenges and work still to be done in this emerging sector. For one, the FDA has yet to provide guidance on determining the interchangeability of biosimilars and innovator biologics. Questions remain over the reimbursement of biosimilars used in Medicaid. Industry is challenging the FDA's biosimilar naming policy, which differs from what is being used successfully in Europe and other world markets. It also remains to be seen how the Supreme Court will rule later this year with respect to key provisions in the law establishing the biosimilar regulatory approval pathway. What we must avoid is allowing these challenges to prevent timely biosimilar market entry. In April 2015, The AAM established the Biosimilars Council, which works to ensure a positive regulatory, reimbursement, political and policy environment for the biosimilars industry.

Going forward, how will the AAM continue to support the generic and biosimilar industries?

AAM will continue its mission of being the lead advocacy organization on legislation and regulations impacting the generic drug industry. Among other efforts, AAM is working to block an ill-advised generic drug labeling proposal that would threaten patient safety, repeal the Medicaid inflation-based rebate penalty for generic drugs that is jeopardizing generic competition, secure a unified drug development regulatory system between the FDA and the European Medicines Agency, and win legislation, such as the CREATES Act, that would end the abuse of restricted access programs that prevents timely generic drug development.

◂ 9

Regardless, there continues to be increasing pressure on cost and drug pricing, which could impact companies' choice of components within their portfolios. As drug development costs rise, companies are likely to pursue treatments and cures for rare diseases to take advantage of expedited review at the FDA to allow more time once in the market to recoup their investment under patent protection.

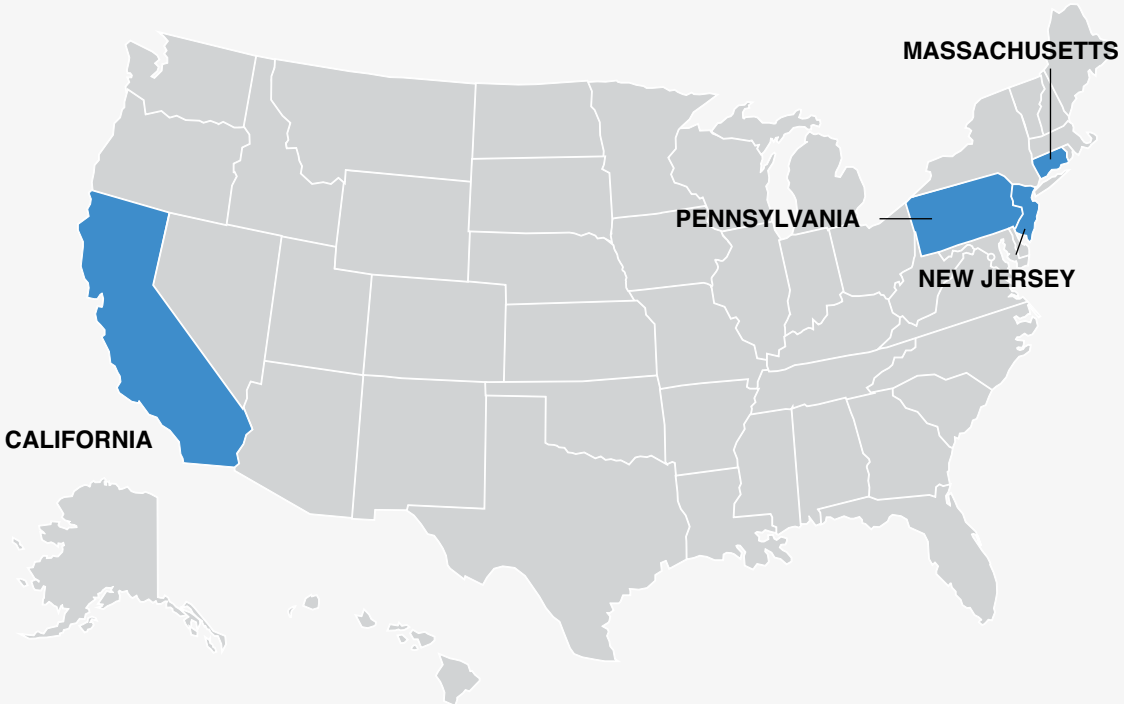
Tax reform is also under a great deal of speculation and, with corporate tax rates among the highest worldwide for developed countries, there could be some positive changes to the framework on the horizon. Equally anticipated is the proposed Border Adjustment Tax: "There are two schools of thought within the Republican party regarding tax reform," outlined Ira Loss, executive vice president at Washington Analysis. "The House of Representatives' version includes the Border Adjustment Tax (BAT), but this is not included by the Senate. Where the White House comes out on the BAT will be critical. We believe there is a 60% chance of no BAT, or that it will be watered down in the final bill, primarily because the retail sector is adamantly opposed."

Nevertheless, international companies are set on increasing their U.S. footprint, with many companies based in Europe and Asia making U.S.-based acquisitions and opening new facilities in regional hubs. —

> "As U.S. companies wait for clarity on the timing of tax reform, there is a window of opportunity where international companies may be more aggressive in acquiring targets in the United States. The attitude might be that it is better to buy now before the U.S. companies make the acquisitions."
>
> - Andrew Forman,
> Life Sciences Global Sector Resident,
> Ernst & Young

Introducing the clusters

Despite the presence of many multinational companies operating across the country, the U.S. biopharmaceutical industry is characterized by a number of hubs. The Boston/Cambridge area is ranked first in Genetic Engineering & Biotechnology News' (GEN) top U.S. biopharma clusters list in 2016, followed by the San Francisco Bay area, having seen greatest progress in R&D through commercialization of academic research projects. Ranking third, the New Jersey/New York hub nevertheless maintains its reputation as the "medicine chest of the world". Cross-industry collaboration is on the rise across the board, with associations and research institutions increasingly recognizing the benefits of pooling efforts and fostering an innovation ecosystem. —



Debbie Hart

President and CEO
BioNJ

BioNJ is a non for profit association representing research based life science companies and stakeholders in New Jersey

Since its establishment in 1994, BioNJ has grown to support some 400 members. Could you briefly outline the development of the association and its main objectives?

At BioNJ, our mission is to ensure a robust life sciences ecosystem in New Jersey in which science is supported, companies are created, drugs are developed, and patients are paramount. We deliver our services in four categories. The first is public policy, making sure that state and federal government advance the industry by supporting medical innovation. The second is networking and education–we know that the number one reason that people come to BioNJ is to meet other people in the ecosystem. We therefore create approximately 40 opportunities annually, allowing our members to network and educate themselves in the fields they are interested in. The third category is services, of which an example would be our negotiation of a high volume purchasing agreement with Fisher Scientific, resulting in savings of up to $6 million last year for our members. Other service areas include insurance, delivery and relocation. Finally, the fourth category is workforce development; making sure that talent finds the right companies, and companies find the right talent. Over the years, the industry in New Jersey has grown from about 30 companies, strictly in biotech, to over 400. Our Members include those in biotech as well as big pharma, medical devices, academic institutions and service providers that support the life sciences industry.

What are some recent examples in which BioNJ has been involved in the state's policy making?

in the last few months, BioNJ was actively involved in having two important initiatives signed into law. One was the establishment of the Biotechnology Task Force. BioNJ will have seats on that task force appointed by the governor. This allows us to go throughout the state and look for opportunities in policy, incentives, and programs that will help to support and strengthen the industry. Even more recently, the governor signed into law another initiative that established a governmental entity intended to facilitate business and academic partnerships across the state. BioNJ will also have a seat on this commission.

Have there been any recent developments or shifts in R&D focus?

There is currently a strong focus on personalized medicine, and this will continue to be the way many medicines are developed and patients are treated. New Jersey is a leader in personalized medicine and immunotherapies, and we are very proud of the developments in immunotherapies being developed by a number of our companies.
A challenge that needs to be addressed is the time frame (10 to 15 years) and cost (upwards of $2 billion) to develop a drug and bring it to market. Since this is such a risky and expensive process, especially for smaller companies, a key initiative of BioNJ is to connect these companies with VC's and investors of all types that are willing to invest in them.

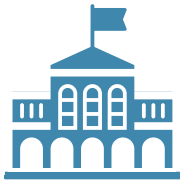
New Jersey was at the forefront of legislation for biosimilars in 2015. How is this area developing?

New Jersey was indeed a leader in passing biosimilar legislation. Biosimilars is a growing industry in New Jersey with many large companies developing their own biosimilars. Also, several smaller companies are coming to New Jersey to develop and manufacture biosimilars. New Jersey is proud to be developing a strong business in biosimilars, in addition to the significant presence of a biopharmaceutical branded and generics industry. The composition of New Jersey's industry reflects the entire spectrum of companies and support organizations.

How do you expect the industry to develop, and what will BioNJ's role be in its growth?

I am bullish on the industry and on New Jersey. While there will be policy and financial challenges in the future, the opportunities are immense. BioNJ will continue to support companies already in New Jersey and to attract more life sciences companies to our state. Working closely with policy makers in Washington and New Jersey, we will advocate for a policy environment that supports medical innovation and ensures faster treatments and cures for patients. BioNJ is committed to the growth and prosperity of our industry and that patients have access to innovative medicines to improve and save their lives. Because, patients can't wait.

New Jersey



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The Number of Academic Institutions

3,180

The Number of Life Sciences Establishments

22,000

The Number of Students Graduating with Degreed in Life Sciences from NJ State Universities

13

Teaching Hospitals

$1.6 Billion

NIH Funding in 2016

312,943

Total Direct, Indirect & Induced Jobs

3,200

The Number of Academic Patents from 2010-2014

65,783

Direct Jobs

$14 Billion

Corporate R&D Funding

14 out of 20

of the World's Largest Pharmaceutical Companies are Based in NJ

#1 State

for Biotech Growth Potential

Dean J. Paranicas

President and CEO
HEALTHCARE INSTITUTE OF NEW JERSEY (HINJ)

A trade association for the research-based biopharmaceutical and medical technology industry in New Jersey

HINJ has acted as a voice for New Jersey's life sciences industry for over 20 years. How has the association developed?

Having earned the reputation as the "medicine chest of the world", biopharmaceuticals is both the largest industry sector in New Jersey and one of the largest such clusters in the United States. HINJ was a response to the need to elevate awareness and advocate for a supportive environment that would nurture and enable our companies to continue to flourish here.

Of the top 20 research-based pharmaceutical companies in the world, 13 have their global, North American or U.S. headquarters in New Jersey, or at least have a substantial presence here. Including biopharma and medical technology, the industry generated about $109 billion in 2014 in direct and indirect economic impact–second only to California–and accounts for nearly 20% of New Jersey's GDP. Because of this considerable impact, HINJ's main goal is to ensure that the elements are in place for New Jersey to continue to be a life sciences leader.

What makes New Jersey an attractive and competitive investment destination amid increasing trends to pursue cheaper costs?

New Jersey possesses high value elements: the infrastructure and transportation system are terrific, it is proximate to the major capital markets in the United States, it has a highly educated, very skilled workforce, great research universities, tremendous cultural appeal, and an extremely well-developed network of goods and service providers that can support the industry locally. For all these reasons, in addition to manufacturing, R&D and distribution, New Jersey is also home to many companies' core functions. These companies also benefit from being proximate to each other.

How has the industry in New Jersey developed from a regulatory standpoint?

The FDA continues to watch over the industry as the global gold standard of review, with ever-growing accountability. 25 years ago, it was recognized that Congressional appropriations were insufficient, so a user fee structure was established that has grown in five-year increments to meet the increasing demand, and is up for renewal in 2017. Also, the 21st Century Cures Act, which became law in December 2016, provides a large supplemental appropriation to the National Institutes of Health to enable more of the core research that it does.

In what ways has the focus shifted in terms of R&D and innovation?

The most significant development in recent years in New Jersey has been the continuing maturation of our innovation ecosystem, which relies on the public, private and academic sectors coalescing to enable the success of innovator industries. As a result of the merger of the former University of Medicine and Dentistry of New Jersey (UMDNJ) with Rutgers University, we now have a real research powerhouse. Coupled with the emergence of Rowan University in the southern part of the state and its acquisition of the UMDNJ medical school in southern New Jersey, we have two public research universities focusing on the life sciences.

These consolidations are starting to gain traction now, and we have seen increasing engagement and collaboration with the life sciences industry, providing better clinical approaches for patients as well as institutions around the state. There also is the New Jersey Institute of Technology (NJIT), which created a 501(c)(3) organization a few years ago called the New Jersey Innovation Institute, to provide innovative solutions to innovator industries, including the life sciences.

Do you have a final message regarding New Jersey's life sciences industry?

The future of the industry in New Jersey remains bright and the signs are encouraging. We continue to see investment and commitments to the state, which is indicative of its core strength as a life sciences venue of choice. It is vital in the current environment that the value of medical innovation, both to human health and to areas such as health care spending and positive economic impact, continues to be recognized.

Because Patients Can't Wait®

Like the journey to freedom represented by the Statue of Liberty along New Jersey's shores, our State is the gateway to new treatments and cures that help free the world from sickness and disease. New Jersey companies have created a legacy of unmatched innovation and achievements.

BioNJ is a network of 400 Members representing research-based life sciences companies and stakeholders dedicated to propelling a vibrant ecosystem where:

- **Science is Supported**
- **Companies are Created**
- **Drugs are Developed**
- **Patients are Paramount**

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Chris Molineaux

President and CEO
LIFE SCIENCES PENNSYLVANIA

Life Sciences Pennsylvania is a non-profit association representing and connecting the state's diverse life science sector

Life Sciences Pennsylvania was first established in 1989 as Pennsylvania Bio. How does its new branding better reflect the association's priorities?

The association was formed in 1989 by two biotech executives out of Penn State University to raise awareness of the growing biotech community in Pennsylvania, which had previously not been considered a hub. In the 1980s, biotech was a very hot new field of science and business primarily focused on biologics. However, the term today refers more to a business model and includes a wider range of companies. The makeup of the association therefore grew and diversified to reflect this and include all other sectors of the life sciences, including pharmaceuticals, medical devices, diagnostics and academic research institutions. We now have about 120 companies out of 726 that are truly biotech, so about 17%. We now also have 49 colleges and universities in our membership and 56 contract research organizations, for example. The name of the organization clearly did not match the makeup of the membership, so we started a brand exploration process towards the end of 2015 and throughout 2016 to determine the most appropriate name. Given the diversity of the life sciences industry in Pennsylvania, we ended up with Life Sciences Pennsylvania. The motivation was really to ensure that the members, whether current or prospective, feel they are included in our mission and properly represented.

What are the characteristics of Pennsylvania's life sciences industry as a hub?

Pennsylvania is very unique among the states – we have all the ingredients to make a life sciences company successful. The cost of living in and around Philadelphia is dramatically lower than areas such as New York, Boston, San Francisco and Washington D.C. We also sit equidistant from the financial markets of New York and the regulatory agencies in Washington D.C. and Maryland, at only an hour-and-a-half train ride. State-wide, there are over 77,000 people working directly in life sciences. There is a job multiplier effect of about five to six jobs outside the industry in the way of service providers. In Philadelphia alone, one out of every six jobs is in life sciences or healthcare.

Pennsylvania is home to the entire value chain across all sectors, from pharma and biotech to medical devices and diagnostics. We have some of the best world-class academic research institutions, and a fast-growing community of contract research organizations. Two of the top five institutions funded by the National Institute of Health (NIH) are located in Pennsylvania– the University of Pennsylvania is number four and the University of Pittsburgh is number five. Companies based in Pennsylvania can find support across areas such as early discovery through to commercialization, approval processes and manufacturing.

How attractive is Pennsylvania's policy framework, and what incentives are offered?

There have not been many recent changes on the policy front at a state level, largely because the state has faced a budget deficit for the last few years so there has not been much appetite for the state capital for investing in new programs. However, there is one very successful program called Innovate in PA, which received $80 million of funding in 2015. That is probably the greatest success story in terms of new programs. Pennsylvania also has Keystone Innovation Zones. We have also been trying to hold onto programs such as the Research and Development Tax Credit, which is now a pool of $55 million for companies to access. Furthermore, those research and development tax credits can be sold, so a small company with a tax credit can sell that credit for cash. Some companies will do this to generate cash to cover their operating expenses.

How will Life Sciences PA continue to grow its membership base and support existing members?

Our overarching mission is to make Pennsylvania the most attractive place in the United States to open and operate a life sciences company. In part, this involves advocacy and fostering an attractive policy framework. The other part is to facilitate strategic connections, connecting businesses with the resources they need to grow and succeed. We now have 39 board members, which is enormous, but is reflective of our membership and serves as an extension of that network. Ultimately, we want to create a supportive and thriving ecosystem.

Pennsylvania

$6,3 Billion
Investment in Regional Companies

1,200
The Number of Life Sciences Establishments

6
The Number of Medical Schools

10
Medical Centers

$3.5Billion
The Value of Pharmaceutical and Basic Chemicals Exports

>$1 Billion
NIH Funding in 2016

$460,4 Million
Venture Capital Investing in 2015 in Bioscience Industry

$103,761
Avarage Annual Wage

48,900
Direct Jobs

5,400
Life Science-related Patents Since 2010

77,000+
Total Direct, Indirect & Induced Jobs

Sara Radcliffe

President & CEO
CALIFORNIA LIFE SCIENCES ASSOCIATION

CLSA represents California's leading life science industry ensuring that it retains its competitive edge

Could you provide us with a brief introduction to California Life Sciences Association (CLSA)?

California Life Sciences Association (CLSA) is California's largest and most influential life sciences advocacy and business leadership organization, with hundreds of members from across the state ranging from small organizations to large multinationals and spanning various applications of life sciences, such as health, industrial, environmental, food and agriculture, device companies, diagnostic, biotech, and pharmaceutical. We work closely with industry, government, academia and others to shape public policy, improve access to innovative technologies and grow California's life sciences economy. The association as it is known today was formed in March 2015 through the merger of two organizations: the Bay Area Bioscience Association, commonly known as BayBio, and California Healthcare Institute (CHI). Both organizations have been in existence for a combined 40 years so; in that sense, our organization has had a long and impactful presence in California.

Could you give some insight into the characteristics of the industry and any recent developments?

California's life sciences sector is strong and growing. Not only does the sector boost patient care for unmet medical needs, it is an economic engine that provides good paying jobs to more than 287,000 people, while generating $147.7 billion in revenue. By our count, there are over 3,000 companies now in the life sciences sector and the life sciences ecosystem in California is extremely impactful in terms of creating life-saving products. For example, right now there are over 1,200 investigational new drugs (IND) in the development pipeline, and in 2016, over 260 medical devices from California companies were approved. Another exciting aspect of our life sciences ecosystem is how cutting edge it is with regard to new, exciting transformational development. In the Bay area, we have been able to build on the proximity to Silicon Valley in terms of growing digital health, such as wearables, biosensors, and robotics. It is a wonderful combination of the historic strengths of the Bay area.

In what ways does CLSA help to ensure a supportive ecosystem for life sciences innovation?

We have two primary areas of focus. The first is advancing innovation in California through our advocacy for effective national, state, and local policies. Protect Access and Innovation is our flagship initiative within a very large body of advocacy work that we do at the national, state and local level, with the purpose of raising topics with policy makers and legislators that will help to improve the environment for innovation and helps patients and consumers. Within this initiative, we are responding to the very robust public debate about how to fund innovation. Alongside the current concerns surrounding drug pricing, other factors such as timelines for getting products to market, regulatory barriers to approval and the complexity and sometimes labyrinthine nature of reimbursement policy are all of keen interest to our members, and we lobby on all those issues.

Another equally important component of our mission is supporting entrepreneurs, life sciences businesses, education and career development. We have a robust portfolio of business solutions services that is unmatched by other organizations, including group purchasing savings via our Business Solutions program, medical and dental insurance plans for life sciences companies and more. We also spearhead opportunities for sources of capital, industry events to bring the sector together, development programs, entrepreneurial support programs – all in addition to our federal, state and local advocacy offerings.

How would you describe the investment climate at the moment?

Because California life sciences organizations have such a strong track record of translating lab science into products that help patients and consumers, the state has long been a magnet for investment. As in past years, California was the top state for life sciences venture capital (VC) investment in 2016 with $4.4 billion: $3.3 billion in biotech and $1.1 billion in medical devices. The life sciences are second only to software in California for VC funding. There are some concern right now about the general unpredictability of the regulatory and reimbursement environment. There is a lot of discussion at the federal level about policies that might be extremely problematic for life sciences organizations, including importation of drugs that have not been approved by the FDA, reworking Medicare, and direct negotiation between the government and manufacturers.

California

California's Life Sciences Ecosystem

3,040
Life Sciences Companies

$1.6 Billion
#1 in State for Digital Health VC Investment in 2016

The Most Universities
in the Shangai Index World Top 100: 11th

1,269
The Number of Medicines Currently in the Pipeline of California Companies

$3.6 Billion in Grants
Leading the Nation in NIH Funding in 2016

884,200
Total Direct, Indirect & Induced Jobs

$116,000
Avarage Wage

287,200
Direct Jobs

$4.4 Billion
Venture Funding

$22 Billion
Total Exports

$15.6 Billion
Federal, State and Local Taxes Paid

Bob Coughlin

President & CEO
MASSBIO

A not-for-profit association representing over 975 organizations across Massachusetts' life science and healthcare industries

Could you start with a brief introduction to MassBio?

MassBio was founded in 1985 as likely the first state biotech association in the country. Our objective is to improve the healthcare system and ultimately improve patients' lives by creating a positive environment for our member companies to operate. Our policy and advocacy efforts are engaged and sophisticated, with a state policy team and a federal policy staff working with representatives at the U.S. House of Representatives, NIH, and the FDA. Our purchasing consortium is one of the largest group purchasing consortiums for our industry in the country, and we also host networking events and professional development forums. We have a wonderful economic development team that works to help our member companies grow, as well as help other companies locate here.

Our Innovation Services group, a key differentiator from many of the other state associations around the country and worldwide, works with Tech Transfer offices and entrepreneurs to not only create companies, but also help them raise capital and advance through the business cycle. In essence, our Innovative Services group is a concierge service for people looking to start companies in this space, offering mentors and providing access to capital. Because of this work and our other assets, in 2016 alone 192 companies joined MassBio. Today, we have over 1,000 member companies, compared to just 120 a decade ago.

What are some of the key characteristics of Massachusetts' biotech industry?

The life sciences industry continues to grow and expand here. Many new companies are being formed from the huge amount of research happening locally because of the large amount of NIH funding received throughout the state. Massachusetts has received more NIH funding per capita than any other state in the country, while Tech Transfer offices at our universities help create small, breakthrough, cutting-edge companies. Over the last decade, we have also been very successful in attracting large Pharma companies to undertake R&D here and allocate business-development dollars to help stimulate and assist with capital formation for our small companies.

Industry, academia and government are all on the same page and we act as partners. Any problem can be overcome if those three parties come together to find a solution. Additionally, there is a thriving public private partnership – the Massachusetts Life Sciences initiative -- thatcreated a ten-year, $1 billion life science initiative to help fund and grow new companies and jobs here. This initiative has greatly helped the economy in Massachusetts; we have experienced 37% growth in employment in the biotech space.

Could you elaborate on the environment and innovation framework in Massachusetts?

Being a small state, one-sixth the size of California, creates an atmosphere, environment, and culture of collaboration. Massachusetts is also home to 122 colleges and universities, adding a high level of talent, the most important ingredient for any industry based on innovation. The number of new ideas created and turned into companies is truly a great advantage to growth here..

Massachusetts created a series of investments through the Massachusetts Life Science Center (MLSC) to directly finance the growth of the industry. Their funding includes refundable tax credits, tax credits granted as a job-creation incentives, a capital fund that can help with equipment, construction needs and growth. They also have a section for improvements to infrastructure, and seed funds for early-stage investment, which is sometimes the most difficult money to raise.

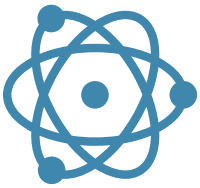
What are MassBio's objectives going forward?

As the state's ten-year life science initiative comes to an end, we find ourselves at a crossroad. We will focus on the challenges moving forward, of which our number one priority is workforce development to fill the constant opening of biotech positions; we are confident that the next rendition of a state life sciences initiative is going to help in that area. We look forward to focusing more on convergence. Many entrepreneurs and established companies are focusing on combination products and companion diagnostics, and we are seeing a huge pipeline of companies created in this space. Moving forward, MassBio will be focusing on these new companies that are going to truly revolutionize healthcare and the life sciences industry.

Our objective is to stay ahead of the curve and continue to invent breakthrough therapies and treatments that change the course of disease and healthcare. We are not competing with other states; it is our responsibility to work together and get better at what we do collectively. Doing this will help make drugs more affordable because they will be less expensive to invent. The source of the treatment and cure is unimportant: our focus is on the result and the patient.

Massachusetts

Massachusetts' Life Sciences Ecosystem



500+

Companies in the Biopharmaceutical Industry

1645

The Number of Investigational Drugs Currently Researched in MA

#1

Harvard University is the Top University Based on Shanghai Ranking

5,506

The Number of Products Have Been Developed at MA-headquarted Companies

$2,573 Billion

NIH Funding in 2016

13,000+

Total Direct, Indirect & Induced Jobs

$147,432

Avarage Salary

63,026

The Number of employed in biopharma industry

$2.1 Billion

Venture Investment

13

The Number of IPOs from MA-headquarted Companies in 2015 Reference

Drug Affordability

Drug makers are "getting away with murder" said President Trump in his first press-conference as President-elect, unsettling prospects of a favorable industry partnership with a condemnation of high drug prices that laid blame on pharmaceutical companies, sending share prices tumbling for a short period.

Trump's comments follow on the tail of controversy, widely covered in mainstream media, over the price hikes of Mylan's EpiPen and Turing Pharmaceuticals' Aids drug. Price increases have long been the norm in the industry, but companies have now been forced to defend and justify drug costs, which are broadly misunderstood by the general public, and even by politicians. Whilst the blame is widely placed on the drug makers themselves, the wholesalers, insurance companies and pharmacy benefit managers (PBMs) have also come under a great deal of fire.

Allergan recently announced a social contract to limit annual list price increases to below 10%, pledging to make its medicines more affordable and accessible to a greater number of patients by increasing eligibility for more than 40 medications in its Patient Assistance Program (PAP). Through the PAP, Allergan now provides free medicines to eligible patients earning up to four times the Federal Poverty Level (FPL), and up to five times for certain complex medicines. "Based on data from the Kaiser Family Foundation almost 200 million Americans fall below those income levels, many of whom are uninsured or underinsured and may need our treatments," said Robert Stewart, Allergan's Chief Operating Officer. Generally, the key outcome of the drug price discussion thus far has been an increasing emphasis on drug price transparency, a complicated topic in the U.S. healthcare system due to the high number of components that make up the final price as quoted to the patient.

Gaining a realistic picture of spending on prescription medicines requires accounting for the significant rebates, discounts and distribution costs, amongst many other factors. Brand companies are not the only stakeholders when it comes to drug spending, with wholesalers, PBMs, pharmacies and the government being only a few of the others with a share. Furthermore, spending growth actually slowed in 2016, despite widespread claims of rapidly escalating medicine costs. "Companies want to be more transparent, and in this new era that includes POTUS tweets, many companies have dialed back annual price increases," stated Andrew Getz, partner, deal advisory at KPMG. "But the reality is that they are required to negotiate prices within the system that exists, complete with payers and PBMs. The real pricing premiums are generally much lower than the public and politicians believe."

If price pressures continue to increase in tandem with the cost of drug development, companies are likely to alter their drug selections based on time to market and speed at which investment is recouped once in the market.

Competition Breeds Cost Savings

Current rhetoric around increasing drug affordability and generally lowering drug prices will not only affect branded drug companies, but will impact the interplay between the branded and generic markets. "With the swirling healthcare dynamic of cost control at the healthcare policy level, generics are flourishing because those companies are looking to capitalize on launching products in the market," commented Andrew Getz.

The 1984 Drug Price Competition and Patent Term Restoration Act, otherwise called Hatch-Waxman, provides the current framework for balance between stimulating generic competition and supporting incentives for the development of new branded medicines. The balance is incredibly important as

Image courtesy of Piramal

tipping the scales in either direction would result in a lack of more affordable alternatives on the one hand, or a lack of new medicines and scientific breakthroughs on the other.

According to the Association for Accessible Medicine (AAM), nearly nine out of 10 prescriptions out of the 12 million taken each day is a generic. In 2016, 3.8 billion of the total 4.2 billion prescriptions dispensed were generic. Meanwhile, these generics account for only 27% of the amount spent on prescriptions, apparently saving the health

> “The key focus should be transparency amongst the insurance companies, the payers. Nobody understands how much the Pharmacy Benefit Managers (PBMs) are making on the backside, and yet they control everything and receive a significant rebate on reimbursements. Whilst only managing the benefit, they make more than any pharmacy that we service, also receiving money from the manufacturers to make sure their product is on the formulary versus another product; this is what they call a slotting allowance. They do not have the bricks and the mortar, the six years of education or the expense of keeping the product on the shelf. They do not have the liability. And yet, they are making a great deal more than our pharmacies.”
>
> - Larry Doud,
> CEO,
> Rochester Drug Cooperative (RDC)

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Today, generics are supplying 90% of the nation's prescription drug demand while consuming only 27% of the prescription drug spend. It is not even debatable—generics drive savings, not cost... Brand drugs are sold in a high-margin monopoly market and typically increase in price year on year. Generic drugs are sold in a highly competitive, low-margin commodity market and typically decrease in price year on year.

- Chip Davis, President and CEO, AAM

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care system $240 billion annually. The AAM, previously the Generic Pharmaceutical Association (GPhA), is the key national representative body for the generic industry. The association rebranded in February 2016 to better represent its member base. State-specific associations also play an active role in their industries, promoting networking and collaboration, as well as advocating at a state policy and national level.

With interest at the healthcare policy level to control costs, generic drug approvals may increase, creating more competition. When coupled with pricing pressures, this may result in further consolidation in the generic sector to increase scale.

Biosimilars pose another challenge; although not themselves innovative by definition, they are inherently high value. With four FDA-approved biosimilars, two of which have entered the market, and another 64 enrolled in the FDA's biosimilar product development program, the biosimilars market is beginning to come to life. “Congressional reauthorization of the biosimilar user fee program later this year will boost funding for the biosimilars program through fiscal year 2022, and will help hasten the pace of biosimilar approvals,” commented Davis. AAM established the Biosimilars Council in April 2015, which works to ensure a positive regulatory, reimbursement, political and policy environment for the biosimilars industry. This includes providing education about the safety and effectiveness of biosimilars, advocating for policies that facilitate access to biosimilars and defending against initiatives that would slow biosimilar development and approval or dampen the use of biosimilars throughout the health system.

While it is undebatable that generics and biosimilars drive cost savings, it will be essential for policy makers not to lose sight of the necessity to maintain innovation incentives, especially as development costs continue to rise. Reimbursement for drugs is always a debate; a pill reaching a consumer might have cost as little as five cents to make, but the first pill and the entire enabling process cost upwards of $2 billion. “The debate over the costs of pharmaceuticals is a big challenge,” commented Bob Coughlin, president and CEO at MassBio. “In Massachusetts, we are not creating generic or ‘me-too’ drugs; we are trying to invent breakthrough therapies that add value to the healthcare system, improve the lives of patients and change the course of disease, if not end disease. Whilst these therapies cost a lot of money upfront, they will also save a huge amount of money in the long run through reduced hospitalizations and reduced surgeries, for example.”

Whilst a focus on accessibility and affordability is commendable, the drive should come in tandem with a push for a supportive innovation framework with adequate incentives. An industry that favors cheaper alternatives and fails to support an effective framework for reimbursement of drug development costs for branded companies will limit innovation and restrict improvement of treatments and the discovery of cures.

Value-Based Pricing

Payers, insurers and hospitals are increasingly favoring contract models in which fees depend upon a product's success based on measurable outcomes, as opposed to the current approach of fee-for-service. The trend reflects the general drive within the health care system to improve patient outcomes while lowering cost and increasing access to affordable care. Payers often play on competition between relatively undifferentiated therapies to obtain discounts; value-based contracting is one way to draw differentiation.

U.S.-based insurers such as Aetna, Cigna, Humana and Harvard Pilgrim have all begun to pursue this model, including some of the following examples: Cigna with Sano, Regeneron and Amgen in May 2016 for cholesterol lowering drugs, with discounts agreed if cholesterol reduction is insufficient following therapy; Harvard Pilgrim Health Care with Amgen's PCSK9 therapy Repatha in November 2015, with rebates agreed if patients do not hit pre-specified cholesterol targets; Eli Lilly's diabetes drug Trulicity in 2016; Amgen's Enbrel in 2017; and with Cigna and Aetna with Novartis' Entresto drug.

Value-based contracts may necessitate pharmaceutical and biopharmaceutical companies refining their value propositions: a large shift in value-based pricing may demand greater product advocacy or a competitive advantage. In light of potential additional requirements to demonstrate the value of drugs to be brought to market for specific therapies, companies may form different decisions regarding which drugs to pursue. —

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We have innovated far beyond what the current payer system can absorb in our country. This has led to robust debate about how treatment and cures should be paid for in the future. There is legislation in Massachusetts that tries to define transparency of drug pricing, and MassBio is part of groups that are looking at value-based contracting so that when these future therapies are approved, there is a plan in place to pay for them and make sure patients have access to them. The industry must find a solution and put it forward nationally so that our federal government can build a healthcare system that will enable us to bring cures to patients.

- Bob Coughlin, President & CEO, MassBio

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Trump's Push for Direct Medicare Drug Price Negotiations Addresses Only One Piece of the Industry's Drug Pricing Puzzle

By Jamie Kendall, Brad Welsh and Alexandra Schulz
The Kendall Law Firm PC

Currently, the life sciences industry is facing more uncertainty than at any other time in recent memory. With the beginning of the President Donald J. Trump ("Trump") era upon us, the industry waits day-to-day for new legislation and its potential impacts. The uncertainty began on January 30, 2017, when Trump set the stage to reduce regulatory oversight in an Executive Order mandating that for every new federal regulation adopted, two existing ones must be eliminated. The very next day, Trump told pharmaceutical industry leaders gathered in the White House that his administration would reduce taxes, regulations and the time it takes for product approval, but in turn they must lower drug prices and bring manufacturing jobs back to the United States.

In March 2017, Trump chose Scott Gottlieb to run the FDA as Commissioner. Gottlieb, someone who is closely tied to the pharmaceutical industry, has a history of calling for faster approvals, greater regulatory transparency and a realignment of the balance of power between the FDA and doctors. It appears that the Trump administration expects Gottlieb to address several industry issues that align with Trump's viewpoints including speeding up the FDA's drug approval process, shaping the future of clinical trial requirements, terminal patient access to investigational drugs, the FDA's control over off-label uses, and drug pricing/drug importation. While all issues are important to industry, the most closely watched issue in the short term with potential long term effects relates to drug pricing.

Drug Pricing

Unlike in many parts of the world where governments control prices, in the United States drugmakers may set their price at any amount the market will bear. This market price is then whittled down through various pricing methods whereby different payors pay different prices for the same drug. This system creates a complex and dynamic environment for policymakers to navigate while attempting to regulate and curtail high drug prices.

Trump is a strong advocate for one policy proposition in particular – enabling the government to directly negotiate the cost of drugs reimbursed by the Medicare program. Current U.S. law prohibits the government from negotiating the prices its Medicare Part D prescription drug plan recipients pay. Instead, third parties, mainly commercial insurers and pharmacy benefit managers (PBMs), negotiate on behalf of the government.

Rather than lower drug prices, it is argued that this system raises them. Conceptually, this system is supposed to drive down the cost of drug prices by creating competition in the market place as PBMs compete against each other for eligible Medicare enrollees. However, an understanding of the PBM business model illustrates how PBMs may not actually prefer lower prices; PBM contracting practices generally provide that PBMs receive service fees for administration of the plans which are a set percentage of the drug's price. What this means is that higher drug prices actually increase the revenue stream of PBMs.

If government is given the ability to directly negotiate drug prices, it is true that Medicare's large share of the marketplace will likely incentivize pharmaceutical companies to lower drug prices for Medicare Part D prescription drug plans. However, lower drug prices for Medicare prescription drug plans do not necessarily equate to lower drug prices universally; 70% of the marketplace will not receive such discounts and will still be negotiated under separate payor systems (most likely through PBMs). In fact, it is probable that the market will adjust itself to account for the lower prices Medicare prescription drug plans will receive. By way of analogy, under the current system Medicaid programs receive statutory minimum discounts and they must receive the lowest and "best price" offered on a specific drug. Pharmaceutical companies understand this mechanism and employ sophisticated price modeling when developing a drug's price. This modeling allows for prices to be set to maximize profits; when drugmakers know that a large percentage discount will be required for certain payors, they can simply adjust the offering price upwards to all payors and achieve the same net profits. If Medicare prices are drastically lowered through government direct negotiations, pharmaceutical companies will again seek to recover this loss through higher prices for other payors.

One solution to this issue is to propose regulations that are applicable universally throughout all payors. One means to achieve this is through government pricing regulations similar to those in place for commodities. A similar pricing structure for drug prices may eliminate the complications that arise under the current payor system.

Image courtesy of Genomind

NAVIGATING THE **REGULATORY FRAMEWORK**

"The FDA's presence in India and China has greatly increased and seemingly every month a major player gets knocked out with a warning letter or import alert. This can have huge repercussions throughout the supply chain, with manufacturers in the United States experiencing drug shortages, and so on."

- Melissa Authelet,
Director, Regulatory and Compliance,
Rochem

Navigating the Regulatory Framework

Balancing Regulations, Safeguards and Incentives

The FDA continues to set the gold standard globally, governing the U.S. industry and responsible for approvals for any international company with interests in the U.S. market. Providing the benchmark for quality, its Center for Drug Evaluation and Research (CDER) regulates over-the-counter and prescription drugs, including biological therapeutics and generics, with the aim of enabling availability of safe and effective drugs.

Drug Approvals

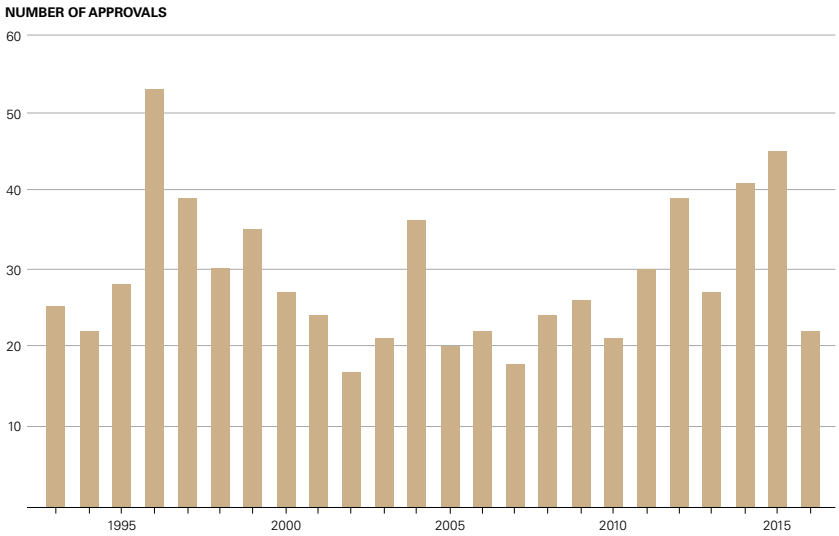
With Rob Califf leaving his FDA position in January, Scott Gottlieb has taken over as the new commissioner. Widely considered a positive choice, Gottlieb is an advocate for faster, more flexible drug approvals. Changes to the drug approval process, especially related to efficiency, are welcomed by the industry. The FDA cleared only 22 new medicines in 2016, a huge step down from 2015's 45 approvals and the lowest number in six years. Generic drug approvals were also down. "As an industry, there has been a drive for the FDA to really streamline and clear up the backlog of ANDAs, of which there are more than 3,000 still unapproved," said Alok Sonig, executive vice president at Dr. Reddy's Laboratories, the Indian generics company. "It is still critical for us to focus on reducing the cost burden by accelerating competitive generic entries vs. slowing them down through tariffs or other forms of blockage. Any disruption can create challenges for the industry's ability to produce new generic high-end equivalents at competitive prices."

Beyond resource challenges within the FDA, increasing hurdles within the approval process and rising development costs disrupting development, another impacting factor has been that a number of applications were turned down due to problems at the prospective manufacturing facilities. 2016 was a record year for complete response letters being issued. "The FDA will not approve a drug if the factory is not in order," explained Ira Loss, executive vice president at Washington Analysis. Instances such as these can be hugely disruptive to drug development and hinder patient access to important new drugs. As proclaimed by Loss: "This is equivalent to showing up to an automobile race with a flat tire. Those are inexcusable reasons for not getting out of the starting box."

Whilst safety is the primary concern, streamlining and accelerating approval processes would be hugely beneficial to the industry. Currently, as the cost of drug development rises, long approval timelines result in limited patent life once commer-

U.S. FDA DRUG APROVALS

Source: U.S. Food and Drug Administration



cialized and greater challenges in return on investment. The industry may be focused on helping patients, but it is also an incredibly high-risk business with a large number of failures and currently limited time to recoup expenses in the market. Investment is, however, hugely important and needs to be incentivized. Operating in a country with one of the highest net corporate income tax rates in the world, rigorous defense of intellectual property and accelerated approval processes are a necessity.

Some companies and R&D groups are looking increasingly into treatments and cures for rare diseases with very specific patient populations, registering under designations such as orphan drug to take advantage of expedited review so the drug can be brought to market faster. Orphan drug designation can grant seven extra years of exclusivity, in addition to the standard five years under Hatch-Waxman. There is also the 505(b)(2) mechanism, which allows companies with re-formulated compounds to forego pre-clinical and Phase 1 trials.

Intellectual Property and Exclusivity: Timelines and Patent Life

The United States is well regarded for its innovation, for which its favorable intellectual property (IP) laws form an essential support. Underpinning discovery of new medicines and development of treatments, innovation must be protected from competition to increase incentives.

Prolonging exclusivity increases incentive by extending timelines for reimbursement and profit before copycat drugs enter the market. According to PhRMA, IP-intensive industries in the United States accounted for 83% of annual R&D spending across all U.S. manufacturing industries between 2000 and 2010, with R&D investment growing by 53% compared to 34% for non-IP-intensive industries. Within the IP-intensive industries, the pharmaceutical manufacturing industry outperformed all others, accounting for 27% of all R&D investment.

The Drug Price Competition and Patent Term Restoration Act, passed in 1984, is a U.S. federal law enabling generic manufacturers to forego a second clinical study program or risk liability for patent infringement. Informally known as the Hatch-Waxman Act after its sponsoring representative and senator, the Act provides a supportive framework to the generics industry and the resultant competition to their brand counterparts. By abbreviating and alleviating some of the financial pressure of the FDA approval process, the generics market has grown to account for nine out of 10 prescriptions dispensed in the United States.

Even within the boundaries of the Hatch-Waxman framework, the industry has seen an increasing trend for post-grant proceedings, such as post-grant review (PGR) and inter partes review (IPR) processes at the patent office. By making minor changes to a product and pursuing new patents, brand companies prohibit their generic-producing competitors from market entry. Taking place outside of the court system, IPRs are an alternative to litigation and, as such, are more efficient. The process allows generic and biosimilar manufacturers to challenge new patents and, if the innovation is deemed too tenuous at the U.S. Patent and Trademark Office (USPTO) to warrant additional patent protection, the patent will be invalidated.

"Specifically, with respect to pharmaceutical IPRs, when it comes to formulation and compound patents, it has been observed that compound patents tend to be invalidated less than formulation patents," commented Vishal Gupta, partner at Steptoe and Johnson, a 600-attorney international law firm specializing across all areas of IP. "Looking forward, in addition to IPRs we will see the PGR area grow in the life science space," he added.

Generic and biosimilar manufacturers take the view that the IPR process expedites patient access to more affordable drugs. According to the Association for Accessible Medicines (AAM), previously the Generic Pharmaceutical Association (GPhA), exempting pharmaceuticals from the IPR process could add around $1.3 billion in increased government spending on medicines. The association claims that the IPR process works in favor of patient access by promoting generic and biosimilar competition.

However, a key challenge is that this opens up the landscape to the entire industry; not just for the two companies involved. Equally, decisions reached in IPR can still be challenged by the original patent holder.

Patrolling Borders

Companies overseas exporting products into the United States will be very familiar with the FDA, which has long monitored all drugs entering the U.S. market tracing back to the 1848 Drug Importation Act. However, as the FDA increasingly crosses over the U.S. border, ramping up inspections of overseas facilities to ensure that the highest quality requirements are met, some companies may find their ties to the United States quickly severed.

The FDA continues to crack down on compliance at facilities to ensure good manufacturing practice (GMP) requirements are met, with an increase in presence and 'zero-notice' inspections at Asia-based facilities in particular. Although potentially disruptive, greater focus on compliance is highly valued in an industry in which quality and safety are of utmost importance. "As the FDA and other regulatory agencies continue to push back more and more, we have seen a trend with the FDA being very hard in Asia," related Anil Kripalani, president at Ash Ingredients. "In 2016, 14 warning letters were issued to manufacturers in China (44 worldwide). In 2017, between January and March, it has been 6 in China (17 worldwide). When we started, the supply chain was not so closely scrutinized. We welcome the increasing scrutiny as it has given us an advantage over our competitors as we have taken proactive steps to be in compliance."

Ash Ingredients, based in New Jersey, specializes in the manufacturing, sourcing and development of advanced intermediaries and fine chemicals. In conjunction with Longchem Chemical Co., based in China, the company forms half of Ash Longchem. Increased inspections, warning letters and import alerts across the board are however taking their toll on the market. "The FDA's presence in India and China has greatly increased and seemingly every month a major player gets knocked out with a warning letter or import alert," stated Melissa Authelet, director, regulatory and compliance at Rochem, a U.S.-based distributor focused on bringing Chinese products into the U.S. market. "This can have huge repercussions throughout the supply chain, with manufacturers in the United States experiencing drug shortages, and so on."

By being more stringent and ensuring adherence to the same quality standards and regulations the FDA continues to protect patients by barring low-quality and potentially harmful products from the U.S. market.

Harmonizing the Global Framework

With increasingly globalized supply chains and companies expanding their geographical footprints the differences in regulation between markets pose a challenge for many companies.

Speaking from the perspective of a manufacturer, Kristin Brancato, vice president and general manager at Cyalume Specialty Products, asserted: "We may characterize the period that lies behind us as one of a "double standard" of regulatory requirements for the manufacture of API's: the level demanded by the U.S. FDA and that required by the rest of the world. Fierce competition on one hand, coupled with the very strict limitations imposed by regulatory requirements in only some parts of the market have been the source of numerous dilemmas for the API industry. The fact that FDA compliance and high manufacturing costs go hand-in-hand has made it extremely difficult for manufacturers to supply the entire global market and at the same time maintain competitiveness."

Whilst the most pronounced disparities are between the U.S. market and less-regulated ones, there are also some key differences between the U.S. and European framework which are now being addressed. For example, the FDA and EMA agreed in March 2017 to recognize each other's audit reports through a reciprocal agreement. Previously, companies in Europe were required to audit suppliers every two to three years after inspection by the regulatory authority, whereas in the United States, the product can be received with impunity once the producer has been passed by the FDA. The result will likely be fewer inspections and greater cohesion and efficiency. The general trend is towards increased global alignment. —

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Another big difference is that European companies have a qualified person (QP), who releases the product from the factory to the general public on behalf of the marketing authorization holder. That QP has special recognized qualifications and is personally responsible for releasing the batch. This is the lynch pin of the safety of the consumer, because it focuses the QP completely and increases accountability. There is an equivalent mechanism in the United States, but there is no designated individual to take responsibility; each company may select and allocate a person with this responsibility.

- Rino Coladangelo,
CEO,
Rephine

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Jamie Kendall

A specialist life science consulting company offering compliance and regulatory solutions.

Founder and Principal
KENDALL LIFE SCIENCES LLC

Could you give a brief introduction to Kendall Life Sciences and the Kendall Law Firm?

Kendall Life Sciences started from a decision to start a compliance consulting practice group that offers cost-effective services to small- to mid-sized life sciences companies across various pre- and post-launch commercialization phases. Early in its launch, clients would repeatedly ask the former practicing attorneys to act as their lawyers. As a result of the demand, and what we felt to be a void in the legal industry regarding a focused life sciences legal practice, the Kendall Law Firm was established. Navigating through the life sciences industry requires experience and an extensive understanding of how the industry operates as a whole. We have that.

How is the drive towards lower drug prices likely to affect the industry?

Similar to the U.S. tax system, the entire industry pricing arena will likely face changes as the new Administration has made it clear that a top priority is to enact industry "competitive bidding" for drugs. What this means or how that "bidding" process will be enacted is yet to be seen but it does raise industry concerns between brand versus generic competition and direct brand versus brand competition. Competitive bidding requires interchangeable medications which is not always possible.

Many states are introducing legislation focused on transparency. How do you see the situation playing out over the next year or so?

Once again, the views and policies of the new Administration will be a main challenge to state transparency drug pricing initiatives. By statute, Federal government healthcare programs, such as Medicare, are required to receive the best price on a drug. It's unclear at this time how the state drug pricing transparency mandates will affect the best price statutory requirements and in turn how the Administration views such initiatives.

In addition, in U.S. hospitals, all drugs must be on an approved formulary list in order to be prescribed at the hospital. Since hospitals have their own committees selecting the prescriptions to be included on such lists, it will be interesting to see how the state drug pricing transparency initiatives affect such selections and if the hospitals will be beholden to follow the individual states' transparency initiatives.

What are the objectives of both Kendall Life Sciences and Kendall Law Firm over the next few years?

We will continue to learn our clients' business from the ground up, quickly and efficiently, and ensure that they are set up for long-term success. To add value as a counsellor at law, it is essential to remain apprised of the ever-changing industry laws, pending legislation, known government investigations, political industry influences and the like. Clients also benefit from our knowledge of how life sciences companies operate both nationally and internationally, and laws and regulations related to each.

We prioritize and provide recommendations as to what a company should do now, in six months, in 12 months, and so on. Being able to see the larger picture, project, and work with a company to prioritize compliance and regulatory need(s) is an approach that a lot of other consulting groups do not take.

Manu Goel

Senior Vice President
GENPACT

Genpact provides business process management services to the life science industry

2017 marks Genpact's 20th anniversary. How has the company developed over the last two decades?

Genpact started as a 100% owned subsidiary of GE providing end to end business process management services in 1997. After successful expansion as a GE subsidiary, we were commercialized and spun off as an independent entity in 2005. One of our first non-GE clients was a Tier 1 Life Sciences company headquartered in UK.. Over the next few years, we expanded our understanding as well as presence within the Life Sciences industry and became a significant and a relevant partner to Tier 1 pharma organizations. We demonstrated expertise and delivered services in multiple business processes, key ones being finance and accounting, sourcing and procurement and commercial reporting and analytics.

About five years ago, we reviewed our business strategy and decided to go 'narrow and deep' with our focus on nine key industries, of which life sciences was one. In our attempt to become more 'relevant' for our clients, we also expanded our footprint into core industry oriented services for those selected industries. For Life Sciences, we identified three main service areas within core operations: multi-channel customer experience, contract management and regulatory affairs. In deciding the priority of service portfolio, we kept the following in consideration: ability to make a difference through use of lean and six sigma, our ability to analyze underlying data and challenge the status quo, and drive outcome improvement for our clients. We have used a combination of 'build and scale' as well as 'buy and integrate' to mature our service footprint in the chosen core operations areas.

Could you elaborate on Genpact's 'Lean Digital' approach?

Two years ago, we embarked on an innovation roadmap, enabled by our 'Lean Digital' approach, to further our transformation agenda for our clients. With the advent of various digital technologies, customer expectations surpassing anything that had been delivered to date as well as agility needed to thrive in the evolving and ever volatile business environment, we developed our proprietary approach to drive innovation for our clients within the industries that we operate in. Lean Digital brings together 4 key components: Design thinking to re-imagine end to end business processes across front-middle-back office to align to customer expectations, Lean principles to drive agility, embedded digital technologies, and holistic industry and domain knowledge. Genpact being the largest sandbox for business processes, we are in the best position to enable this transformation for our clients.

How have client priorities changed over time, particularly with regard to adopting new technology?

Whilst life sciences is all about innovation and finding the next drug to improve patient health outcomes, majority of their investments, rightfully so, go into drug discovery rather than business processes. The industry is very risk averse and compliance is top of mind for everyone. As they have emerged from the patent cliff and on an upswing path with regards to NME approvals, the functional teams face huge demands for cost effective business partnering. They are looking for superior quality of service aligned to meet their customer expectations.

The market evolution is immense, and whilst cost optimization is still key, the discussion these days is all around improving outcomes, better effectiveness, variable capacity and agile innovation. Our focus is on end to end customer experience, while improving efficiency and effectiveness. We are able to make the most difference to our clients when we partner with them on their strategic agenda for their business.

What are some of the more innovative ways in which Genpact is supporting clients?

We are bringing our 'Lean Digital' approach to support clients in the Life Sciences industry across a breadth of business outcomes which range from reducing leakage in contract management to improving compliance in pharmacovigilance to predictive analytics in improving product sales performance. A great example is our PVAI Software as a Service offering for automating AE Processing through the application of Natural Language Processing, Machine Learning, and Process Automation technologies. PVAI will revolutionize Pharmacovigilance by establishing a highly scalable and sustainable operating model that drives improved compliance, significant cost savings and unprecedented data quality, and insight.

Another area in which we have developed innovative solution is 'digital health'. We are working within the ecosystem of pharma companies, providers and patient, to utilize the patient interaction and engage in a proactive management of health. We have developed global solutions to be used by patients, dieticians and providers to streamline the patient lifecycle journey.

What is the outlook for Genpact's life sciences business?

Life sciences is an exciting space and one of the core growth engines of our organization We are proud to be able to partner with our clients in the journey to improve patient outcomes..

Image courtesy of Frontage

Keeping Up with Compliance

Regulatory affairs as an internal-company function encompasses a range of areas, but largely concerns the maintenance of already-approved drugs. Because filings vary slightly internationally and need to be harmonized at a global level to remain compliant, just keeping a license to sell, keeping it consistent and maintaining transparency is a huge task. These functions are likely to be increasingly outsourced to specialists rather than maintaining the internal infrastructure required to run individual transparency reporting systems and respond immediately to changes in guidance.

In the clinical trial space, companies such as TrialScope are offering services to manage data volumes related to compliance. Trialscope, based conveniently in Jersey City, offers its PharmaCM platform to take data from company's source systems and import it into an environment in which the data can be edited to the specific requirements for disclosure and then routed for approval. "Our system assists with data accuracy and pushes this information out to the registries," explained Thomas Wicks, chief strategy officer at TrialScope. "It is designed to assist with timelines and ensure compliance with the law. Our system can actually translate data from clinicaltrials.gov to fit the European requirements and vice versa. The software service is hosted by us, so customers do not have to develop their own solution."

TrialScope also recently launched ATLAS Global Compliance, which helps companies manage global disclosure compliance across different sites and markets.

Pricing transparency is also a topic under a great deal of discussion. PhRMA expects 15 to 20 states to have legislation in place for price transparency by the end of 2017. Drug pricing is extremely nuanced and, as drug development costs continue to rise, there is a larger sum for which to seek reimbursement once in the market. "With higher cost drugs, there is clearly more nuance in how those drugs and classes of drugs are being restricted by the evolving Payer/PBM market access policies, and companies have needed to develop more sophisticated market-access strategies in those classes, both from a competitive standpoint and how they communicate factors such as availability to physicians," said Gregory Haskins, senior vice president at MMIT. "In exacerbated disease states, for example, physicians have to know what is available for

Image courtesy of Mission Pharmacal

that patient at that particular time. Oncology is an area in which we are seeing a number of utilization management tools used, and traditional formularies are not at an indication level. The formulary does not always cleanly delineate between disease states, so it has been paired with a number of nuanced policies at a payer-to-payer, channel-to-channel level. Manufacturers have therefore had to revisit their strategies on where they position themselves with the payer to get their drugs prescribed."

MMIT offers solutions across three market segments, trying to drive consistency in how payers, manufacturers and HCPs communicate and utilize market access information. The company is focused on market access and bringing transparency to market access everywhere across healthcare. In terms of market access, one way in which MMIT helps payers is in communicating therapeutic alternatives through its tools.

Equally challenging to navigate in the United States is the requirement for states to track all financial interactions involving physicians and teaching hospitals under the Sunshine Act. "Vermont has a total gift ban, for example, and some medical centers require sales reps to complete courses or have certain credentials before interfacing with its practitioners," commented John Oroho, executive vice president and chief strategy officer at Porzio Life Sciences. "In part, these restrictions stem from a drive by some states to set up road blocks and hurdles in an attempt to prevent pharmaceutical companies with branded products from interacting directly with physicians and other healthcare practitioners. Their thinking is that by reducing the interactions, they will lower the number of prescriptions written for branded pharmaceuticals, and increase the number of prescriptions written for the cheaper generics products."

Porzio Life Sciences, a subsidiary of law firm Porzio, Bromberg & Newman, specializes in state-specific regulations, tracking information and making it available to the industry. Porzio has developed online databases to which companies can subscribe, which track the laws, regulations and pending legislation across all 50 states.

As trends towards digitization continue, new technologies will hopefully drive a greater deal of harmonization both at state level and internationally. —

John Oroho

Executive Vice President and Chief Strategy Officer
PORZIO LIFE SCIENCES

Porzio Life Sciences helps companies to operationalize compliance with legal and regulatory requirements

Porzio Life Sciences was established in 2004 as a subsidiary of Porzio, Bromberg & Newman. What unmet market needs did Porzio Life Sciences address?
In 2002, Porzio, Bromberg & Newman, previously focused on product liability litigation in the pharmaceutical and medical device space, decided to diversify and launched Porzio Life Sciences at a time in which several trends were converging. Firstly, states were starting to become increasingly involved in regulating life science companies, imposing license requirements for the distribution of drugs and devices in their states. Secondly, the number of mid-level practitioners with the right to prescribe drugs and devices grew, whilst doctors became busier with patients and had less time to see pharmaceutical sales reps. When Porzio Life Sciences was first established, law firms were mostly focused on FDA and Congress and the framework at a national level. Porzio Life Sciences cut its niche in catering to state-specific regulations, tracking this information and making it available to the industry.

In what ways does Porzio Life Sciences serve the industry?
We developed online databases to which companies could subscribe, in which we would track the laws, regulations and pending legislation across all 50 states to show how to sell, market and distribute products in every state, and indicate who had prescriptive authority for various products, and so on. Before long, we became specialists at a state level and a point of reference for other firms.
Today, we carry out a lot of work in compliance monitoring and auditing, but are probably best known for how to operationalize compliance with legal and regulatory requirements.

What are the main challenges companies face at a state level?
Possibly the greatest challenges faced by companies are the state restrictions on interactions employees can have with physicians and hospitals; this is one of the big areas we are involved in. Vermont has a total gift ban, for example, and some medical centers require sales reps to complete courses or have certain credentials before interfacing with its practitioners. In part, these restrictions stem from a drive by some states to set up road blocks and hurdles in an attempt to prevent pharmaceutical companies with branded products from interacting directly with physicians and other healthcare practitioners. Their thinking is that by reducing the interactions, they will lower the number of prescriptions written for branded pharmaceuticals, and increase the number of prescriptions written for the cheaper generics products.

In December 2015, legislation was passed in New Jersey to forego the requirement for companies to have FDA approval prior to granting a license. What is the importance of this legislation to the industry?
At some point, the head of New Jersey's licensing program decided that in order to be licensed in New Jersey, a company was required to have an already-FDA-approved product. This would generally also mean that biotech companies would be unable to get a license in any other state. With the short patent life of drugs and devices following approval, and companies likely having to delay launches because they are unable to get a license to distribute the product, this could have killed New Jersey's biotech industry. Porzio Life Sciences and Porzio Governmental Services were the impetus behind the new legislation, and helped to shepherd it through.

Several states have introduced bills and legislation relating to price transparency. How will an increasing emphasis on transparency impact the industry?
Today, the cost to bring a drug to market is north of $2 billion. We have even seen a concentration from President Trump's administration on drug pricing, and PhRMA expects about 15 to 20 states this year to have legislation for pricing transparency. This could have a big impact on areas that companies pursue. Companies will avoid putting significant dollars into more expensive therapeutic areas if they cannot get a certain return on investment. Pricing transparency legislation may also impact where companies choose to sell and market a drug. Just as companies in Europe do not necessarily receive or seek approval in every country, likewise the market in the U.S. could become much more fragmented by state.

What are the next steps for Porzio Life Sciences?
Transparency will drive our growth. The more regulated the industry becomes, the more need there will be for our services to help companies understand how to do business within different frameworks. We can assist companies with distribution and entering new markets, and are also able to help companies develop methodologies to report pricing in different states and countries.

Image courtesy of Rutgers

THE "MEDICINE CHEST OF THE WORLD": FOCUS ON THE EAST COAST AND SURROUNDING ECOSYSTEM

"New Jersey is proud to be developing a strong business in biosimilars, in addition to the significant presence of a biopharmaceutical branded and generics industry. The composition of New Jersey's industry reflects the entire spectrum of companies and support organizations".

- Debbie Hart,
President and CEO,
BioNJ

The "Medicine Chest of the World": Focus on the East Coast and Surrounding Ecosystem

Introducing the Medicine Chest of the World

Ever since Johnson & Johnson set up shop in New Brunswick in 1886, New Jersey and its life science industry have grown hand-in-hand. The state has long held its reputation as the "Medicine Chest of the World", and today is home to 14 of the world's 20 largest pharmaceutical, medical technology and diagnostics companies. Gracing the grounds of the Garden State are, amongst others, Bristol-Myers Squibb, Merck, Novartis, Pfizer, Sanofi, Novo Nordisk, Bayer Healthcare, Daiichi Sankyo, and of course Johnson and Johnson.

As the industry continues to generate huge economic impact, the state government and associations maintain a supportive framework through which the industry can continue to thrive. Although Massachusetts carries the torch for biotech, followed by California, New Jersey's incentives for small companies and startups have also attracted a number of biotechnology companies; more than 400 were recorded as operating in the state in 2016.

New Jersey's favorable geographic location, over 30 public and private universities including Princeton University and Rutgers University and strong talent pool all contribute to the favorable view taken by companies operating there. According to the New Jersey Economic Development Authority, the state boasts the highest concentration of scientists and engineers anywhere in the world, at around 225,000 per square mile.

The Keystone State

Moving down the East Coast, Pennsylvania also demonstrates a diverse ecosystem, from prominent, well-established companies down to emerging biotech startups. Growing alongside familiar names such as those of generic giants Teva and Mylan is a community of contract research organizations (CROs) and two of the top five institutions funded by the National Institute of Health (NIH)–the University of Pennsylvania is number four and the University of Pittsburgh is number five.

"Pennsylvania is very unique among the states – we have all the ingredients to make a life sciences company successful," said Chris Molineaux, president and CEO at Life Sciences Pennsylvania. "The cost of living in and around Philadelphia is dramatically lower than areas such as New York, Boston, San Francisco and Washington D.C. We also sit equidistant from the financial markets of New York and the regulatory agencies in Washington D.C. and Maryland, at only an hour-and-a-half train ride. State-wide, there are over 77,000 people working directly in life sciences. There is a job multiplier effect of about five to six jobs outside the industry in the way of service providers. In Philadelphia alone, one out of every six jobs is in life sciences or healthcare."

Previously Pennsylvania Bio, the association rebranded in 2016 to Life Sciences Pennsylvania so as to better represent the growing PA life science industry and the increasing diversity of its members.

The main challenges faced by the state are its visibility alongside other states as an investment destination and its tax climate– Pennsylvania's corporate net income (CNI) tax is one of the highest in the country, second only to Iowa. Nevertheless, companies continue to be attracted to the state, taking advantage of opportunities presented and services offered by the surrounding industry.

Innovation Incentives: Fostering an Ecosystem

Already ranking third for life science patents in the United States, New Jersey continues to focus on supporting innovation.

Particularly notable is New Jersey's Net Operating Loss (NOL) program, which is unique to the state. Officially called the Technology Business Tech Certificate Transfer program, the program allows companies not yet seeing financial return to sell their losses to for-profit companies. The for-profit companies use that credit to offset some of their profits, and in turn offer a certain percentage on each dollar bought. In addition, there is the Grow New Jersey program, centered around job creation in the state, and the state's angel investor programs also carry huge appeal.

Top 10 Company Profiles

REVENUE: $70 BILLION

Core areas of research:

Cardiovascular and metabolic, immunology.

REVENUE: $51.4 BILLION

Core areas of research:

Cardiology, hematology, women's healthcare, ophthalmology, radiology, oncology.

REVENUE: $49.4 BILLION

Core areas of research:

Cardio and metabolic, ophthalmology, respiratory, neuroscience, oncology, immunology, cell and gene therapy.

REVENUE: $48.9 BILLION

Core areas of research:

Diabetes and cardiovascular, oncology, immunology, rare diseases, neurology, skin diseases.

REVENUE: $48.1 BILLION

Core areas of research:

Oncology, neuroscience, infectious diseases, haematology, immunology, ophthalmology, respiratory.

REVENUE: $39.5 BILLION

Core areas of research:

Cardiovascular disease, respiratory disease, oncology, neuroscience, infectious diseases, immunology and women's health.

REVENUE: $34.5 BILLION

Core areas of research:

Diabetes and cardiovascular, multiple sclerosis, oncology, immunology, rare diseases.

REVENUE: $32.6 BILLION

Core areas of research:

HIV/Aids, cardiovascular, oncology, respiratory, liver diseases.

REVENUE: $24.7 BILLION

Core areas of research:

Cardiovascular and metabolic, oncology, respiratory, inflammation and autoimmunity, neuroscience.

REVENUE: $23.92 BILLION

Core areas of research:

Respiratory, HIV and infectious diseases, oncology, immuno-inflammation and rare diseases.

"251 applications were approved through New Jersey's Angel Investor Tax Credit Program in 2016, representing the injection of more than $96 million in private capital into technology and life sciences companies in the state," commented Melissa Orsen, CEO of the New Jersey Economic Development Authority. "Interestingly, a little under 40% of investors within the angel investor program were actually from New Jersey, showing a larger percentage investing into the state from the rest of the United States and from abroad."

New Jersey is also home to the largest incubator; the Commercialization Center for Innovation Technologies (CCIT). Established in 2002, CCIT's tenants have so far generated more than $130 million in revenue, and graduates include successful ventures into a variety of areas. Genewiz, a global leader in research and development genomics services, grew from a two-person operation at CCIT into a 700-person, internationally recognized operation headquartered in South Plainfield with 12 facilities at major biotech hubs around the world. Advaxis, Chromocell, Amicus Therapeutics, Agile Therapeutics and ContraVir are just some of the other notable companies that originated at this facility.

Industry associations such as BioNJ, the New Jersey arm of BIO, and the Healthcare Institute of New Jersey (HINJ) act both in support of individual companies and as industry advocates. BioNJ was recently involved in signing two initiatives into law: the establishment of the Biotechnology Task Force, and the establishment of a governmental entity to facilitate business and academic partnerships across the state. BioNJ will have a seat on both. "Working closely with policy makers in Washington and New Jersey, we will advocate for a policy environment that supports medical innovation and ensures faster treatments and cures for patients," stated Debbie Hart, president and CEO at BioNJ. "BioNJ is committed to the growth and prosperity of our industry and that patients have access to innovative medicines to improve and save their lives."

Pennsylvania has also started to attract a number of biotech companies. Some have emerged from research conducted at Pennsylvania's universities, most notably the University of Pennsylvania. Whilst the state has faced a budget deficit for the last few years, resulting in fewer policy changes, there are nevertheless a number of initiatives in place, such as Innovate in PA, which received $80 million of funding in 2015. In addition, there is the Research and Development Tax Credit with a pool of $55 million for companies to access, which can also be sold for credit or cash.

The Pennsylvania Biotechnology Center seeks to advance biotechnology in the region, part-funded by a grant from the Commonwealth of Pennsylvania, and home to the Hepatitis B Foundation and its research institute, the Baruch S. Blumberg Institute, as well as other research organizations.

> "New Jersey is in fact the only state that offers NOLs. I am on a committee called the Capital Formation Committee at BIO, and we are always trying to figure out ways for other states to pick up the program. For companies like ContraVir that only spend money, the program allows the sale of these losses to for-profit companies, often energy companies such as JCP&L and PSE&G. They use that credit to offset some of their profits, and they give us a certain percentage on each dollar we sell to them. For us in New Jersey, it is a terrific advantage."
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>
> - James Sapirstein, CEO, ContraVir

These life science hubs recognize the importance of not only supporting their existing companies, but attracting new market entrants. The industry is built on innovation, and innovation must be constantly fed into it to strengthen its foundations and sustain its growth. —

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Image courtesy of Genomind

THE INDUSTRY'S BACKBONE: RESEARCH AND DEVELOPMENT

"The pharmaceutical industry is under a great deal of pressure from investors to keep profitable, and in order to reduce expensive internal R&D resources companies have been increasingly outsourcing early stage research. Universities can benefit from this trend by partnering with pharmaceutical companies in these early research phases."

- Chris Molloy
Senior Vice President,
Office of Research and Economic Development,
RUTGERS UNIVERSITY

The Industry's Backbone: Research and Development

Paradigm Shift

When it comes to advancing medicine, the United States takes center stage, producing more than half of the world's new molecules in the last decade. One of the most R&D-intensive industries in the United States, the pharmaceutical sector is accountable for a huge portion of global innovation and new medicine, investing over $50 billion into R&D annually. Also extremely varied, the U.S. biopharmaceutical industry comprises large companies overseeing diverse development pipelines and their commercialization, all the way down to biotechnology startups, some with only one product in development. The source of innovation is also shifting, with academic institutions playing an increasing role and the number of biotechs on the rise.

There are more than 7,000 medicines in clinical development worldwide and, from 2000 to 2015, more than 550 new medicines were approved by the FDA. Through a deeper understanding of disease, coupled with novel technologies and approaches, the industry is moving towards more specialized treatments, stepping away from the blockbuster model that has long been the standard, and further towards the discovery of cures. Also notable is the greater focus on biologics rather than small molecule chemically synthesized drugs, since biologics have been proven to be more effective in treating the underlying cause of disease.

Oncology continues to be a key therapeutic area and treatments have come a long way, now becoming more targeted. Cancer death rates have declined 23% since peaking in the 1990s, with approximately 83% of survival gains attributable to new treatments, including medicines, according to PhRMA. Treatments for Hepatitis C have also advanced greatly, with cure rates upwards of 90% in as little as eight weeks with minimal side effects.

However, whilst science may be coming along in leaps and bounds, the financial framework is becoming harder to navigate and approval hurdles are becoming higher. The United States has one of the highest corporate tax rates in the world and reimbursement on the market is becoming increasingly difficult. This proves particularly problematic for the biotech startups from which a great deal of innovation is stemming.

The framework

Well reputed for its favorable intellectual property (IP) laws, the United States is the global epicenter for biopharmaceutical innovation and drug development. As the basis for innovation, and therefore the improvement and discovery of treatments and cures, IP protection is paramount as an incentive to innovate, protecting against competition.

Nevertheless, drug development costs are on the rise, the development and review process is long and can take over a decade, while reimbursement on the market is therefore becoming more of a challenge. Only 22 new molecular entities (NMEs) were approved by the FDA in 2016, compared to 45 in 2015.

With no revenue from the drug over this period and development costs often more than $2 billion, only two out of ten medicines generate returns exceeding average

The Price to Pay: Potential Impacts of Drug Price Pressure

R&D costs, and more than 90% of U.S. biopharmaceutical companies do not earn a profit. For an industry relying on innovation and the required investment, the stakes are incredibly high. Fewer than 12% of drugs entering clinical trials result in an approved medicine.

These challenges could greatly influence product pipelines as companies are likely to pursue more niche fields in which they can expect less competition and higher return. Certain FDA designations may be applied in particular circumstances to fast-track the approval process. For example, orphan drug designation is applicable when addressing treatable patient populations of fewer than 200,000 people in the United States, or where the treatment drug is not expected to recover the costs of its development and marketing.

A number of other designations have also been introduced to streamline approval pathways and reduce high market-entry barriers to enable drugs to reach patients. One example is the Qualified Infectious Disease Product (QIDP) designation. Infectious diseases are an extremely important area to keep addressing, as pathogens develop resistance to new antibiotics after about eight to ten years, after which point resistance grows exponentially. "There will never be an antibiotic that maintains complete efficacy forever," commented Marco Taglietti, CEO of Scynexis, a New Jersey-based company focused on an antifungal compound, SCY-078. "As a doctor, I believe that one day we will find a treatment for cancer, Alzheimer's disease, Parkinson's disease and many other afflictions, but there is a group of diseases which we will continue to fight forever, and these are infectious diseases. No matter the antibiotic, at a certain time the pathogens will become resistant. The first antibiotic was introduced 80 years ago. Back then, there was no resistance, and now we have burnt out so many antibiotics that there are less and less effective antibiotics on the market."

The last class of antifungals introduced was echinocandins in 2000, and about 3% to 5% of pathogens are resistant today.

Companies need access to external funding and, as the pool increases, so will competition for investment. Grants and other forms of financial support will be essential in fostering innovation and further scientific progress.

The United States is generally considered very attractive where innovation is concerned, particularly due to protective IP laws providing good incentives for R&D. On the flip-side, however, is the drive to lower drug prices, which could lower attractiveness and incentives for innovating and bringing new drugs to market.

PhRMA's recently launched GoBoldly campaign seeks to showcase the industry's cutting-edge research and advances, and goes some way to offsetting the recent somewhat negative portrayal in the media. Universities and research institutions continue to play an increasingly key role as larger companies outsource early-stage development, and the number of projects spun-out into commercial ventures is on the rise.

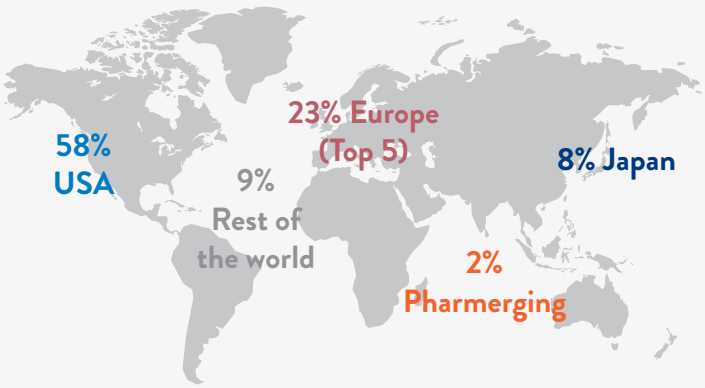
Beyond the immediate effect on companies' profits, lowering drug prices would greatly reduce incentives to innovate in an industry where the average drug costs upwards of $2 billion to develop and bring to market. The pharmaceutical industry is indeed one of the most R&D intensive in the United States, with annual investment of over $50 billion, and companies allocating between 15% to 20% of revenue to this area. As the backbone of the pharmaceutical and biotechnology industry, innovation needs to be supported and encouraged to drive these industries forward. Concerns had already been raised following a drop in drug approval rates in 2016 as the bar is pushed increasingly higher for approval and evidence of safety and efficacy. Following a shifting trend from mass-market drugs to those targeting smaller patient populations, whilst hurdles are rising, addressable market sizes are shrinking, and reimbursement once in the market is therefore more difficult even before considering the impacts of lowering drug prices.

"The industry needs to do something about pricing, plain and simple," asserted James Sapirstein, CEO at Contravir and chairman at BioNJ. "If the industry does not figure out a way to be more transparent, the government will. The system in the United States allows us to innovate, and reference pricing as seen in Europe and around the world would hinder our progress to helping people with hard-to-treat diseases. Patients might be in favor of reference pricing to lower drug costs, but removing the incentive for profit will kill invention. In countries such as Russia, prices might be low, but there is no innovation, and what is invented is not tested adequately enough to be safe."

A certain degree of support is required for companies to enable continued development and research into new areas, and whilst this is recognized at a state level, the industry would benefit from wider nationwide support. First and foremost, companies need adequate incentives and minimal barriers for projects to make commercial sense to support the various stages of drug discovery and development. The drive to make drugs more affordable is commendable, but should not come at the expense of the innovation that enables these treatments and cures in the first place.

Biopharmaceutical industry in the United States at a glance

GEOGRAPHICAL BREAKDOWN (BY MAIN MARKETS) OF SALES OF NEW MEDICINES LAUNCHED DURING THE PERIOD 2010–2015*



326 MILLION PEOPLE

Current Population of the United States of America

48 MILLION PEOPLE

Population Over 65

$1,49 TRILLION

Government Healthcare Expenditure

$1,3 TRILLION

Private Healthcare Expenditure

$70 BILLION

Generic Sales

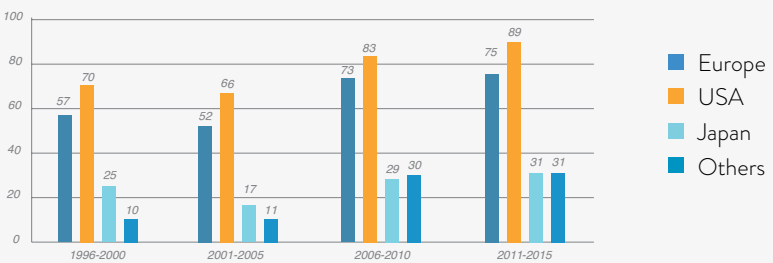
$244 BILLION

Patented Sales

$19 BILLION

OTC sales

NUMBER OF NEW CHEMICAL OR BIOLOGICAL ENTITIES (1996-2015)

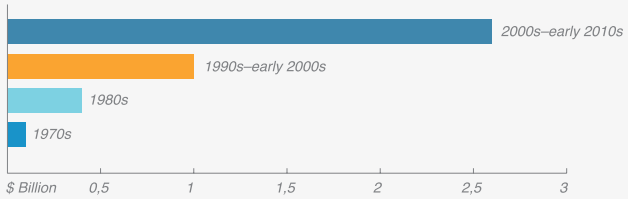


10 TO 15 YEARS

Average Time to Develop a Drug

AVERAGE COST TO DEVELOP A DRUG

(INCLUDING THE COST OF FAILURES)



854,000

Direct jobs (Innovative Biopharmaceutical Industry)

1,882,000

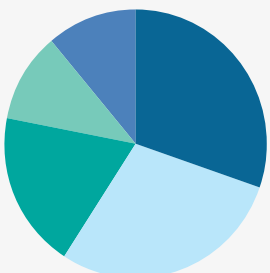
Induced Jobs (Additional Private Economic Activity)

1,710,000

Indirect Jobs (Vendors and Suppliers)

#1

Biopharmaceutical Sector Invests More in R&D Compared to Other Manufacturing Industries

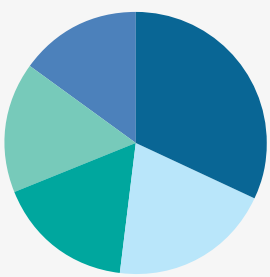


U.S.'S TOP FIVE SOURCES OF IMPORTS OF PHARMACEUTICALS (2015)

- Ireland: $15.2 billion
- Germany: $14.5 billion
- Switzerland: $9.4 billion
- Israel: $6 billion
- India: $6 billion

$11,8 BILLION

U.S. Pharmaceutical Industry R&D Spending Outside the U.S.



U.S.'S TOP FIVE EXPORT DESTINATIONS FOR PHARMACEUTICALS (2015)

- Belgium: $6.4 billion
- Netherlands: $4.2 billion
- Canada: $3.8 billion
- U.K: $3.7 billion
- Japan: $3.6 billion

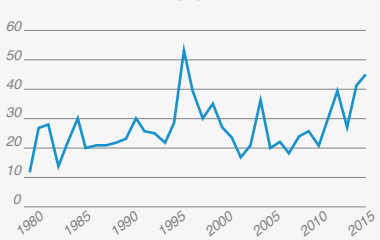
3500

Compounds Currently Being Studied in the United States

$47 BILLION

Volume of Biopharmaceutical Exports

MEDICINES APPROVED BY THE FDA'S CDER



Leading Research through Cross-Collaboration

Whilst larger companies continue to drive R&D programs and bring drugs to market, academic institutions and their off-shoots are playing an increasing role in innovation. Cross-collaboration between industry and academia is on the rise and larger pharma companies are increasingly outsourcing early-stage R&D, with many products of companies such as Johnson & Johnson, Merck and Bristol-Myers Squibb initially developed by biotech companies. Financing is a key challenge for companies lacking already-commercialized products in their portfolios and whilst the United States' appealing IP laws might offset potential deterrents such as high corporate tax rates, financial incentives and support are needed for these trends to continue. This has been better recognized at a state level, although there are some grants and initiatives nationwide. The 21st Century Cures Act, which became law in December 2016, also provides a large supplemental appropriation to the National Institutes of Health to enable more of its core research.

Universities such as Rutgers and Princeton are taking advantage of trends to outsource early-stage development and are positioning themselves as strong partners for industry. Princeton plans to increase research expenditure from industry, already increasing this figure to 12% in 2016, where it had previously been between 5% and 6%. Despite being relatively small in size, Princeton saw 191 patents filed, 31 issued and 29 technologies licensed in 2016. Rutgers is leading the way in areas such as continuous manufacturing (CM), partnering with companies such as Johnson & Johnson, which recently used CM processes developed and optimized at Rutgers to produce HIV treatment drug Prezista.

Chris Molloy

Senior Vice President,
Office of Research
and Economic Development
RUTGERS UNIVERSITY

Rutgers University is the largest university within New Jersey's state university system, and has a history dating back to 1766. How has the university evolved?

Today, Rutgers is a top 30 research university in the US with nearly 70,000 students, and spends more than $650 million per year in research. We are also part of the Big Ten Academic Alliance, a group of mostly large state universities that generates more than $10 billion a year in research expenditures in the U.S.–more than the Ivy League universities or the University of California system together spend.

Rutgers Biomedical and Health Sciences (RBHS) is an important component of the university that was formed in 2013 through the merger with the University of Medicine and Dentistry of New Jersey (UMDNJ) as a result of the New Jersey Medical and Health Sciences Education Restructuring Act. The division has vast expertise in a wide variety of biomedical research areas including oncology, neuroscience, immunology, anti-infectives, and cardiovascular diseases.

What attracts students to the Rutgers Biomedical and Health Sciences (RBHS) division?

Students are attracted in part to the "Rutgers brand", and equally drawn by the fact that Rutgers is a leading national research university. A recent article in USA Today ranked the university second in the U.S. among the best places to study health professions, with careers such as nursing, pharmacy, physician assistant, physical therapy, and so on.

We also have very good relationships with many surrounding industries. We are continuously expanding our student internship programs and seek to invite companies to interview our students on a regular basis. For example, the Rutgers Ernest Mario School of Pharmacy coordinates the largest national pharmacy post-doctoral program, placing top pharmacy school graduates throughout the US in one- or two-year fellowships at more than a dozen biopharmaceutical companies.

Could you elaborate on the emphasis placed on research in New Jersey, and the role Rutgers plays?

New Jersey is actively working to foster and expand a research-intensive ecosystem in a variety of areas that leverages the large professional talent pool available in this relatively small state. State universities like Rutgers contribute by recruiting top students and producing world-class research that attracts and expands our corporate industrial base, leading to job growth. We believe that expanded public-private partnerships among the state's universities and industry will spur private investments and economic development as has happened in other areas of the US, such as Massachusetts and California.

In what ways is Rutgers taking advantage of trends for companies to outsource early-stage R&D?

The pharmaceutical industry is under a great deal of pressure from investors to keep profitable, and in order to reduce expensive internal R&D resources companies have been increasingly outsourcing early-stage research. Universities can benefit from this trend by partnering with pharmaceutical companies in these early research phases; for example, in disease target identification and target validation, and we are expanding our industry collaborations to take advantage of this at Rutgers.

In this regard, my office has developed an in-house preclinical translational research team, staffed by scientists with many years of pharmaceutical industry experience that work with our academic faculty to identify and advance new therapeutic research projects and develop new patented technologies. The expertise of this translational team spans medicinal chemistry, cell biology, in vivo pharmacology, imaging technologies and histopathology, which complements many of the academic strengths of Rutgers in the life sciences. This core group and their facilities are also available to provide expert help with external partners from the biotechnology industry, further extending the university's reach in economic development.

What are the key priorities and objectives for Rutgers going forward?

Rutgers' main priority continues to be the education of our students in the best possible way. However, as a prominent state-funded research university, our mission also includes research and service, and we readily accept our role to support the economic growth of the state and industry through productive collaborations with state agencies and companies across the entire research continuum.

My office at Rutgers University has worked hard to foster a user-friendly business environment with respect to corporate relations, sponsored research, and technology transfer. We are flexible in terms of our IP positions and how we work with companies.

Coleen Burrus & Pablo Debenedetti

CB

FD

CB: Director, Corporate Engagement & Foundation Relations
PD: Dean for Research
PRINCETON UNIVERSITY

How focused is the university on life sciences and its associated industries?
CB: Our location in central New Jersey, between Philadelphia and New York City, makes life sciences a very natural and significant focus for us. New Jersey is a major life sciences hub with about 3,000 life sciences companies and 13 of the world's 20 largest pharmaceutical companies. So, we have many world-class, life science research partners right in our backyard. And these same companies are also potential future employers for our students when they leave Princeton.

How strong is the relationship and collaboration between the university and the life sciences sector?
PD: The enhancement of our interactions with the industry is a key goal in my office. Traditionally at Princeton, between 5% and 6% of our research expenditures come from industry, and we would like to see an increase in this figure. The primary motivation behind increased cooperation with industry for research is the intellectual drive. Many interesting questions are being asked at the interface between the biomedical industrial sector and the academic sector across several areas, and particularly in life sciences.

What measures is Princeton taking to attract industry collaboration?
CB: We have joined organizations and associations, like BioNJ, and raised our profile at summits and conferences with display booths and brochures. We also have strong corporate affiliates programs. One example is our E-ffiliates program at the Andlinger Center for Energy and the Environment, which is designed to bring companies in to have a closer look at our research.
PD: A further example is that we run several competitions for funding within the faculty called Innova-tion Funds. One of these, named New Industrial Collaborations, has a very interesting funding model. Every year, we have a call for proposals, and every faculty participant must have a letter from industry stating their interest in this research. In year one, the faculty member can receive up to $100,000 from the University. In year two, Princeton will match whatever the company provides, up to $75,000. Through a contribution of $75,000, a company can thereby see results of $250,000 worth of research. This is a way of incentivizing collaborations by making it more attractive for industry to collaborate with faculty.

Could you elaborate on some of the opportunities offered to students through industry partnerships?
CB: The faculty's interaction with industry offers many benefits to students, such as greater ease in placing PhD students at various companies such as Bristol-Myers Squibb, Merck and Boehringer Ingelheim. We also have a proactive internship program through our Keller Center for Innovation in Engineer-ing Education. In the summer of 2016, Keller started placing students in start-ups in New York City, and this summer, we are also sending students to internships in Israel, to be immersed in Israel's entrepre-neurial culture. Our large Merck catalysis and Bristol-Myers Squibb research centers provide a high level of support for student research.

Princeton is a relatively small university, yet 2016 saw 172 patents filed, 25 issued and 25 technologies licensed. How does the university support this extent of research and innovation?
PD: We have a very proactive and supportive Office of Technology Licensing that works closely with fac-ulty members on intellectual property developed on the Princeton campus. The basic legislative frame-work, centered around the Bayh-Doyle Act, strongly encourages the protection of intellectual property and the commercialization of inventions at universities under governmental funding.

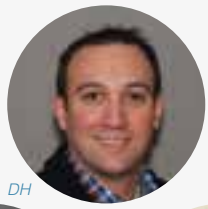
What are the objectives in terms of industry collaboration and education?
PD: A very distinctive feature of Princeton is that we can confidently say we are excellent across the board in every single department. Maintaining this reputation is an objective, and requires large in-vestments in hiring and retaining a world-class faculty. Another very important objective articulated by our president is for Princeton to be proactive in its interactions with the innovation ecosystem. Princeton is a community of scholars, so we need to have greater opportunities to engage with that ecosystem.
CB: A core part of Princeton's mission is seeing the University's fundamental research turned into prac-tical applications that benefit the world. Our faculty wants to see that happen. So we are motivated to work with industry because industry is the conduit to those practical applications.

Continuous Pharmaceutical Manufacturing: A New Beginning

Fernando J. Muzzio, Douglas Hausner, Marianthi Ierapetritou, and Alberto Cuitino

School of Engineering, Rutgers University

FJM



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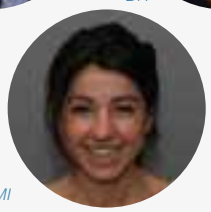

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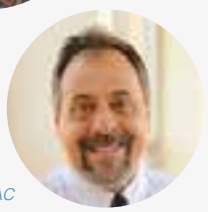


AC

New Approaches to Pharmaceutical Manufacturing

The dramatic increases in costs and time to develop new drugs necessitates new approaches to pharmaceutical manufacturing. Batch processing, which has been the trend for the last 100 years, is no longer sufficient in an era in which drugs need to be developed faster and produced more flexibly to better address patient needs. Continuous Manufacturing (CM) addresses this need. It is a methodology which has been successfully applied in other industries and which is already attracting support from the FDA to meet the needs of accelerated development (i.e. Fast Track, Breakthrough Therapy, Orphan Drug).

This approach has been under development over the course of the last decade through public-private partnerships involving major universities, corporations, and the government and is now making its way into commercial utilization. Regulators are welcoming these new CM methodologies as a science based approach that supports major FDA initiatives for Quality by Design, Process Analytical Technology, and Continuous Process Verification.

The main focus of the NJ-based C-SOPS alliance is small molecule oral solid dose continuous manufacturing (i.e., tablets and capsules). C-SOPS is the most mature alliance with the first two FDA product approvals occurring within the last two years and many more expected in the near future. This area of application is at the point where industry-wide efforts are now focused on easing adoption, aligning technical approaches for regulatory approval, and workforce development. As technology adoption accelerates and eventually reaches, at full maturity, an expected 50% penetration of all pharmaceutical manufacturing, this creates enormous opportunities for building an innovation ecosystem capable of impacting manufacturing activities accounting for hundreds of billions of dollars in annual output.

The Impact of CM on the Pharmaceutical Industry

CM for small molecule medicines, both for drug substances and for finished products, has already been shown to be an effective approach for accelerating product and process development, decreasing manufacturing cost, and improving pharmaceutical supply-chain efficiency. Moreover, continuous manufacturing of large molecule biologics is also beginning to receive attention from industry, providing significant additional opportunities. The need to support efforts in CM technologies across the product portfolio is easily demonstrated: While small molecules represent the overwhelming majority (> 90%) of prescriptions currently dispensed worldwide, large molecules represent the fastest growing segment and are becoming a critical component of drug manufacturers pipelines, already accounting for >20% of gross revenue.

As a result, CM for both small molecules and biologics has become a priority for biopharmaceutical companies, its technology suppliers, the FDA, BARDA, OSTP, and the USP. Companies such as Johnson and Johnson, Merck, Sanofi, Bayer, Glaxo SmithKline, Novartis, Eli Lilly, Vertex, and Pfizer, have declared corporate goals of converting to CM more than half of their total production volume in the next few years. Many other companies are following suit.

The potential economic impact, both direct and indirect, is very large. In our opinion, within the next decade, we will witness a worldwide conversion to CM, which at maturity could reach 50% or more of total output. Many other related industries will benefit as well. The total direct investment in equipment, instrumentation, and facilities required to implement the new manufacturing platforms could easily exceed $100 billion. Specialty ingredients will need to be developed and commercialized to facilitate CM. An entire new generation of scientists, engineers, and technicians will need to be trained to implement, optimize, carry out and regulate the new manufacturing methodologies required to manufacture products continuously. Countries (and states) that are able to implement these methods effectively will capture much of this activity.

Bringing New Technology to Market

Importantly, the rate of adoption of this new technology is currently limited by access to know-how and trained personnel. Thus, technology transfer hubs developing and transferring efficient CM technologies to the pharmaceutical industry will transform manufacturing during the next decade, triggering enormous economic development in synthetic and biopharmaceutical manufacturing infrastructure, impacting not only drug companies, but also technology suppliers (manufacturing equipment, raw materials, instrumentation and control, technical and regulatory consulting, etc.). The Rutgers Engineering Research Center for Structured Organic Particulate Systems (C-SOPS), which was the origin of this technology revolution for small molecule solid dose, is a demonstration of this cascading effect: While the first ten industrial members of C-SOPS were all pharmaceutical manufacturers, 80% of the next 50 companies to join the Center were technology suppliers. The great majority of these companies are currently engaged in using or supplying solid dose CM technology, and two of the members were the first to receive FDA approval for the manufacture of tablet products manufactured continuously; Janssen Pharmaceutical's Prezista and Vertex Pharmaceuticals Orkambi.

Today's Innovation is Tomorrow's Medicine

The U.S. biotechnology industry is booming with companies sprouting from a variety of sources. Many have been set up around a specific molecule or technology spun out from larger companies, and many others have grown out of university research.

From Volume to Value

The entire pharmaceutical industry is going through a shift in paradigm. Until now, the general model has been to manufacture blockbuster drugs for the mass market for a substantial commercial return. However, the proliferation of breakthroughs in the realms of medicine, technology and biotechnology has vastly increased the understanding of diseases and how to cure them, enabling a move into targeted treatment solutions and into personalized medicine. Moving from mass-market to solutions to more targeted patient populations does, however, result in shrinkage of the total addressable market for the respective drugs. This means higher value but lower volume.

A better understanding of disease states and their underlying causes has allowed novel approaches to come to the fore. The use of biomarkers has become widely used to monitor and predict the effects of drugs in the human body, for example. Pennsylvania-based FlowMetric utilizes flow cytometry to identify cells based on associated markers. Monitoring multiple parameters simultaneously, the company is able to analyze a billion cells per day. "The first prerequisite is the safety of the drug and whether the drug has any reaction that was not anticipated," stated Renold Capocasale, CEO at FlowMetric. "We look primarily at the immune system for specific modulatory responses, as the cells of the immune system are great sentinels for understanding whole-body wellness. We also can identify cytokine storm, a potentially fatal immune reaction that can take place after the introduction of a therapeutic drug into a patient for the first time…We hone in on answers that allow our clients to determine mechanism of action in order to aid them in understanding how their drug is effective in their patients."

Although FlowMetric offers mechanism-of-action studies, functional assays, signaling assays, and proliferation assays, immunophenotyping is its primary service to the pharmaceutical and biotech industry. "Flow cytometry is the perfect platform for advancing drug development," said Capocasale. "Its specificity, precision, and high-throughput nature allow for efficient tracking of drug efficacy and safety… What differentiates us is our ability to develop, validate and analyze high-complexity flow cytometry (up to 18 colors/20 parameters on one cell, simultaneously). This is not common for CROs–we are at the highest level of ability in the market. Our capacity allows our clients to assess a greater number of biomarkers in one small sample and evaluate the data across those markers at one time."

FlowMetric is increasing its U.S. footprint as well as opening a facility in Asia focusing next on point-of-care diagnostics. In 2015, FlowMetric Europe was incorporated in Italy at the PTP Science and Technology Park. Personalized Medicine Otherwise known as precision medicine, a more targeted approach enables better care for the individual patient. An increasing focus on patient centricity is apparent across the healthcare industry, and more tailored solutions fit in perfectly with these strategies. 25% of FDA approvals for new molecular

entities (NMEs) in 2016 were personalized medicines, a huge leap from only 5% in 2005. PhRMA estimates that 42% of medications currently in the pipeline have the potential to be personalized.

Platforms such as flow cytometry, as utilized by FlowMetric, allow the identification of ways to separate patients within a heterogeneous disease into different categories in order that the treatment may be personalized leading to improved response rates. A key therapeutic area into which this could be applied is cancer.

Advancing Oncology

Since 1990, new therapies have contributed to almost a 23% decline in cancer deaths, with two out of three people diagnosed today surviving at least five years. However, due to a high level of activity in this area and concern over a diminished treatable patient population, there has been a recent dearth in new programs and treatments. Meanwhile, shifting trends in clinical trials and financing will impact the ways in which these molecules are developed. Oncology markets are becoming better defined thanks to more specialized treatments, but this will also reduce patient population sizes whilst raising the value of each molecule.

Until the late 1990s, the main treatment options for cancer were surgery, radiation and chemotherapy, but these treatments have several drawbacks, including a range of side effects. However, over the last two decades, two new treatment paths have new been identified: targeted therapies and immunotherapies.

Advaxis, founded in 2002, is furthering innovation in this area using listeria monocytogene (Lm) technology to get the bacteria to communicate to present an antigen to the immune system. "We are currently the only company globally sponsoring a phase 3 clinical study in cervical cancer today," stated Daniel O'Connor, president and CEO at Advaxis. "Whilst HPV vaccines Gardasil and Cervix, of which Cervix is no longer being marketed, were a great step forward in public health, they also took the pressure off of drug development, fueled by the belief that the treatable patient population would be eliminated."

Avastin is the only drug to have been approved in cervical cancer in the last three decades, and is generally thought to add about three months to patients' lives. Advaxis' axalimogene filolisbac (AXAL) candidate, its first and lead product, was shown to demonstrate the highest survival rate ever achieved at 12 months in a recent study carried out by the Gynecologic Oncology Group (GOG). The concept behind Advaxis' development pipeline was to reteach the immune system to view a tumor as such and to eliminate it. "When there is bacterial presence, antigen presenting cells, sentinels in our immune system, will engulf the bacteria in an attempt to break it down then present it," explained O'Connor.

Recognizing that bacteria preferentially infects dendritic cells but would escape the destructive process, instead gaining access to the cytosol of the presenting cell, Advaxis pursued the opportunity to bioengineer the bacteria to present the antigen in the cytosol setting. AXAL is now in phase 3 clinical trials.

Another approach pursued by companies in the oncology area is to develop medicines that work in conjunction with other chemotherapy treatments. For example, New Jersey-based Cornerstone Pharmaceutical has five indications–pancreas stage 4, AML, t-cell lymphoma, MDS and burkitts lymphoma–for its CPI-613 drug, of which three are in combination with other therapeutic agents, whilst MDS and burkitts are single-agent trials. CPI-613 originated from the company's Altered Energy Metabolism Directed (AEMD) platform, which targets enzymes involved in cancer cell energy metabolism and are located in the mitochondria of cancer cells. "Our drug is one of a kind, and it is the only drug that simultaneously inhibits two targets in the TCA cycle," commented Sanjeev Luther, chief operating officer at Cornerstone. "Our competitors, Argos and Calithera, are publicly-traded companies that are not going after the whole range. Our side-effect profile is also preferable, and there is little added toxicity to chemotherapy when our drug is used.

CPI-613 is intended for use in conjunction with other chemotherapy treatments to enhance their activity. "For example, the t-cell trials are in combination with Teva's drug, Bendeka," said Luther. "When used in combination with CPI-613, the response rate is 86%. Our longest-living patient today is an MDS patient who has been on the drug for six years and three months now."

The company is also currently working on a trial to extend the survival time frame for relapsed burkitts lymphoma patients; although 80% of patients with burkitts lymphoma can be treated, 20% relapse, and in these instances the patient dies within three months. The trial aims to extend the time frame by another 27 days.

Two further molecules, CPI-1818, which is an oral formulation and CPI-3220, a next generation inhibitor, are currently in their IP stages and hinted to be an improved CPI-613.

A product of research into quiescent cells at Roche, Felicitex addresses cell availability as more cells are sent into dormancy as a by-product of new technologies that target more cells. Felicitex's drug candidate is also intended as a combination therapy.

Quiescent cells are clinically defined as non-proliferative and documented as unresponsive to treatment, and identified as in a reversible 'G0' state. "While normal healthy cells also take advantage of this stage because it is a normal stage in a cell cycle for normal cell regulation, cancer cells specifically use the G0 state as a niche to hide from treatment and therapies, whether it is radiotherapy, chemotherapy, or targeted therapies," explained Maria Vilenchik, Felicitex's founder, CEO and scientific director. "No drug currently available on the market can reach quiescent cells."

Felicitex's concept is that when cells are pushed out of G0, they are not just exposed to the drug, they are also sleep-deprived. Cancer cannot survive without this G0 or resting state. Felicitex is currently in the late pre-clinical development stage and hope to initiate pre-IND studies by the end of 2017. Felicitex expect to begin Phase 1 clinical trials a year and a half later.

Having recently been awarded a Small Business Technology Transfer of $300,000 by the National Cancer Institute, Pennsylvania-based Atrin has a diversified portfolio of small molecules and is now exploring brain cancer. Its lead product, focused on ATR, is water soluble and orally bioavailable, and has produced promising preclinical data in ovarian, pancreatic, prostate and colon cancer indications.

Every patient is unique

Although widely used in oncology for some time, biomarkers have been less common in other medical circles until relatively recently. Now, the application of companion diagnostics is becoming more widely recognized as a way to greatly improve treatment options and provide greatly improved patient outcomes.

Companies such as Genomind, based in Pennsylvania, have begun to address needs for genetic testing in other areas, such as mental health and neurology in this particular case. "When we first launched the company, the notion of personalized medicine was emerging, but biomarkers were a foreign concept in medical circles outside of oncology," explained Jay Lombard, Genomind's co-founder and chief strategy officer.

Increasing awareness has, however, led to a demand for more tailored treatments over a one-size-fits-all approach. "The unmet need is astounding," elaborated Lombard. "Psychiatric diseases are highly ubiquitous and pervasive across societies…The need itself centers around the status quo of traditional mental health treatment which is truly empirically based. Medication is chosen by clinicians based on a trial and error process, and statistics show that resistance, treatment failure and non-compliance within the mental health population across diagnoses are high. Using personalized biomarkers to help predict response can increase the efficacy of treatment in this population."

New medicine for unmet needs

As well as using innovative technology to identify different treatment pathways, many biotechs are utilizing proprietary technology to select targets and identify and develop effective treatments based on new molecules.

In the area of pain management, Chromocell is using its Chromovert technology and NaV1.7 pain receptors to find highly-specific molecules. Due to the opioid crisis, alternative pain blockers are in high demand. However, it is in fact Chromovert's application in the food industry that has allowed the company to grow and attract investment. Chromocell was asked to use its technology to create taste receptors, make a high-throughput screening campaign, and look for natural ingredients that could make foods taste more salty or sweet. "We were able to build an impressive franchise around flavor applications such as screens for bitter blockers, salt enhancers, sweet enhancers, and so forth," said Christian Kopfli, Chromocell's CEO. "To our delight, big companies like Nestlé and Coca-Cola began to work with us, which remains the case today. These companies allowed us to grow in a special way, but they did not prevent our pursuit to benefit the bio-medical field."

Chromocell's program is based on the discovery that without the NaV1.7 gene, humans lack pain receptors and do not feel pain. Chromocell's Chromovert technology enables the creation of receptors ideally suited for high-throughput screening and very similar to human receptors, giving accurate results in screening campaigns. "It is fair to say that there is a large unmet medical need at the moment, and severe pain is a large, unresolved issue," asserted Kopfli. "Whilst there are many

pain medications available, most are not very effective for severe and chronic pain, and while opioids help, they come with a lot of side effects. There are other companies with impressive programs, but our particular strength and main advantage is the combination of high potency and high specificity in our compound. There is currently nothing available to patients that specifically target the sodium-channel (NaV 1.7) area."

Chromocell has received fast-track designation for its lead candidate and is also working on NaV1.8, another pain channel.

> "The decision to move a therapeutic into the clinic needs to be supported by the science and there needs to be a strong indication that the drug will be successful through clinical trial. Having the knowledge of good assays measuring if the drug will be safe, effective, and how effective it will be relative to what is already on the market, is key to developing a strong drug package for approval. FlowMetric's sweet spot is in the ability to develop assays that allow companies to move forward with their therapeutic candidate by giving them a data package with actionable results."
>
> -Renold Capocasale, CEO, FlowMetric

Repurposing the Wheel

Many companies focus on entirely new discoveries to formulate new treatments. However, there are often further improvements that could be made to products already in the market and, by focusing on a specific application or therapeutic area, the scope might be narrowed beyond a product's potential. Over time, medicines are often found to have additional benefits or demonstrate efficacy in other disease areas, either in combination with another drug or independently.

Reformulated products, also known as specialty pharmaceuticals, can either enhance the original product, or address a new application area. Commenting on the decision to establish a business based on reformulating compounds, Jingjun (Jim) Huang, CEO at Ascendia, explained: "We recognized that a high percentage of new chemical entities (NCEs) were very difficult to formulate and often had very low solubility and negligible bioavailability. We also looked at medicines that were already on the market, and noticed that drugs are sometimes rushed into the market without first being optimized, indicating another area of our business focus. We developed our nano-technology platforms to address the majority of issues associated with these NCEs or existing marketed drugs."

Ascendia is a biotech company based at New Jersey's Commercialization Center for Innovative Technologies (CCIT), the states leading incubator. The company's pipeline is built around its three technologies: Emulsol, AmorSol and NanoSol. Through these technologies, Ascendia is able to improve factors such as stability, bioavailability, food effects, and side effects.

Another company pursuing this pathway is Nevakar, a specialty pharmaceutical company addressing unmet needs of existing molecules in the injectable and ophthalmic space through extensive formulation, drug delivery and clinical development efforts. "Nevakar's drug repositioning efforts are focused on the design and development of improved formulation, functional packaging, novel drug delivery approaches, and regulatory and clinical strategies," commented Navneet Puri, Nevakar's CEO. "Resulting new and repositioned products are expected to provide patient-centric benefits while ensuring incremental value proposition for the healthcare system."

Puri founded Nevakar in 2015 after completing the integration of his previous venture, InnoPharma, which was sold to Pfizer.

For these specialty products, the FDA has introduced the 505(b)(2) regulatory pathway, allowing companies to skip over pre-clinical and Phase 1 trials. Nevakar's new products, with their proprietary enhancements, are primarily filed under this pathway. "The 505(b)(2) pathway has certainly been evolving, and is a channel where we are able to leverage on some existing clinical and preclinical data, while generating new data subjective to the product differentiation," said Puri. "Such an approach provides a risk managed portfolio development cost, timeline and probability of clinical and commercial success."

Funding can however be a challenge for companies pursuing this route. Levolta, a Pennsylvania-based biotech, is currently working on its VOLT01 and VOLT02 candidates. The first is a combination of zoledronic acid and a steroid, methylprednisol, expected to minimize some of the side effects experienced by patients from zoledronic acid. The second is a progesterone-based compound, with two ongoing Phase 3 trials to show that progesterone crosses the blood-brain barrier and would be a protectant for injuries to the brain. On the subject of state initiatives or external financial support, Levolta's CEO, Richard Becker, commented: "We have tried, but we have not been successful in Pennsylvania, even when partnering with major institutions and having them act as a primary author in submitting. I think if there is a new concept and a new molecular entity that is being discovered, by bias, they are going to get more of a favorable outcome than a combination of old, generic products."

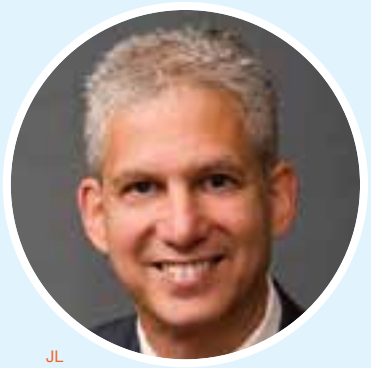
Whilst specialty pharmaceutical companies may present a less exciting investment opportunity, they are certainly lower risk and set to make some interesting advances in existing formulations and medicine.

Natalie Cummins & Jay Lombard

NC: SVP & Chief Strategy Officer
JL: Co-Founder and Neurologist
GENOMIND

A personalized medicine company applying genetic testing to treatment in mental healthcare

NC



JL

Can you briefly introduce the company and outline its development?

NC: Genomind was founded in 2009 by a psychiatrist and a neurologist, addressing a need for genetic testing in the area of mental health and neurology, where it had previously only been utilized in other areas of healthcare. Dr. Lombard and co-founder Dr. Dozoretz developed the Genecept Assay®, a proprietary saliva-based test that helps predict response to medication so that the clinician can find the optimal treatment for a particular patient. We have seen a huge amount of growth over the last several years, from 3,500 tests in 2012, to an overall volume of about 100,000 tests expected to have been run in our CLIA-certified laboratory by the end of 2017. Adoption has been strong, with about 4,000 clinicians in the United States utilizing our tests. Furthermore, we plan to expand internationally through 2017, and have actively identified or are seeking partners in 15 countries.

What is the gap in the market for this approach and what is the unmet need?

JL: Psychiatric diseases are highly ubiquitous and pervasive across societies, from the increasing frequency of autism diagnoses on a pediatric scale, all the way to patients developing depression and cognitive dysfunction as the population ages. The need itself centers around the status quo of traditional mental health treatment which is truly empirically based. Medication is chosen by clinicians based on a trial and error process, and statistics show that resistance, treatment failure and non-compliance within the mental health population across diagnoses are high. Using personalized biomarkers to help predict response can increase the efficacy of treatment in this population.

When we first launched the company, the notion of personalized medicine was emerging, but biomarkers were a foreign concept in medical circles outside of oncology. In the last several years, we have seen a transformation in awareness across certain areas of medicine including psychiatry, resulting from patient demand as well as clinician demand that drug companies develop more specific treatment addressing a particular biological makeup, as opposed to a one-size-fits-all approach. New drug development today is often based on companion diagnostics.

Could you give some insight into the clinical evidence and data supporting the Genecept Assay?

NC: There is a large body of evidence supporting the 18 genes analyzed by the Genecept Assay. In addition, we have run our own studies, including an open label study that identified how the physicians are utilizing this test, what the clinical utility is and what the patient impact is. These findings have been very positive. Patients reported that after taking the Genecept test and having their medication therapies adjusted using the Genecept Assay, their depressive systems, side effects, and anxiety all decreased and their quality of life improved.

In addition, we have seen very positive adoption from providers, who are reportedly seeing improvement in their patients nearly 80% of the time after they have changed the therapeutic direction based upon the Genecept Assay. Most recently, we have just completed a large study with Aetna, which will be published in the very near future. This study shows that when pharmacogenetic testing is used in mental health, we see a reduction in inpatient stays, outpatient stays, slight reductions in pharmaceutical costs and reductions in ER visits.

Is there a capability to utilize collected data to inform trials and drug development?

JL: One of our main objectives is to develop our bioinformatics unit, through which we will collect all the data and translate it into useful and meaningful information for outside sources. Biopharmaceutical companies are expected to be our main client, but we also see potential for private-public partnerships with bodies such as the National Institutes of Health (NIH) to provide them with pharmacogenetic insights.

What are the strategies for Genomind's growth?

NC: Our main objective is always to improve patient care through innovative technologies within mental health. Our international strategy is key in meeting that objective, developing new products that can address market needs such as ADHD is an area on which we are likely to focus in 2017. Another area of focus is our drug-gene-drug interaction tool that we have recently introduced to the market, which will assist clinicians as they prescribe medication using our pharmacogenetic information. This tool will assist them in avoiding drug-gene-drug interactions that could occur upon prescribing.

Marco Taglietti

CEO
SCYNEXIS

A drug development company developing and commercializing anti-infectives

How has Scynexis developed as a company since its initial establishment?

The company started in 2000 as a spin-off of Sanofi, and was created in North Carolina's Research Triangle Park as a contract manufacturing organization (CMO). As part of its synthetic chemistry activity, Scynexis was able to identify some interesting compounds, one of which we are currently developing. The compound, SCY-078, is an antifungal for severe hospital-based fungal infections, and was initially developed for Merck, which then conducted all the initial development. In 2011, Merck decided they were no longer interested in developing an antifungal, so the product came back to Scynexis, and the company decided to move away from simply being a manufacturing organization to becoming a true biotech in order to develop and bring this novel antifungal to the market.

When I became CEO, in April 2015, I restructured the company, sold the manufacturing business, which was no longer strategic for us, and brought the company to New Jersey from North Carolina's Research Triangle Park in order to take advantage of the incredible pool of talented pharma executives and people on the research, commercial and investment side.

Could you provide some further insight into SCY-078?

SCY-078 is a new class of antifungals in phase 2, and has the potential to treat fungal infections that are becoming resistant to current treatments.

SCY-078 is a broad-spectrum product that works across resistant strains, and one important feature is that it can be administered both orally and intravenously, a flexibility of use that not many antifungals have.

Drug resistance is a major issue. How long do you expect SCY-078 to maintain its efficacy?

There will never be an antibiotic that maintains complete efficacy forever. Usually, it takes about eight to ten years before some pathogens begin to become resistant to a newly introduced antibiotic. However, after the first few resistant strains appear, resistance begins to grow exponentially. The last class of antifungals introduced was echinocandins in 2000 and resistance to echinocandins started to be reported around 2010. Today, probably 3% to 5% of pathogens are resistant to echinocandins. At a certain point, about 15 years after introduction of a new antibiotic, resistance becomes more and more common, limiting the use of these old antibiotics only on those cases where the pathogen is sensitive.

As a doctor, I believe that one day we will find treatment for cancer, Alzheimer's disease, Parkinson's disease and many other afflictions, but there is a group of diseases which we will continue to fight forever, and these are infectious diseases. No matter the antibiotic, at a certain time the pathogens will become resistant. The first antibiotic was introduced 80 years ago. Back then, there was no resistance, and now we have burnt out so many antibiotics that there are less and less effective antibiotics on the market. For this reason, the United States introduced the QIDP designation–to support companies that are developing new products.

What are the next steps for SCY-078, and are there any other products in the pipeline?

We are planning to do phase 2b in 2017, and phase 3 in 2018. If everything goes well we hope to file for an application here in the U.S. in 2020 and launch the product on the market shortly thereafter. A new pathogen has recently surfaced, known as Candida auris. This specific strain has a mortality rate of 60% to 70%, as opposed to the usual 20% to 40%, and is resistant to almost everything available on the market. Case Western University tested 11 different drugs against 16 strains of Candida auris, and the only one that showed consistent activity at a low concentration was SCY-078. This is an important way to demonstrate the value of the product. The strain is still rare in the United States, with only about 30 infected patients, but in India it seems that 5% of Candida isolates are now Candida auris.

Since we believe we have a good product, we believe the future of Scynexis is very bright. As yet, SCY-078 is our only asset in development but this product is developed for several different indications, and we are now ready to make further additions to our pipeline either from our internal platforms or from opportunities readily available in the market.

Daniel O'Connor

President & CEO
ADVAXIS

Advaxis is a biotechnology company focused on targeted therapeutic cancer immunotherapies using its Lm Technology™ to create immunotherapies that specifically target cancer without affecting normal tissue.

Advaxis was founded in 2002 and has developed around its Lm platform. Could you briefly introduce the company?

The underlying premise behind all cancer therapies is to get the patient's own immune system to fight the tumor to forego the use of chemicals, radiation or surgery. Humans are built with an ability to rid themselves of cancer and a problem is that the system is no longer able to illuminate the cancer. In the 1990s, a researcher at the University of Pennsylvania reasoned that a patient with cancer still has an immune system that will recognize a bacteria. She then thought of getting the bacteria to communicate with the immune system in a way that we can present an antigen to the immune system.

What are the underlying principles of Advaxis' Lm technology platform?

The Lm technology is in essence a bacterial antigen presenting system. Known as listeria monocytogenes (LM), giving the technology its name, this bacteria was selected because of its unique lifecycle. The idea was that this bacteria could be used as a way to interact with the immune system to basically reteach the immune system to view a tumor as such and to eliminate it. Currently, the arsenal of weapons for treating cancer patients include surgery, chemo and radiation, and certain targeted therapies. All of these therapies have drawbacks, and there has always been a quest to find something better.

Could you provide some further insight into Advaxis' lead immunology candidate?

Our first ever product candidate, axalimogene filolisbac (AXAL), is our lead candidate and now in phase 3 clinical trials. We are currently the only company globally sponsoring a phase 3 clinical study in cervical cancer today. Whilst HPV vaccines Gardasil and Cervix, of which Cervix is no longer being marketed, were a great step forward in public health, they also took the pressure off of drug development, fueled by the belief that the treatable patient population would be eliminated. However, the vaccinations are not rolled out to every individiaul globally, and only help people not yet exposed to the virus. About 80-85% of sexually active women in America have a strain of the virus, and in a very small number this will develop into a malignancy associated with that virus, and an even smaller number will develop an associated cancer. The only drug to have been approved in cervical cancer in three decades is Avastin, which has been approved in multiple solid tumors and is generally thought to add about three months to patients' lives. A study recently carried out by the Gynecologic Oncology Group (GOG) showed that AXAL demonstrates the highest survival rate ever achieved at 12 months. They have done multiple studies with other drug candidates, and we were able to show about a 50% increase in expectations for survival at the 12 month mark, from 24.5% based on current treatments to 38%.

Advaxis' preclinical immunotherapy candidate, ADXS-NEO, is expected to enter the clinic in 2017 as part of a collaboration with Amgen. Could you elaborate on the collaboration and the drug itself?

We are pursuing protein secretion that relates to the individual patient's tumor and genetic profile. Amgen invested $40 million in cash and $25 million in market equity, and so own about 8% of Advaxis. We were able to get the IND within the 3 day review cycle, andwere able to get through in the first 30-day request, which is remarkable considering that this is a very different approach to treating cancer patients. One of the issues with cancer is that it is difficult to treat as it is an individualized disease. It is a disease of genetic mutation. Our key differentiator is the avoidance of the one-size-fits-all approach.

We also took a step back and designed our own program, ADXS-HOT, which also targets new public antigens, rather than private ones; not patient-specific tumor biopsy-driven neoantigens, but instead neoantigens identified from bioinformatics. We know that there are certain driver mutations called hotspots and there is commonality amongst patients with that certain type of cancer where we can premake those plasmids instead of targeting the tumor, finding out what the mutations are. We then build plasmids to the hotspots. Our plan is to get the IND ready this year for that program.

What are the key objectives for Advaxis?

Our AXAL program aims to prevent or delay recurrence in patients following chemo radiation as their primary care treatment before the disease recurs. We give them AXAL as a monotherapy, and are comparing the effects against placebo in women of high risk of recurrence. The other study we want to do is in late-stage cancer, so we are taking a book-end approach. We also have the ADXS-PSA program for prostate cancer, looking to stop or decrease progress of the disease. Another program is pediatric astrocytoma, borne out of work at the University of Pennsylvania into bone cancer in dogs. This is a very rare disease, with only about 400 patients, mostly children and young adults.

James Sapirstein

CEO
CONTRAVIR

ContraVir is a biopharmaceutical company focused on the development and commercialization of targeted antiviral therapies with three candidates in the pipeline.

How has ContraVir developed since its conception?

We founded ContraVir three years ago as a publicly traded company, and 15 months later were listed to Nasdaq. The first product with which we founded the company was FV-100, now known generically as Valnivudine™, a treatment for shingles. We entered our phase 3 clinical trial about nine months later. Around the time the FDA allowed us to go into phase 3, I licensed another product from Chimerix called CMX157, now known as Tenofovir Exalidex (TXL™). TXL™ is a lipid analog of Tenofovir, the same drug that I launched at Gilead. We are now in phase 2 and recently finished a trial in Thailand. Our other asset originates from a company we acquired last year called Ciclofilin, which we are looking at for Hepatitis B and for liver fibrosis. CRV431, which is a cyclophilin antagonist, is pre-IND, and we are doing all the IND studies now. We hope to file our IND by the end of the year and move into clinical studies in 2018.

We have two further research centers outside of New Jersey. The first is a Hepatitis B laboratory in Edmonton, Canada, where our chief scientific officer sits with his staff. We also recently opened a facility in Doylestown, Pennsylvania, as part of the Hepatitis B Foundation, the Blumberg Institute.

How supportive is New Jersey's Net Operating Loss (NOL) tax credit program, of which ContraVir has taken advantage?

New Jersey is in fact the only state that offers NOLs. I am on a committee called the Capital Formation Committee at BIO, and we are always trying to figure out ways for other states to pick up the program. For companies like ContraVir that only spend money, the program allows the sale of these losses to for-profit companies, often energy companies such as JCP&L and PSE&G. They use that credit to offset some of their profits, and they give us a certain percentage on each dollar we sell to them. For us in New Jersey, it is a terrific advantage.

What could some of the major changes to the industry framework be as a result of pricing pressure?

The industry needs to do something about pricing, plain and simple. If the industry does not figure out a way to be more transparent, the government will. The system in the United States allows us to innovate, and reference pricing would hinder our progress to helping people with hard-to-treat diseases. Patients might be in favor of reference pricing to lower drug costs, but removing the incentive for profit will kill invention. In countries such as Russia, prices might be low, but there is no innovation, and what is invented is not tested adequately enough to be safe.

What are some of the key considerations when bringing ContraVir's drugs to market from a competition standpoint?

We have data that shows that TXL™ is as good as both of Gilead's products. Our goal is to show that we are a little better, then the sky is the limit. We hope to be safer and outdo our competitors in dropping the amount of virus. Hepatitis B will be a combination like HIV, and there are about 40 products currently in development, but it remains to be seen which combination will work best. We hope that our drug will work better within combination than other drugs out there.

Valnivudine, now in phase 3, has already been proven in our studies to be superior to Valtrex, the current treatment for shingles and the associated pain. It is now a question of completing phase 3 to move towards approval and commercialization.

How does ContraVir plan to build its pipeline beyond its three key assets?

We are currently trying to pivot over to Hepatitis B, and are looking for a partner for Valnivudine. We were going to wait until phase 3 was over and we had an approvable drug, but Hepatitis B is much more attractive from an investor perspective, and we are too small to build up a commercial organization. My responsibility is to create shareholder value, and the best way to do that is by creating a stronger pipeline in Hepatitis B. CRV431 is also certainly going to be a piece of the combination to Hepatitis B. It is a whole new class of drugs, and we are the only ones developing a cyclophilin for Hepatitis B.

Navneet Puri

CEO
NEVAKAR

A specialty pharmaceutical company that develops enhanced products to address unmet clinical and/or commercial needs of existing molecules in the injectable and ophthalmic space.

You previously had great success with InnoPharma, which was eventually sold to Pfizer. Could you provide some insight into your new venture, Nevakar?

InnoPharma's acquisition was a strategic move by Pfizer; its product pipeline and track record of successfully developing and commercializing complex generic injectable products provided Pfizer a platform for further growth in this area. This was a great exit for InnoPharma's shareholders as well as its team. After completing integration, I left Pfizer to found Nevakar in 2015.

Nevakar is a specialty pharmaceutical company that develops enhanced products to address unmet clinical and/or commercial needs of existing molecules in the injectable and ophthalmic space. We do so through extensive formulation, drug delivery and clinical development efforts. We are a U.S.-centric company. Our New Jersey facility is about 27,000 square feet, half of which is lab space, and the other half of which is office space. The labs provide infrastructure for pre-formulation, formulation and process, drug delivery and analytical R&D. Besides that, we have pre-clinical and clinical development capabilities, along with all support functions to grow Nevakar as a fully integrated specialty pharmaceutical company.

How is Nevakar's pipeline currently structured?

We have several products in our portfolio undergoing active development. Nevakar's drug repositioning efforts are focused on the design and development of improved formulation, functional packaging, novel drug delivery approaches, and regulatory and clinical strategies. Resulting new and repositioned products are expected to provide patient-centric benefits while ensuring incremental value proposition for the healthcare system. These new products with proprietary enhancements are filed with the FDA, primarily under the 505(b)(2) regulatory pathway.

Is Nevakar utilizing a particular technology to develop its pipeline?

Nevakar utilizes technology as a tool, and not a primary way of developing a business model, so for us it all starts with the problem we are trying to solve. The technology is therefore selected according to what will best address and solve the specific problem. In addition, we leverage on our mechanistic understanding of physical, chemical and biological sciences, in molecules specific manner, to come up with solutions, before proceeding with utilizing technology based tools.

Have there been any particular trends in the drug delivery area?

Specifically in the injectable segment, we are seeing greater emphasis on controlled delivery, although this trend is not necessarily new. We are also seeing developing trends in colloids, nanoparticles, suspensions, and so on. Depending on the industry segment in which we operate, we utilize the available tools to optimize our results according to the specific target.

How well paved is the path to market?

Nevakar's product pipeline is diversified; there are some very big and ambitious products, and then there are products with a relatively simpler path to development and market. The 505(b)(2) pathway has certainly been evolving, and is a channel where we are able to leverage on some existing clinical and preclinical data, while generating new data subjective to the product differentiation. Such an approach provides a risk managed portfolio development cost, timeline and probability of clinical and commercial success.

Nevakar raised $55 million in 2016; a large sum for a young company. How supportive has the innovation framework and investment climate been?

In terms of funding, it helps to have a successful track record and credibility that provides investors with a certain degree of comfort. Securing funding is never easy, and investors need to have a level of confidence and belief, primarily in the team and then in the business model.

On another side, the state of New Jersey has been very supportive in growing technology based companies by incentivizing investors through angel investor tax credit, which Nevakar investors have taken advantage of. New Jersey is considered the pharma belt of the United States, and its talent pool presents an additional advantage.

What are Nevakar's plans for growth and building its pipeline?

The list is ever-growing. Taking a broader perspective, we are focused on becoming a leading and fully integrated specialty pharma company, to which we dedicate ourselves 100%. As we grow, we will become stronger and continue to expand, and will continue to partner and collaborate with other companies and research entities where we find value.

Jingjun Huang

CEO
ASCENDIA

Ascendia is a contract development and manufacturing company

Ascendia was established in 2012 and its primary focus is on creating new formulations for poorly soluble drugs. Could you elaborate on the unmet market need that Ascendia is addressing?

We recognized that a high percentage of new chemical entities (NCEs) were very difficult to formulate, and often had very low solubility and negligible bioavailability. We also looked at medicines that were already on the market, and noticed that drugs are sometimes rushed into the market without first being optimized, indicating another area of our business focus. We developed our nano-technology platforms to address the majority of issues associated with these NCEs or existing marketed drugs. Our company's mission is "aspiring for better medicine"; we aspire to make compounds work better, and make medicines work better via developing different routes of administration, expanding labels, seeking new indications, and creating better safety and efficacy profiles.

Although we are a small company, we have a highly-skilled workforce consisting of about 20 people globally. In the United States, we have a 4,000 square foot lab area, where we can also manufacture cGMP clinical supplies. We conduct our work per the FDA's ICH standards and have some international collaborations in our pipeline. At the moment, our main focus is the United States but we are also looking at Asian markets, particularly China, and down the road we may look to European markets as well.

Could you elaborate on Ascendia's EmulSol, AmorSol and NanoSol technologies?

Our leading technology is EmulSol, a nano-emulsion technology that is essentially an oil -based drug carrier. We put this technology through certain stabilizing processes to make the oil droplet nanosized so that it can act as the carrier for the drug. When making nano-emulsions below 50 to 100 nanometers, without a high level of surfactant, it can be challenging to load a certain level of the drug and make it very physically stable for adequate long-term stability. Despite not using solvents or high levels of polymers, the EmulSol technology is still able to achieve a nano-emulsion oil droplet size below 100 nanometers. The result is an optically-clear liquid with very good stability for shelf-life. This technology has been utilized for injectable, topical, and oral dosage forms.

AmorSol is an amorphous nano-particle formulation technology mainly used for oral dosage forms to address drug bioavailability issues. Our aim is not only to boost bioavailability, but also to reduce or eliminate food effects, an area that is critical for oral drugs, because the timing of meal consumption has an important impact on drug absorption and bioavailability. Our technology can address that issue to give similar bioavailability, or PK profiles, before and after meals. This reduces patients' over- or under-exposure to the medicine. Our third technology is NanoSol, a nano-particle engineering technology for oral bioavailability enhancement and topical permeation enhancement. It can also enhance drug loading and drug infusion rates for injectables and reduce injection related side effects such as irritation. We have intellectual property for making nano-particles that can be used for sustained release of injections, which is important for parenteral dosage forms. For each technology platform, we have significant expertise, capabilities, and proprietary intellectual property.

How much competition does Ascendia face?

We are a key player in a very niche area. Very few companies in the market can offer all three of these platform technologies, which gives us a distinct advantage because one technology is not suitable for all applications. By having these three major technologies in-house, we can ensure that the right technology is selected for the right formulation, which can then have a higher probability of success down the road.

What are your current R&D focus areas?

Our long-term goal is for Ascendia to be a specialty pharma company with leading nano-technology and nanomedicines on the market. A very exciting development is our ASD-002 program, for which our U.S. patent has been issued, and for which we are at the point of initiating a clinical study. If we advance this drug into the market, we will address a real unmet need for patients with Acute Coronary Syndrome (ACS). ASD-002 addresses the current onset-of-action delay of the current standard-of-care tablet product. An injectable version of this drug can deliver a high dose in a short period of time, allowing the plasma concentration to be titrated to the desired level quickly, and overcome some patients' resistance to the drug when administered orally. Previously, injectable dosage forms were thought to be unfeasible, but we have made them feasible through EmulSol. Furthermore, we are working on using EmulSol to enhance the efficacy of ophthalmically administered cyclosporin. Our formulation has the potential to improve the patients' response to the eye drops and reduce the required dosage frequency. With respect to side-effects, our EmulSol formulation could potentially address the burning sensation faced by some patients thanks to its low surfactant levels, and also potentially address blurred vision issue thanks to its optically clear appearance. Our regulatory pathway to the market is mainly the NDA 505(b)(2) route, for making existing drugs work better.

What are the next steps for the company?

Our next step will be to advance our pipeline products into clinical trials. We will be moving into a bigger facility in the New Jersey area, and looking to increase business revenue by increasing collaborations with companies and increasing our formulation service capacity. Our business model is a hybrid model; we conduct pipeline development and licensing, and we seek co-development partnership projects. We currently have several co-development projects underway with some large pharmaceutical companies - developing nano-particle based products with challenging controlled release requirements.

Biosimilars: The Dissimilar Twin

Biosimilars remain a hot topic, but the program is so far walking rather than running. Europe is ahead of the United States in terms of approvals, and the U.S. regulatory framework is still under development; four products have been approved, with two on the market so far, with another 64 enrolled in the FDA's biosimilar products development program. "The action is likely to be more focused in the patent court than around the FDA because the law surrounding biosimilars, unlike generic drug law, does not take patents into account; the approval process centers only around the science," commented Ira Loss, executive vice president at Washington Analysis. "The whole patent battle is fought separately from the FDA, and the agency will continue to approve products of which the patent status has not yet been settled."

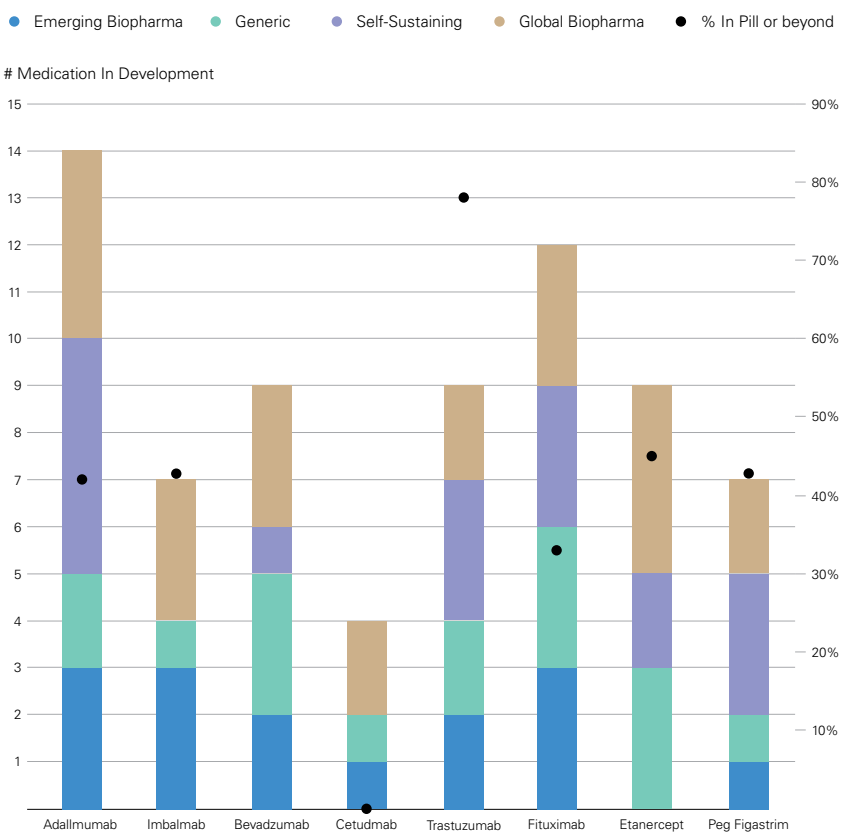
In the United States, biosimilars currently have access to an abbreviated approval pathway via the Biologics Price Competition and Innovation Act of 2009 (BPCIA). The BPCIA includes a process for the resolution of potential patent claims, commonly referred to as the "patent dance." In early 2017, the U.S. Supreme Court agreed to review the process and six-month wait time after FDA approval before launching the products, in response to the Sandoz vs. Amgen court battle. The case concerned Sandoz's Zarxio, a biosimilar version of Amgen's Neupogen, which had been approved by the FDA in March 2015. Although then recognized as the first biosimilar in the United States, the product's entry was delayed by 180 days through a provision under the BPCIA, effectively granting Amgen an extra six months of exclusivity.

Despite expecting a speedier pace of approvals due to Congress' reauthorization of the biosimilar user fee program boosting funding, AAM's president and CEO, Chip Davis, voiced some uncertainty over challenges in the framework: "For one, the FDA has yet to provide guidance on determining the interchangeability of biosimilars and innovator biologics. Questions remain over the reimbursement of biosimilars used in Medicaid. Industry is challenging the FDA's biosimilar naming policy, which differs from what is being used successfully in Europe and other world markets. It also remains to be seen how the Supreme Court will rule later this year with respect to key provisions in the law establishing the biosimilar regulatory approval pathway."

In April 2015, the AAM established the Biosimilars Council, which works to ensure a positive regulatory, reimbursement, political and policy environment for the biosimilars industry. "What we must avoid is allowing these challenges to prevent timely biosimilar market entry," Davis concluded.

SECOND WAVE BIOSIMILARS IN DEVELOPMENT BY COMPANY TYPE AND STATUS

Source: PharmSource



Biosimilars – An Update on Recent FDA Industry Guidance

By Vishal Gupta
Partner, Steptoe and Johnson LLP

Biosimilars are a type of biological product (e.g. therapeutic antibodies) highly similar to an already approved biological reference listed product (RLD). While biosimilars are highly similar to a RLD, they are not exactly the same and some physician concerns exist regarding the potential for patients to respond differently to a biosimilar than the RLD in certain contexts. For this reason, a pharmacist cannot simply substitute a biosimilar for an RLD without instruction from a prescribing physician. However, if the FDA determines that a biosimilar is "interchangeable", then in addition to being highly similar to an RLD, it is expected to produce the same clinical result as the reference product in any given patient. A pharmacist can substitute such a product for the RLD without additional physician approval.

Guidance on Demonstrating Biosimilar Interchangeability

In January of 2017, the FDA issued a draft guidance regarding demonstrating interchangeability with a reference product. This guidance is important because it provides insight into what type of data the FDA will want to consider for this inquiry: "The data and information to support a showing that the proposed interchangeable product can be expected to produce the same clinical result as the reference product in all of the reference product's licensed conditions of use may vary depending on the nature of the proposed interchangeable product". This may include analysis of differences between the RLD and proposed interchangeable product, immunogenicity issues, pharmacokinetics and toxicity issues. The FDA advises industry sponsors intending to develop a proposed interchangeable product to consult with the FDA early in the process regarding development plans, scientific justifications and potential data submissions to streamline the process.

Switching studies appear to be a key piece of information considered by the FDA in interchangeability inquiries. "The main purpose of a switching study or studies is to demonstrate that the risk in terms of safety or diminished efficacy of alternating or switching between use of the proposed interchangeable product and the reference product is not greater than the risk of using the reference product without such alternation or switch." Depending on the complexity of the biologic at issue, the FDA may also require additional data from post marketing studies of a biosimilar before granting interchangeability status.

Overall while more clarity regarding exact requirements is to be desired, this draft guidance is an important document providing insight into what the FDA is looking for.

FDA Guidance on Biosimilar Naming and Labeling

Last year, the FDA also issued a draft guidance regarding biosimilar labeling. The FDA recommended labels contain a statement that a product is biosimilar to a RLD. However, it did not require an interchangeability statement (e.g. a non-interchangeable biosimilar does not have to disclose in its label that it is not interchangeable). This caused some controversy. Some organizations opined that a label should contain a statement about whether or not a biosimilar is interchangeable. They argued that this would help avoid a situation, for example, where a physician mistakenly believes that a biosimilar is interchangeable (some physicians only consult the label before prescribing).On the other hand, other organizations opine that the interchangeability statement is unnecessary and could artificially decrease physician preference for prescribing a biosimilar. We will see how this is dealt with in the FDA's final guidance.

In January of this year, the FDA issued a final guidance on biosimilar naming. In addition to a core name, a four character suffix is also required (e.g. filgrastim-sndz). This will help avoid any confusion regarding origins of a biologic.

Trial, No Error: Facilitating the Best Possible Outcome

Clinical trials are inherently high risk and any errors can result in major disruptions or completely collapse the trail. It is extremely telling that only 12% of medicines in clinical trials make it to patients and, whilst there are many reasons that a trail could be unsuccessful, there is potential to mitigate some areas of risk and error.

When the trial fails the drug

Diligence from all parties involved is of course key, but a great deal of potential error comes from the supply and delivery side. Equally, as the market shifts to biologics, which are higher value, the importance of preservation and maintaining efficacy will only increase. This demands increasing control over all aspects of the supply chain and its components.

Regulations are becoming more stringent and companies offering clinical trial support and services have to be highly adaptable to stay ahead of the curve. For instance, Almac Clinical Technologies has created a product called TempEZ™ in response to regulatory requirements to monitor all supplies across ancillary and room temperature requirements. TempEZ™ tracks and monitors all clinical trial supplies, with a particular focus on ensuring product stability and optimal temperature are maintained.

Approaches to medicine are changing, particularly with the uptake in personalized medicine and patient centricity. As a result, the old blockbuster, one-size-fits-all approach, is no longer applicable. A 2016 Accenture survey of over 200 patient services executives stated that 85% of companies are raising their investment in patient-centric capabilities over the next 18 months and 95% of companies are planning to invest in patient engagement technologies over the same time period.

"Today, an increasing emphasis on precision medicine and therapies such as CAR T-cell show that the current model does not work," stressed Gerald Finken, founder and chief scientific officer at CSM. "Rather than the old model of mass production, the patient now goes through tests that have to be relayed to the manufacturer and then back to the patient. The process cannot take place in the manufacturing setting."

> "It is our belief that the slow rate of adoption boils down to a misalignment of incentives. Scientists care about quality, operational executives care about speed, and the outsourcers care about cost. Having all three elements coincide is a challenge. Centralized rating costs more from a transactional perspective but less from a system perspective. Innovation costs more on a transactional level, but fewer clinical trials need to be run if the right answers are found. However, outsourcing does not care about fewer trials because they are compensated to make sure each trial does not cost more than a local assessment. Whilst we are now getting a lot of notice, there are still a lot of paper-based trials."
>
> - Paul M. Gilbert, CEO and Cofounder, Medavante

> It is primarily the regulations that pose a dilemma. In clinical research, companies tend to adhere primarily to FDA regulations. However, when looking at drug supply, it is necessary to contend with global and national regulations versus local and regional regulations. In the United States, for example, each state has its own requirements... Factoring the national regulations, the question then is which set of regulations to comply with. In Europe, there is nothing stopping direct-to-patient supply at a national level, but some countries require shipment from a pharmacy. There is a need for greater harmonization and in the United States specifically clinical research must be regulated at a national and global level with minimal state involvement.
>
> - Gerald Finken, Founder and Chief Scientific Officer, CSM

CSM is a clinical supply solutions provider, utilizing its On-Demand and Direct-to-Patient platforms. "The industry is going virtual because of cost, but this requires Direct-to-Patient capabilities," said Finken. "This is changing the way we think about clinical supplies, which has always been considered on the GMP side. Now, however, we are really starting to get into the GCP side."

The platforms also facilitates trials for products with a shorter shelf life, with the ability to package, label and ship within eight hours at the most anywhere in the United States. "We can have that medication to the patient within 24 hours, allowing a company to undertake an efficacy study even if the product has a shelf life of only 48 hours, for example."

Overcoming subjectivity

Whilst some results are measurable, many trials have endpoints that are either challenging to quantify or can only be measured subjectively. There are also many causes for bias and variability. Paul M. Gilbert, CEO and cofounder of Medavante, focused on CNS clinical trials, explained: "There are three forms of bias, the primary one being misaligned economic incentives. This occurs due to significant pressure to enroll patients into the trial, resulting in inappropriate patient selection and inflation of patients' scores. Once the investigators are paid and the patients come in for their follow up, their real scores may give the illusion that they have improved. These patients would show improvement even if only on placebo and the results would therefore indicate that patients both on the drug and on the placebo are getting better, making it impossible to determine whether or not the drug is working better than the placebo."

The second form is expectation bias, due to a natural human tendency to look for improvement, and the third is therapeutic alliance, described by Curtis Wilson, director, marketing and communications at Medavante, as follows: "Getting to know somebody better results in different ways of evaluation. A patient may simply feel better because the investigator is showing care on a weekly basis. Another therapeutic bias is where the patient simply wants to feel better because they are in a clinical trial and taking medicine."

Medavante aims to replace variability with standardization and bias with objectivity by providing systems for centralized ratings and centralized interviews. So far, the company has raised $49 million to invest in innovation to improve the success rates of CNS clinical trials.

Utilizing data

So far, results data has not been particularly useful to patients because the scientific format and clinical language of the available data is not easily accessible. However, the European Union now requires plain-language summaries of clinical trials to be made available to participants and many sponsors outside the European Union are following suit.

To make access more patient friendly, TrialScope has established a Trial Results Summaries portal intending that any individual that has partaken in a trial can find such a summary explaining the outcome of their trial. As well as its focus on patient-centered transparency, TrialScope specializes in regulatory compliance and positions itself as a partner to all clinical trial sponsors globally by providing a single source of relevant clinical information to trial registries and participants.

With digitization and Big Data rocketing and companies increasingly taking a more patient-centric approach, the prospects for processing and utilizing recorded data to inform patient treatment and trials are immense. —

Valarie Higgins

President & Managing Director
ALMAC CLINICAL TECHNOLOGIES

ACT is a specialized technology and expert consultancy for pharmaceuticals and is part of the Almac Group

Almac Clinical Technologies (ACT) is one of five business units within the Almac Group. Where does ACT fit in?

Almac Clinical Technologies, headquartered in the United States, provides our biopharmaceutical partners with innovative software and professional service solutions to simplify the management of the most critical elements in clinical trial conduct. More specifically, ACT designs and deploys complex software that helps trial sponsors automate complex decisions that occur in clinical trials – such as randomization, patient dosing, titration, eligibility/enrollment criteria from 3rd party centralized laboratory tests, and medication inventory management. Many of these functions are combined as part of a web-based software system commonly known in the industry as 'Interactive Response Technology,' or IRT for short.

What are some of the biggest hurdles faced in clinical trials in terms of compliance?

The biggest challenge that the industry faces is keeping abreast of potential shifts in the regulatory landscape. Our clients consistently depend on us to advise on the implications of specific regulations. For instance, while oversight of temperature-sensitive clinical supplies, or "cold chain," has always been important, the regulations have now changed to require monitoring of all supplies, including ancillary and room-temperature supplies. As a result, Almac has created a product called TempEZ™, which tracks and monitors all clinical trial supplies, with a particular focus on ensuring product stability and optimal temperature are maintained. This area of oversight is becoming more crucial by the day, especially as we see the biopharmaceutical landscape shift focus from small-molecule compounds, to large-molecules (biologics) that are extremely expensive to produce.

Another area of focus is the challenge of data privacy as the use of cloud and encryption technologies increases. Traditionally, the pharmaceutical industry has been slow to change, but there is currently a greater need and financial pressure. Because of developments in healthcare and pressures around costs, companies and the industry at large are accepting change at a more aggressive rate than I have seen in my 20 years in the industry.

Could you elaborate on Almac's IXRS Technology and its advantages?

IXRS® 3 focuses primarily on randomization, drug assignment and maintaining the blind in a clinical trial. Over the years, the platform has grown to automate dosing decisions and titration decisions, thereby improving data integrity over manual processes, which can be subject to suspicion. We also now bring in a more global and broad supply management possibility. Unlike virtually all of our competition, we do not rely on acquisitions for new technology systems; we build them internally using our own expertise.

What do you see as the major challenges for the industry in the short term and how should they be addressed?

By their very definition, clinical trials are high-risk. There is no room for error, whether in patient randomization or in the assignment of a product kit or dose. The supply side is equally critical and is becoming increasingly important due to the costs associated with costly investigational products, like biological compounds. Clinical site selection and retention are becoming increasingly important, and we are focused on providing visibility and analytics in these areas to aid success.

The industry needs to work together in a cross-functional manner to drive speed, efficiency and cost in trials. We have seen some fresh thinking in the industry at a leadership level and companies are coming together to share their knowledge and experience to create industry standards across countries, like the TransCelerate initiative. These types of broad-reaching consortiums are well poised to drive meaningful change in an industry which has historically been risk-averse and slow to implement new solutions.

How does Almac plan to develop its services going forward?

Our focus has always been on reducing complexity in as many aspects of clinical trial conduct as possible. We are developing new forms of automation like barcode scanning instead of manually inputting kit numbers for accountability logs, which saves time and reduces instances of human error. We are also looking at leveraging our data, another big industry trend, to produce unique analytics to help our clients stay informed and enable them to make smarter decisions at high-cost inflection points. Any area in which there are frustrations or pain-points is where Almac Clinical Technologies will look to innovate.

Disruptive Technologies

A major trend in the life science industry and far beyond is digitization and a convergence of the Internet of Things, which has interesting applications and ramifications in analyzing data sets and processing information. Artificial intelligence and machine learning are also likely to play a role in recording, processing and distilling information. One application is the processing of adverse events; every drug has associated adverse events and side effects that need to be assessed and acted upon. By applying artificial intelligence, modern analytics and machine learning, this process can be automated.

For example, global professional services firm Genpact currently has a pilot system running for a machine that does just that: intakes and processes adverse events. The company is focused on delivering digital transformation for clients through its Lean Digital approach, an integration of elements including lean principles, design thinking, analytics and digital technologies. "The market evolution is immense and whilst cost optimization is still key, the discussion these days is all around improving outcomes, better effectiveness, variable capacity and agile innovation," said Manu Goel, senior vice president and Genpact.

In March 2017, Genpact announced the acquisition of Rage Frameworks, a leader in knowledge-based automation technology and services, adding enterprise-level AI capabilities to further Genpact's ability to drive digital transformation. "As clients evolve their digitization journeys, AI is moving from experimentation into the mainstream," said Sanjay Srivastava, Genpact's senior vice president and chief digital officer, in a press release. "Enterprises are looking for comprehensive solutions which they can successfully deploy without an army of AI specialists…"

Implementation

Technology and computational power continue to increase by huge increments, and it would be a challenge to remain at the forefront of process innovation. However, the life science industry seems not so much to be impeded by a lack of capability but by a lack of desire to implement new technologies. Because the industry is very high risk, life science companies tend to eschew cutting-edge innovation in favor of "tried and true" processes and technologies. However, there are some key factors driving faster adoption of new technology. "Traditionally, the pharmaceutical industry has been slow to change, but there is currently a greater need and financial pressure," emphasized Valarie Higgins, Almac Clinical Technologies' president and managing director. "Because of developments in healthcare and pressures around costs, companies and the industry at large are accepting change at a more aggressive rate than I have seen in my 20 years in the industry."

Smaller companies are less hesitant and more likely to outsource because they have fewer established tools and specialized personnel in this area.

A key concern and arising challenge is security, which is of great importance to the industry. "External studies show that over 3.6 billion data records were compromised worldwide between 2013 and 2015," highlighted Joshua Grauso, Sales Manager, UL Consumer & Retail Services.

"This covers data breaches in retail, government, healthcare and financial sectors. The cost of this has jumped past approximately $4 million per incident, which does not even account for potential loss of sales and revenue. We have to ensure that as technology changes, there is a level of security that can be trusted."

The Health Insurance Portability and Accountability Act (HIPAA) insures companies collecting data from patients on the commercial side. However, privacy will become increasingly problematic with electronic data.

Image courtesy of Novartis

MANUFACTURING – DEMAND SPURRING DIVERSIFICATION

"As an industry, there has been a drive for the FDA to really streamline and clear up the backlog of ANDAs, of which there are more than 3,000 still unapproved. It is still critical for us to focus on reducing the cost burden by accelerating competitive generic entries vs slowing them down through tariffs or other forms of blockage. Any disruption can create challenges for the industry's ability to produce new generic high end equivalents at competitive prices."

- Alok Sonig,
Executive Vice President,
DR. REDDY'S LABORATORIES

Manufacturing

Managing the Increasing Complexity of Manufacturing and Supply Chains

Home to the world's leading pharmaceutical companies, the United States is the forerunner in the global market with 2015 sales of $333 billion, triple the size of its nearest rival, China. Alongside the vast number of U.S. companies that continue to expand their reach both throughout the United States and internationally, many international companies have also set up shop for greater proximity to U.S. customers and to take advantage of a number of opportunities. Posting a 2.6% increase in worldwide sales on the previous year, Johnson & Johnson tops the leaderboard with worldwide sales of $71.9 billion in 2016. Long an industry leader, the company is joined in the Top Ten by familiar notable names such as Pfizer, Novartis, Roche and Merck. The prominence of U.S.-based companies is significant.

When it comes to manufacturing, whether for the brand or generic market, cost is a primary consideration. For brand drugs, development costs are so high, and reimbursement once in the market so challenging, that companies strive for efficiency and cost effectiveness throughout the process. As the U.S. generic market matures, companies need to focus on cost even more as competition increases. In this respect, a vertically-integrated supply chain can be hugely beneficial. "Outside the cost advantages, which are clearly key, the increased degree of control is also a key factor," stated Robert Cunard, CEO at Aurobindo. "Having presence in API as well as the finished dosage forms mean we have development teams working side by side; we feel that there is much greater efficiency when those teams are working together to address challenges throughout the process, rather than operating independently."

Whilst supply chains are becoming more globalized, they are still often very complex, particularly as many companies spread operations over multiple locations. When it comes to sourcing, many companies prefer their suppliers to be locally-based, although their launch location will be factored in, and repatriation of manufacturing into the United States and Europe continues to be a trend. Tax is another consideration and, whilst previously perhaps a motive to move business elsewhere, other forms of taxation could add pressure to importers under the new Administration. The much-discussed Border Adjustment Tax (BAT), for example, would prohibit domestic companies importing goods and services from deducting those costs from their tax base, while also meaning they would not be charged tax on revenue from exports.

However, recent forecasts predict that the BAT is unlikely to go ahead, at least in its current form. Washington Analysis, for example, believes that there is a 60% chance of no BAT, or that it will at the very least be vastly watered down in the final bill.

Cost savings are of great importance to the industry, but quality is held above all else. Increasingly stringent FDA guidelines ensure that companies operate within a certain set of parameters, and companies are eager to follow best practice to support patient safety and the highest standards.

Image courtesy of CordenPharma

Alok Sonig

Executive Vice President
DR. REDDY'S LABORATORIES

An Indian multinational pharmaceutical company with three manufacturing sites in USA

Dr. Reddy's has become particularly strong in India since its establishment in 1984. How do the company's U.S. operations fit into the global picture?

Dr. Reddy's is a $2.3 billion company, present in nearly forty countries, and the United States is our largest market, accounting for about 55% of our sales. The United States is a key geographical location for us and is home to our proprietary business product, focusing on addressing patients' needs through innovative NDA's and NCE's, alongside the 505(b)(2)'s in the fields of neurology and dermatology. Whilst our headquarters are in Hyderabad and the bulk of our operations are in India, we have three sites in North America: an oral solid and topical facility in Shreveport, Louisiana, an antibiotic penicillin facility in Bristol, Tennessee and an API plant in upstate New York, which works on pre-launch products and dosage forms. Our U.S. pipeline is rich, and we expect to file 20+ products every year and certainly anticipate growth in our U.S. footprint. Within the generics segment in North America we have three key business: the retail business (Rx), which is the standard generic prescription business in the U.S., the hospital business, which is our specialty Rx business, and is mostly injectable oncology products, GPOs and integrated delivery networks. The third is our $200 million OTC business, which has Store brand OTCs as a more significant portion, and also recently added the branded OTC business. We recently acquired six OTC brands from Ducere Pharma: Doan's, Bufferin, Nupercainal Ointment, CruexNail Gel, Comtrex and Myoflex.

What is Dr. Reddy's strategy for strengthening its portfolio, and the importance of recent acquisitions such as the Teva assets?

Our portfolio selection philosophy is strongly driven by one of our key brand promises 'Bringing Expensive Medicines within reach'. As part of this strategy, we have made deliberate choices focusing on categories such as Complex Injectables, Transdermals, and Controlled substances to bring affordable options for the patients and also create sustainable value for the company. We acquired the assets from Teva because some of them were novel dosage forms; complex assets in markets which are likely to have limited competition. The acquisition has also allowed us to leverage our capability in the Rx segment significantly towards commercialized success. In this sense, we will not require incremental resources to commercialize those assets.

We also acquired the Habitual brand from Novartis a couple of years ago, which is commercialized mostly as a private label asset. We therefore have quite a favorable position in the OTC space and will continue to grow that part of the business. The Rx business is of course the bread-and-butter business and accounts for about two thirds of our business in the U.S.

In what ways is Dr. Reddy's pushing development in the biosimilars space?

Biologics and biosimilars are critical to our growth in the long term, and we will be looking to address the high cost burden in the biologics space. We are focused on emerging markets, and our short term strategy is to focus primarily on India, as we feel that we could leverage our work on biologics in India more efficiently and effectively and really address their cost burden. The Indian market tripled in size when we launched biosimilars in therapy areas.

From a regulatory perspective, should there be further developments to make the environment more conducive to new products entering?

As an industry, there has been a drive for the FDA to really streamline and clear up the backlog of ANDAs, of which there are more than 3,000 still unapproved. It is still critical for us to focus on reducing the cost burden by accelerating competitive generic entries vs slowing them down through tariffs or other forms of blockage. Any disruption can create challenges for the industry's ability to produce new generic high end equivalents at competitive prices.

What are the core areas of focus within the business for the next few years?

In terms of emerging markets, we want to increase our presence in key therapy areas, and grow our presence in regions such as Russia and India. We are also looking at expanding our footprint in a few additional emerging markets predominantly leverage our strong Oncology and Biosimilars pipeline. Within the United States specifically, the objectives are to grow the retail, specialty Rx and OTC business.

Robert Cunard

CEO
AUROBINDO

Aurobindo is a provider of broad line generics based in India

Since Aurobindo's establishment in 1986, how has the company's offering developed?

When the company first started it was all APIs, sourcing from other companies and reselling into the market, and then we migrated into manufacturing. For the first 15 years, the company's sole source of revenue was the sale of APIs. Aurobindo then followed a natural progression into the development of finished dosage forms, and grew exponentially in terms of geographical reach and product portfolio.

While the United States and Europe account for about 67% of Aurobindo's business, at about 45% and 22% respectively, Aurobindo is present in more than 150 countries, either on its own or through an affiliate. Our portfolio is extensive and comprises over 2,000 products around the globe, and has continued to evolve across different categories: from the typical oral solid products such as tablets, capsules, and suspensions into injectables. Recently, we announced an initiative on the biosimilar side. Aurobindo has always positioned itself as a broad line generic provider, so it makes sense that our portfolio should reflect the proprietary marketplace.

What are the advantages of Aurobindo's vertically integrated supply chain?

We are now moving into a more mature U.S. generic market where cost will be key. By keeping processes within our own four walls, we forego a number of markups along the way, and can hopefully drive that value to our customer. This will allow us to compete at a higher level in more cost competitive markets and also improve profitability for us.

The increased degree of control is also a key factor. Having presence in API as well as the finished dosage forms mean we have development teams working side by side; we feel that there is much greater efficiency when those teams are working together to address challenges throughout the process.

How well equipped is Aurobindo to deal with complications in the supply chain, particularly in a drive to increase manufacturing within the United States?

In light of recent dialogue around increased manufacturing within the U.S., and in conjunction with our existing U.S. manufacturing presence, we have the ability to pull some of our projects forward, or expand our U.S. operations to meet that need. Nevertheless, Aurobindo's supply chain is long and complex, similar to most generic pharmaceutical companies with numerous API and Formulation manufacturing sites, and all these sites are governed by numerous regulatory authorities for the markets they serve. Rapidly altering the supply chain would be difficult in such a highly regulated environment.

The location of Aurobindo's R&D facilities in New Jersey and North Carolina are clearly strategic. Could you elaborate on the capabilities and recent developments at these facilities?

In total we have seven R&D facilities including two in U.S. We currently have about 25 people at the North Carolina Research and Development facility, which is largely being remodeled. The 140,000 sq. ft. area will be built out primarily for R&D to target inhalation products including nasals, meter dose inhalers, dry powder inhalers, and some transdermal and topical products.

In New Jersey, we have recently decided to expand into injectable, aseptic manufacturing. We have two development teams in New Jersey. The first is working on the controlled substances group, with about 15 projects that we hope to file in our next fiscal year, beginning April 2018, and second on the injectable side with complex injectables, depo injections, microspheres, and liposome technology. These groups also work closely with our R&D groups in India, giving us a large resource pool. In mid-February we also announced the TL Biopharmaceutical acquisition of four biosimilar projects, which we will be combining with eight of our own projects.

Where would you like to see the company in a few years' time?

We would like to see Aurobindo evolve to a $5 billion revenue company. We finished last year at slightly over $2 billion, continuing to diversify in portfolio as well as markets. We are targeting certain emerging markets..

As we continue to expand and work closer with our customers on different fronts, a logical step would be to leverage some of our intellectual property gained through the years and try to expand in different footprints.

Himanshu Brahmbhatt

Vice President of Business Development & Sales
SUNRISE PHARMACEUTICAL, INC.

Sunsrise Pharmaceutical is a generic drug company manufacturing products under its own label

How has Sunrise Pharmaceuticals developed since its establishment in 2004?
Sunrise Pharma started back in 2004 as a private label and contract manufacturer of predominantly over-the-counter (OTC) and prescription drugs. As of 2012, we have shifted our focus and currently Sunrise is solely a generic drug company. The biggest recent development is that we are now commercializing our own generics and expanding our development pipeline. Of our multiple approvals, one of our products was approved within just 13 months, an industry record of which we are very proud of as a company.
We have recently added another building, increasing our capacity by an additional 33,000 sq. ft, which can be used for manufacturing, packaging, and storage. This enhances our current manufacturing capacity to about a billion tablets and half a billion capsules per year.

What prompted Sunrise Pharmaceuticals' move out of the contract manufacturing and packaging space?
It was a clear cut decision considering our new product approvals; we needed to sustain our own product portfolio and to manufacture our own products. Our contract manufacturing projects were tying up our own capacity. Moving forward, Sunrise will be a private label and will only manufacture products under its own label. Our product portfolio has a good mix of products and some are volume based which requires substantial manufacturing capacity. Thus we are now fully dedicated to manufacturing all our own products.

How have you found the approval process in the United States?
For the most part we have been pleased with the approval process given that one of our products was approved within 13 months, though there are approvals which are taking much longer than expected. On the one hand we did not anticipate the GDUFA fees going up, we expected that these fees would accelerate the rate of approval but with the FDA backlog there has been delays. In that respect, it has certainly impacted our business in a somewhat negative way. But we look forward to this year for a faster approval time.

In terms of manufacturing under its own label, where does Sunrise Pharmaceuticals position itself in the market?
Since 2012, Sunrise Pharma has positioned itself as a generics company, while successfully launching several of its generic drugs. We have penetrated all channels of distribution on the commercial side so overall it has been a great start. On the development side, we are looking into new capabilities. We are currently only doing solid doses, but we are looking into different manufacturing technologies. We are exploring some interesting oppourtunities towards topicals, liquids, and biosimilars technologies.
Our competitiveness comes from many different angles; one is our tremendously talented personnel, with a collective wealth of knowledge across NDAs and ANDAs sphere. Also, as a small cohesive unit, we are able to make decisions very fast and can be very flexible.

What are Sunrise Pharmaceutical's plans for growth, particularly in terms of increasing capabilities and market reach?
We are approaching growth from both organic and inorganic perspectives. Our primary focus is expanding our current capabilities including our facility expansion, R&D/new product development, increasing our customer base and grow our personnel. We will steadily continue to invest on this front.
Secondarily, we are looking into acquisitions and investments if we find the correct fit. We have been exploring oppotrunties with potential partners both within the United States and internationally, specifically in Europe and Asia. These partnerships will be crucial not only on the licensing side, but also on the development end. We are seeking partnerships based on established track record, experience with the relevant technology and a good understanding of the regulatory landscape within the United States, EU, and Asia.

Kristin Brancato, PhD

Vice President and General Manager
CYALUME SPECIALTY PRODUCTS

Cyalume Speciality Products manufactures a wide range of APIs

Cyalume Specialty Products is one of three divisions within Cyalume. Could you give a brief introduction to this arm of the company and its areas of focus?
Cyalume Specialty Products manufactures and provides a full range of support services for the specialty chemical products market with focus on the pharmaceutical, medical products, cosmetic and commercial markets. The products we manufacture range from simple raw ingredients, to finished product formulations, to complex high performance polymers. Our company culture is one of prevention, compliance and improvement. We identify and adopt industry best practices, not only to promote safety, but to protect against costly delays. We reinforce these efforts through continuous investments in the latest equipment and processes across our global network.

Could you comment on some of the trends in the United States in the API space, particularly from a regulatory perspective?
The U.S. market for pharmaceutical ingredients is ever-changing, and many companies face challenges with increasingly stringent regulations. We may characterize the period that lies behind us as one of a "double standard" of regulatory requirements for the manufacture of API's: the level demanded by the U.S. FDA, and that required by the rest of the world. There can be no doubt that we are on the verge of entering a new era, in which the market for APIs has become global. However, differences in regulatory requirements for different markets have made this global market an extremely complex one to operate in. Fierce competition on one hand, coupled with the very strict limitations imposed by regulatory requirements in only some parts of the market, have been the source of numerous dilemmas for the API industry. The fact that "FDA compliance" and high manufacturing costs go hand-in-hand has made it extremely difficult for manufacturers to supply the entire global market and at the same time maintain competitiveness.
With the EU adopting regulatory requirements and, importantly, enforcing API inspection systems of a level similar to those of the FDA, with increasingly more countries expected to follow suit, the time is rapidly approaching when there will only be a business future for companies that can meet the new higher and ultimately global, regulatory standards. This will be an enormous step forward in terms of securing the safety of medicines.

Are there any particular areas of focus from an R&D and innovation perspective?
Cyalume's core competency is innovative molecular architecture via synthesis and manufacturing of sophisticated and complex multi-step chemical processing. We spend a lot of time with our customers in their early-stage development work to understand novel chemistries and unique methods of delivery. The idea is to integrate into the customer's project pipeline before the commercialization stage to help jointly build the program and regulatory framework, whether from a sourcing, process development or quality perspective. Being involved early on also means being ahead of the game in knowing investment costs, whether it is capital, human resources, equipment or processes when it comes to launching the product.

What steps has Cyalume taken to ensure quality and best practice?
We made sure to hire the right people and put the right procedures and processes in place, and re-evaluated our entire portfolio of standard operating. In addition, we increased training and awareness, and invested heavily in new laboratory equipment for better results, and digitized the processes. Our New Jersey manufacturing facility is FDA-approved, and meets all regulations and requirements. Some of our customers have shown preference for the manufacturing of the finished products to take place in the United States versus importing. Import regulations are also becoming more stringent. Today, all of our manufacturing is out of this facility, and this is an aspect that attracts customers. We also have ten drug master files (DMFs), all related to APIs, of which seven are active.

What are the core areas of focus going forward?
We will remain very much focused on API manufacturing. We have recently brought a old API back online for use in the prevention of urinary tract infections, which we are selling into both the branded and generic markets. We are also focusing on an active ingredient for anti-itch as an alternative to hydrocortisone.

Jagadeesh Babu

CEO
BIOPHORE

A pharmaceutical company developing and manufacturing niche pharmaceutical products for the generic industry

How has Biophore developed since its establishment in 2007?

We started Biophore with 10 chemists, beginning as a technology development center for APIs focusing primarily on the U.S. and European market. Over the last decade, we have grown significantly, and today have about 300 scientists, 60 drug master files, more than 60 patents filed, and two FDA-approved manufacturing assets. Biophore has grown significantly every year and consistently has double-digit financial growth year on year. Biophore is mostly U.S.-centric. Almost 70% of the revenue comes from the U.S. market and around 30% from the European market. We are currently trying to enter into the other markets with the aim of establishing a global presence by focusing on entering less regulated markets in the coming years.

Biophore's first fully-owned manufacturing is coming online in 2018. What manufacturing assets does Biophore currently have access to?

Biophore is an acting partner in two manufacturing companies. One is Sionc Pharmaceuticals and the other is Azico-Biophore. These facilities manufacture exclusively for Biophore and are located in the Pharma City Industrial Park in Vizag, with a distance of just half a kilometer between them. The third facility will also be located in the same place.

Biophore API manufacturing facility will have multi product manufacturing capabilities, like oncology, steroidal, contrast agents and peptides.

Biophore operates across 30 therapeutic segments. What are the main areas of focus?

Generally, we do not take the therapeutic segment into consideration when selecting a product. However, there are a few exceptions. We focus a great deal on oncology products, contrast media, and diagnostic products, and we have a greater number of products in these areas than in others. Contrast media, APIs meant for injectables for MRI screening, are Gadolinium- based, and only the big companies play a significant role in these products, such as Bracco, GE Healthcare and Bayer. Biophore has, however, succeeded in developing some generic APIs and has done extremely well in the European market in particular.

From an R&D perspective, what are some of Biophore's main focus areas?

Our method for portfolio selection differs from that of many pharmaceutical companies. We do not want to manufacture bulk APIs. Instead, we want to manufacture products with greater complexity and an element of uniqueness. These products are more niche, higher priced, and have better control in the market.

We do not want to be in bulk of API. Instead, we want to make more products with more complexity that have some kind of uniqueness to them in the API niche. As a recent player in the API game, competing with many established players, we want to be differentiated. We can do this through intellectual property, product selection, and uniqueness of product. We work with more complex chemistry towards more unique products.

What are the key objectives for Biophore going forward?

We want to enter more niche areas, such as macromolecular complexes, iron products, carbohydrate chemistry and peptides. Biophore specializes in macromolecular iron products, such as iron sucrose and sucroferric oxyhydroxide. Although the chemistry looks simple in these products, they are more complex in terms of characterization. This will demand a high level of innovation and present barrier to entry. As we have already seen success with similar products, we would like to continue in the same area.

Peptides is an area in which we have developed and commercialized some products. For some of the peptides, the yearly consumption is close to 20 grams per year. There is a lot of value here because only a handful of companies will focus on developing 20 grams of peptides for the generic industry. Even if the product involves a lot of challenges in terms of synthesis and isolation of the impurities, we see it as an opportunity. We do not want to dive into the higher-volume game; we want to succeed in high-complex areas.

Biophore would like to be a key player in the API industry, filing 15 DMF's per year for the US market and to be top 10 players in the API world.

Terry Herring & Peter Valko

TH: President of Commercial Operations
MISSION PHARMACAL
PV: Chief Operating Officer
BIOCOMP PHARMA

Mission Pharmacal is a family of companies comprising wholly-owned subsidiaries that function independently and collectively to offer customizable solutions to customers

TH

PV

Could you give an overview of Mission Pharmacal in 2017?

TH: In addition to Mission Pharmacal proper, the Mission Family of Companies is comprised of Alamo Pharma Services, Inc. ("Alamo"), a contract sales and outsourced sales solutions company; BioComp Parma, Inc. ("BioComp"), the generic arm of the organization; ProSolus, Inc. ("ProSolus"), one of the industry leaders in transdermal patch technology; Espada Dermatology, Inc. ("Espada"), prescription and esthetic dermatology products; as well as BexR Logistix, LLC ("BexR") and their subsidiary company, EPIC Fulfillment, Inc. ("EPIC"), the logistics and fulfillment arms of Mission. Specific to ProSolus, we have our original facility in Miami as well as a newly completed facility in Boerne, Texas, outside of San Antonio. These are significant changes over the last six years for a company that, for most of its 70-year history, has been a specialty pharma company focused in urology and women's health, and we believe this sort of diversification will continue. Very few organizations, if any, can work with a partner company the way we can in terms of providing customizable solutions that can be scaled to meet their particular needs. This is especially true in an industry landscape in which most companies are increasingly focusing in one area. We have partner companies that work with two or three of the different Mission subsidiaries which is a winning combination for all included parties. That is the exciting part to us.

What are some of the main areas of focus in the transdermal space?

TH: Transdermals are a high-tech area with a high barrier to entry. At this point, there are very few transdermal products available to patients–somewhere in the teens–out there as transdermal brands. ProSolus is developing transdermal patches that can be taken off and put back on while maintaining the pharmacological integrity of the product. Customers can expect to see next-generation products working more like consumer adhesive bandages than others in the market in terms of size and flexibility. Aside from the work at ProSolus, Mission is currently bringing in several different products that will improve our ability to manufacture creams, liquids, and semi-solids. Our Dr. Smith's® spray utilizes the Greentek™ Spray System powered by Honeywell Solstice® Propellant and was recognized by the White House for its earth-friendly characteristics due to the product expelling no fluorocarbons. This product feature applies to both our diaper rash spray and our adult barrier spray. Through our relationship with Honeywell, we are looking to introduce this technology to other companies worldwide that utilize spray technology. Our motto is that these sprays are "Mother Nature and Mom friendly."

What is the strategy for the ProSolus business segment?

TH: There is a great opportunity in private-label manufacturing of transdermals in the retail world. We have the capacity to do that at a great price. Secondly, we plan to continue our Abbreviated New Drug Application (ANDA) development. Transdermal ANDA development is a great place to take generic products and put them into a transdermal delivery that increases patient compliance. Then, there is the New Drug Application (NDA) portion. We provide for our own generic companies, but we are also making transdermals for other generic companies via strategic partnerships. Finally, we have a partnership with a consumer-transdermal company targeting branded consumers with consumer private label, consumer brands, and generics. Our facilities in Miami will focus on generics and branded NDA products. The newly configured ProSolus manufacturing site in Boerne, Texas, has a bigger footprint with bigger equipment than what is currently at the Miami location. With the added capacity, the Texas site will focus on higher volume private label and consumer products that have lower-margin requirements.

What are the strategies and the outlook for the family of companies as a whole?

PV: Each of these companies has the support, direction and push from corporate, but each component is a self-sourcing energy center. Together, we are strong and can continue to create solutions where there are needs. In two years, we hope that the legacy of each of these new businesses becomes something that can spin out on its own.

TH: The broad outlook is that within five years we will have a better-defined services group and the leadership required to drive the business development process. We are already moving into the early stages of a client manufacturing and formulation development group. Furthermore, we hope that Mission Pharmacal will have its own international pharmaceutical and consumer companies, and our dermatology business will be its own standalone business.

Sourcing Overseas: The Quality Debate

Despite the strong drive to reduce cost and drive efficiency, previously a major driver for outsourcing in particular, companies have circled back to quality as the most important criteria in drug manufacturing. This renewed emphasis rightly adds pressure and, indeed, several organizations have fallen at the quality hurdle.

Many companies feel that close-to-home translates to better quality and are reassured by reduced concerns surrounding supply chain security. Equally, the increasing emphasis on quality and compliance, coupled with rising labor costs, has narrowed the cost advantage of Asian manufacturers and suppliers. In China especially, the market landscape has changed as the government clamps down on environmental regulations with longer registration periods and a more stringent process. "There was a time in which India and China held a strong cost advantage of about 25% to 40%," stated Anil Kripalani, president at Ash Ingredients, a company focused on the custom synthesis of advanced intermediates. "However, this cost advantage has been reduced in time. Following new regulations in China, our manufacturing partners have invested heavily to remain compliant. Equally, labor costs have risen significantly."

Ash Ingredients, which together with Longchem Chemical Corporation forms Ash Longchem, has its principal office in Glenrock, New Jersey, and subsidiary operations in India and China, alongside a number of strategic partnerships.

Whilst the cost advantage may be receding and compliance requirements are becoming tougher, there remains a preconception that outsourcing to jurisdictions such as India and China automatically equates to poorer quality. U.S.- and Europe-based companies present their local operations and facilities as differentiators and key markers of quality and cite international contract service organizations as responsible for poor-quality products entering the market, which could be detrimental to patients' health and safety.

The FDA is more committed than ever to ensuring quality with increased inspections at plants both within the United States and internationally, with a particular focus on Asia. "Across the board, there have been more inspections, more warning letters, more import alerts, and more zero-notice inspections," noted Melissa Authelet, director, regulatory and compliance at Rochem, a distributor of pharmaceutical, food, nutritional and animal health ingredients working with Chinese manufactur-

> "As the FDA and other regulatory agencies continue to push back more and more, we have seen a trend with the FDA being very hard in Asia. In 2016, 14 warning letters were issued to manufacturers in China (44 worldwide). In 2017, between January and March, it has been 6 in China (17 worldwide). When we started, the supply chain was not so closely scrutinized. We welcome the increasing scrutiny as it has given us an advantage over our competitors as we have taken proactive steps to be in compliance."
>
> - Anil Kripalani, President, Ash Longchem

> It is a binary game: companies have to be right 100% of the time. If a customer loses a major product because they are single-sourced or even dual-sourced, the supplier is out. The higher number of inspections in Asia is something that U.S. and European suppliers have requested for years and, whilst the playing field is not yet level, it is much more so than previously.
>
> - Charles Dodd,
> Executive Vice President,
> Rochem International

ers. "The FDA's presence in India and China has greatly increased and seemingly every month a major player gets knocked out with a warning letter or import alert. This can have huge repercussions throughout the supply chain, with manufacturers in the United States experiencing drug shortages, and so on."

The FDA launched the CDER Office of Pharmaceutical Quality (OPQ) in 2015 to address gaps in drug quality, with the motto "One Quality Voice". As well as endeavoring to enhance quality drug assessment through integrating review and inspection and establishing consistent quality standards, using quantitative metrics to help monitor quality, OPQ also continued to work with international regulators on ICH Q12.

Some efforts are being made to harmonize regulations and compliance requirements internationally. For example, FDA and EMA agreed in March 2017 to recognize each other's audit reports through a reciprocal agreement. "Generally, the trend is towards global alignment," commented Rino Coladangelo, CEO of Rephine, a U.K. company specializing in European regulation and GMP compliance. "PCI/S is trying to get regulatory authorities to sign up to work towards a universal standard all over the world. The challenge is in trying to bring every country into line for a certain degree of harmonization."

The FDA's focus on compliance may be a disruptive force among supply chains, but the benefits in the long term of a closely-adhered-to global standard would be tremendous. Harmonization across international markets would not only increase patient safety but make the framework more easily navigable for the companies operating within it. —

Quality: a means for Value Creation

By Rashida Najmi, Global head of Quality, Regulatory, Pharmacovigilance(PV) and Patents, Piramal Healthcare

Pharmaceutical firms and contract manufacturers that supply into the firms are regularly challenged with balancing the need to bring cutting edge and innovative medicines quickly and cost effectively to the patients, with the need to ensure that there is no compromise on their quality and safety. In a highly regulated industry such as pharma, quality assumes significant implications since sub-standard medicines can jeopardize human life.

40% of the finished pharmaceuticals that are consumed in the US are imported; this figure is close to 80% for active and bulk pharmaceutical ingredients. As per the FDA Safety and Innovation act, GDUFA, signed in July 2012, the agency has to inspect global plants on the same schedule as it does the ones in the US. The FDA has also been tasked with clearing the backlog of drug applications seeking approval within five years. These factors, coupled with some high profile compliance failures, have triggered increased vigilance over the past few years.

Among the multitude of factors cited for non-compliance, two common issues have emerged and have been highlighted by the regulatory agencies: Data integrity (DI) and cross contamination, which affects product quality.

Data integrity issues arise when regulators are not convinced of the data based on which the products are launched in the market. In 2015, 74% of the total warning letters issued by US FDA were linked to DI and the number increased to 79% in 2016.

Compliance derailment can cause value destruction; an import alert or warning letter may trigger significant decline in stock prices of a firm. Moreover,, it results in a delay or unavailability of drugs to patients. For drug manufacturers, recent events have underscored the importance of managing regulatory risk in order to remain a viable business.

CDMOs supply drug substances and drug products to various countries across the globe; as a result they are audited by both the respective regulatory agencies from the country of launch, and by their customers. For CDMOs, customer audits are as critical as regulatory audits as they ensure that the manufacturing sites are perpetually audit ready. The good service providers usually lever this and adopt best practices in Quality and Compliance through engagement with their global customer base. CDMOs must view the current regulatory landscape as an opportunity to provide a differentiated and sustainable advantage in a competitive market. The regulatory landscape is also quite dynamic and is evolving rapidly. At Piramal, we have an internal cell that tracks all regulatory updates including 483s, observations, and new regulations in the industry on a daily basis. Existing practices can be evaluated vis-à-vis these events to identify possible deficiencies.

The nature of regulatory inspections has also undergone significant changes. Earlier, regulators scouted for evidence of non-compliance, whereas they now have a perception of non-compliance and leave it to the firms to demonstrate otherwise. This shifts the onus of proof to the CDMO or the pharmaceutical firm. Until recently, citing deficiencies used to be the norm, however lately regulators have started citing improvement opportunities during inspections. To help reduce the challenges inherent to inspections, it is essential to continuously remain in contact with regulatory authorities. Collaborating with FDA by participating in meetings concerning quality metrics is crucial.

Quality has been long viewed as a means to successfully clear regulatory audits and obtain product approvals. This approach could be attributed partly to the quality issues at the manufacturing sites. Firms must shift focus from Quality for Compliance to Quality as a Culture by keeping the end patient in mind.

Finally, it is our belief that Quality is a collective responsibility and must be woven into the fabric of any organization. Foremost of all, Quality must be aligned as a business strategy within the organization. A strong governance and escalation mechanism is the foundation of any quality organization and it must exercise autonomy and have a reporting structure independent of operations. A robust review process should employ various tools including data integrity calculations and drive towards an audit readiness scorecard that can quantify the quality health of sites within the organization, and potentially, predict quality outcomes. Stringent internal audits at manufacturing sites by the Corporate QA team are a means to proactively identify risks and mitigate them.

"A strong quality culture is best indicated by what is done when nobody is looking. Culture is the cornerstone of Quality"

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THE INDISPENSABLE PARTNER: CONTRACT SERVICES

"Large pharmaceutical companies have grown better at outsourcing and now understand the advantages better. It has become a much more accepted business model and much more complementary to pharmaceutical supply chains."

- Gil Roth,
President at the Pharma and Biopharma Outsourcing Association (PBOA).

The Indispensable Partner: **Contract Services**

From Service to Solution

Outsourcing trends continue to pick up pace as pharmaceutical companies respond to pressure for faster and more cost-effective routes to market. Contract service organizations have recently become a much more widely accepted component of supply chains across all areas of development.

In response to rising pressure to identify new drugs and competition from generics alongside increasing R&D costs, outsourcing of research is increasingly common. Grand View Research expects the global healthcare Contract Research Organization (CRO) industry to reach $45.2 billion by 2022, highlighting stringent timelines as a key driver for increased demand for outsourcing of research activities. Universities are also benefitting from this trend, more able now than ever to collaborate with industry and eager to have the opportunity to commercialize research.

Covance, a global leader in the CRO field, worked on all of the top 50 best-selling drugs available today through its full spectrum of nonclinical, clinical and commercialization services. Today, the company acts as LabCorp's drug development arm since the acquisition in 2015. LabCorp, now the world's leading healthcare diagnostics company, acquired assets of Mount Sinai's Clinical Outreach Laboratories, giving more direct access to the New York metro market health system in January 2017. From October 2016, LabCorp is also the first U.S. laboratory to offer molecular testing, with new fully automated cobas 8800 system from Roche.

For the sixth time in eight years, QuintilesIMS was recognized as the Best Full-service Provider CRO at the 2016 Scrip Awards. The merger between Quintiles and IMS Health, completed in October 2016, is a prime example of companies integrating services to provide a more extensive offering, as indicated by the award. The combination of companies brings together a wide range of capabilities, spanning healthcare information, technology and service solutions, with the intent to drive efficiencies and insights across the entire life sciences product lifecycle, from R&D through commercial execution to real-world patient outcomes.

Following the trend for integration, inVentiv Health's business model is built around a CRO combined with a global Contract Commercial Organization (CCO). In the past five years, inVentiv Health has helped to develop or commercialize 81% of novel new drugs and 79% of novel new oncology drugs approved by the FDA, as well as 70% approved by the EMA.

Years ago, large-scale CMOs began to venture into the development side, resulting in a number of contract development and manufacturing organizations (CDMOs). In addition to offering flexibility and time efficiency, many of these organizations also offer capabilities and innovative processes as an advantage. Large Pharma companies often turn to CMOs and CDMOs for areas of niche or specialized expertise, such as biologics, antibody-drug conjugates (ADCs) and highly potent compounds.

According to business-intelligence provider visiongain, the pharmaceutical CMO market is expected to grow at a CAGR of 6.4% over the next five years, and at 5.7% over the following five, with the market reaching an estimated $88bn in 2021 and $124bn in 2027. "Large pharmaceutical companies have grown better at outsourcing and now understand the advantages better," explained Gil Roth, president at the Pharma and Biopharma Outsourcing Association (PBOA). "It has become a much more accepted business model and much more complementary to pharmaceutical supply chains."

PBOA, established in 2014, is a representative body for CMOs and CDMOs. Recently, the association worked closely with the FDA to negotiate the second five-year iteration of the Generic Drug User Fee Authorization (GDUFA), contributing to the development of a new financial model intended to be less burdensome for contract manufacturers. By lessening the financial burden, GDUFA II is more supportive of new CMOs entering the space and will likely contribute to further growth of the sector, particularly in terms of smaller organizations with more niche

> "Due to a recent change in guidance in China, there are hundreds of studies that need to be redone. Frontage is handling that work on the frontline. With business booming and highly positive forecasts and outlook, 2017 will be a very good year for China-based CROs."
>
> - Azhar Kalim, Head of Business Development, Frontage

and specialized capabilities."Companies are realizing that it is much more efficient to come to [a contract services] company to develop processes and ultimately be able to scale them up as opposed to doing them internally," commented Andrew Brennan, general manager U.S.A. operations at Novasep. "This trend will likely continue because it just makes logical sense."

Highlighting Novasep's specialized expertise in development processes, chemical processes and purification processes, Brennan continued: "Since this is our expertise, we will naturally be more efficient than companies that do not have this expertise at their core. We can often draw on past experience to be able to accelerate the ultimate success of customer programs to greatly reduce the development time."

Catalent leads the pack, continuing to grow and add new technology capacity, investing over $1 billion back into the company, including over $600 million of CAPEX and more than $400 million in M&A, in the last five years. Catalent recently fully acquired Redwood Bioscience, adding an antibody drug conjugate (ADC) technology to its portfolio called SMARTag, and acquired Pharmapak Technologies in 2015. Having been purchased from Cardinal Health by Blackstone Private Equity and a few others in 2015, Catalent is now a fully-public company traded on the New York Stock Exchange (NYSE), following Blackstone's sale of its last remaining interests in September 2016.

In 2017, Catalent has continued to add capabilities, with the acquisition of Accucaps, a Canada-based developer and manufacturer of Over-the-Counter (OTC), high-potency and conventional pharmaceutical softgels. In addition, the CDMO has also completed a $15 million expansion at its Winchester-Kentucky control-release facility, doubling capacity, and in April 2017 completed an expansion project at its Kansas City, Missouri, facility to significantly increase controlled-temperature storage capabilities for its clinical supply business. Further investment and expansion to Catalent's workforce is also to be expected in its clinical supply network at Bolton and Bathgate in the U.K., and in Singapore.

Patheon also recently completed its initial public offering (IPO), increasing cash flow and equity to grow the business. With a diversified client base, including the top 20 pharma firms, Patheon is also very focused on small and emerging companies. In fact, the CDMO has been highlighted on the 2017 PharmSource CMO Scorecard as supporting approximately 30% of new drug approvals (NDAs) in the United States in 2016, more than any other CMO.

These contract service giants are particularly successful in offering a complete set of services, offering clients a simplified supply chain solution that does not necessitate coordinating multiple organizations. For example, Patheon utilizes its simplified development path, OneSource, claiming to eliminate eight to 12 weeks of development time for small molecules and 14 to 20 weeks for large. Meanwhile, smaller companies flourish when working in specific technologies in which they excel, that the larger companies might not have extensive expertise in. Many mid-sized and smaller companies also differentiate themselves based on claims that they are more flexible and adaptable, and therefore better able to respond quickly to unexpected changes and implement client methodologies.

For instance, Alcami Corporation offers a Protect Your Brand service, a no-strings-attached arrangement for companies dealing with sudden supply constraints. "We want to offer a quick, flexible solution to these companies with a fast tech transfer," explained Stephan Kutzer, Alcami's CEO. "Our contractual setup and initial contracting can occur in less than two weeks whereas some larger providers take months to sign a service agreement… We do not require any long-term commitments and are able to set up a project for short-term supply. This is the most flexible offering in the market today because it provides a flexible manufacturing solution to help drug makers protect their supply."

As companies continue to strive for greater efficiency and simplified supply chains, contract service organizations will move away from plugging holes in the process to becoming a valued partner to support the development lifecycle.

Increasing end-to-end service offerings

Most noticeable across the board in the contract services industry has been the trend towards a more integrated service offering and "partnership" model. This model has two benefits. Firstly, the more extensive offering can attract clients through positioning as a partner or 'one-stop-shop', presenting a more simplified supply chain. Secondly, there are advantages for the contract service organization in working across bigger portions of the project lifecycle. For CMOs, an added benefit is the mitigation of risk related to the tech transfer of pulling a drug out of one CMO to another.

"The key trend is the establishment of partnerships," commented Gustavo Mahler, CEO at CMC Biologics. "Outsourcing to individual companies for every requirement is expensive and is sometimes a logistical nightmare. Therefore, the key trend here is to establish a few very strong relationships with preferred specific partners. This will enable companies to have the flexibility to swap products and, as the infrastructure requirement is much smaller, it is more cost-effective."

CMC Biologics, recently acquired by Asahi Glass Corporation (AGC), began as an early-stage development company before moving into manufacturing for commercial production in 2010. With 11 products in the pipeline entering the commercial market over the next ten years, the company is focused on adding capacity at its sites in Copenhagen, the United States and Japan.

Many contract service organizations recognize the benefit of being able to work as a partner across bigger portions of the project lifecycle. However, a consolidation in client base could heighten risk and contract service organizations should therefore be sure to maintain a somewhat diversified portfolio. Whilst companies such as Catalent and Patheon dominate the market and continue to grow their capacity and capabilities through organic and inorganic growth, the CMO and CDMO industry landscape remains somewhat fragmented. Nevertheless, the high level of M&A activity is likely to lead to increased consolidation as companies seek to extend their service offering across the development cycle, increase advanced capabilities, and develop their geographical footprint.

Worldwide growth in API volumes, increasing use of generics and growing opportunities for penetration in developing markets, coupled with these increased outsourcing requirements by large innovator companies, indicate that the industry will continue to experience strong growth. At the same time, the influx of small companies and biotech startups have also resulted in increasing demand due to a lack of internal manufacturing capacity. —

> "The most significant trend is that the whole industry is under considerable pricing pressure. The media attention on drug pricing has never been greater and is trickling down throughout the distribution pyramid ultimately to the manufacturers, so there is a strong focus on cost-saving initiatives such as improving yield. In addition to improving order accuracy and on-time fulfillment, we do a lot of process improvement and pass some of those cost savings on to our customers so they can remain competitive.
>
> - Lee Karras,
> CEO,
> Halo Pharmaceutical Inc

Gil Roth

President

THE PHARMA & BIOPHARMA OUTSOURCING ASSOCIATION (PBOA)

An association representing Contract Manufacturing Organizations (CMOs) and Contract Development and Manufacturing Organizations (CDMOs)

Could you give some background to the Pharma & Biopharma Outsourcing Association (PBOA), its main objectives, and how it realizes them?

PBOA was established in 2014 and is dedicated to representing Contract Manufacturing Organizations (CMOs) and Contract Development and Manufacturing Organizations (CDMOs). We have worked with the FDA to negotiate the second five-year iteration of the Generic Drug User Fee Authorization (GDUFA) and developed a new financial model that will be less burdensome for contract manufacturers. As part of that, we restructured the allocation of the Finished Dosage Form (FDF) facility fee under GDUFA whilst also smoothing a few wrinkles, such as removal of the incursion of a fee until a facility's first ANDA is approved.

This has been the major accomplishment for the PBOA to date. As a result of these undertakings, we have evolved as an association, and our membership has grown to about 25 companies, with several more planning to join in 2017. As we've grown to become the point of contact for the CMO/CDMO sector, we are working with groups such as PhRMA, Bio, GPHA and others to organize a concerted industry-wide response to FDA's Quality Metrics initiative. We have also helped with serialization efforts to ensure that contract manufacturers are prepared for the big Drug Supply Chain Security Act (DSCSA) deadline in November 2017.

What are the key positive changes heralded by GDUFA II?

For CMOs under GDUFA I, companies were paying an annual FDF facility fee regardless of whether there was an approved ANDA, simply if there was a pending generic drug application referencing a site. They were also paying the same flat fee as an in-house generic FDF facility, despite the differences between those two business models. By eliminating "fee-before-first-approval," GDUFA II will permit CMOs to enter the space without putting a great financial burden on them years before they would ever see revenue from a generics client.

Growth rates for contract manufacturing have been much higher than that of the pharmaceutical and biopharmaceutical industries. Could you elaborate on this trend?

Large pharmaceutical companies have grown better at outsourcing. Another key growth driver includes the move, years ago, in which large-scale commercial contract manufacturers began to work on the development side. This is beneficial for a number of companies that can now acquire business in the early phases of a project and remain the preferred partner through to commercialization.

Another area of growth will be drug delivery technologies. One of the biggest problems within the industry on the innovator side is a lack of bioavailability.

What are some of the main advantages PBOA offers its members?

PBOA's members get the direct access we have been building with the FDA, as well as first knowledge about draft guidance in the pipeline, expert analysis of legislative and regulatory trends, help getting their names out in the segments in which they operate, speaking opportunities at major industry events, access to member-only conferences and webinars, and input into our representation of the sector. We are also working to develop and proliferate best practices through the industry, and are building business solutions partnerships with vendors to the CMO/CDMO sector.

How will the drive to shift more manufacturing into the U.S. affect the contract manufacturing sector?

The Republican party has talked about a Border Adjustment Tax (BAT) as part of their broader tax reform concept, which would mean that domestic companies importing goods and services will no longer be able to deduct those costs from their tax base, while they would also not be charged tax on revenue coming from exports.

The infrastructure simply does not exist to make everything in the U.S. – it is a globalized supply chain, and extremely complicated. The common perception is that outsourcing involves cheap offshoring, but this is not the case in the pharmaceutical industry. Pharmaceutical companies are simply not able to do certain things as efficiently or effectively as a CMO, and may not want to invest in niche technologies. Making sure that the administration and Congress understand the complexity of global supply chains is going to be very important for PBOA going forward.

What are the main priorities for PBOA and its members for 2017 and beyond?

As with every industry, we are currently in somewhat of a "wait and see" mode. The number one uncertainty remains industrial policy and tax reform in the U.S. and how that may impact the industry's direction.

Vivek Sharma & Ramesh Subramanian

VS: CEO
RS: Vice President, Strategic Marketing
PIRAMAL PHARMA SOLUTIONS

VS

RS

Piramal has been expanding its services in the outsourcing space both organically and inorganically. How has the group grown within the segment?

VS: In the last two years, we have undertaken a couple of acquisitions, with Coldstream Laboratories for injectable capabilities and Ash Stevens for high potency API capabilities. We constantly engage our customers to identify their future needs and also monitor macro market trends in order to solidify our future investment strategies. Our main focus has always been to meet our customers' expectations collaboratively.

With the addition of Ash Stevens, there are now three North America facilities. Could you provide some detail on the scope of Piramal's operations in North America and beyond?

VS: We have three facilities in North America, with Ash Stevens in Detroit, Michigan for high potency APIs, the Lexington, Kentucky site for injectables, and the API site in Torcan, Canada, right outside of Toronto. In addition, we have two facilities in Europe; an oral solid dosage and API manufacturing facility in Morpeth, England and an ADC site in Grangemouth, Scotland. We also have several facilities in India, including API sites in Ennore and Digwal, and two sites in Ahmedabad, one dealing with Discovery R&D services and the other for oral solid dosages, and an injectables R&D site in Mumbai. Finally, we have an oral solid dosage manufacturing site in Pithampur, India, for oral solids manufacturing.

Could you comment on the shape of the industry and how it has changed since 2015?

VS: Many companies are strategically rationalizing their manufacturing and R&D operations and are increasingly exploring opportunities to expand outsourcing as well. Given our structure, our capabilities and our extensive offering, these macro trends complement our business model well, as customers are increasingly looking for more integrated outsourcing services. We are seeing a number of inquiries from biotechs and big pharma companies looking for end-to-end project support.

RS: Drug approvals reduced dramatically last year compared to previous years- for example, in small molecules, New Chemical Entity (NCE) approvals plummeted from 32 (2015) to 15 (2016). A lower number of NCE approvals leads to consolidation and cost rationalization at the customer's end: this may mean fewer people to manage internal programs. This gap is further widened by the need to drive more programs to alleviate the impact of clinical attrition and lower number of approvals. This gap has led to our customers looking for strategic, integrated partners, who can seamlessly manage globally dispersed teams and deliver on multiple verticals- for example, drug substance and drug product. Piramal Pharma Solutions is currently working on around 30 integrated projects globally. Our leading capabilities in drug substance and drug product development and manufacturing, and our ability to seamlessly blend operations across geographies with flexible scheduling to reduce delivery timelines, has resulted in an integrated offering that is attractive to both big pharma and biotech.

From a drug delivery perspective, what areas are Piramal currently working on?

VS: From an injectables standpoint, some of the things we are doing in drug delivery are very unique. We are sole partners to many of our customers and are humbled by their trust in us. Some of the capabilities at our OSD site are also highly innovative. Generally, we are looking at technologies that provide drugs at a faster pace and cheaper price for our customers and their patients.

RS: We continue to be a leader in Antibody Drug Conjugates, a vehicle for drug delivery, and have supplemented that capability with our High Potency API acquisition and our fill finish capability. Soon, we expect to be able to make the potent active, do the conjugation, and complete the fill-finish, all in-house. In terms of manufacturing technologies, the injectable site in Kentucky utilizes mobile isolators, which ensures high quality batches, and large volume production, even under a small manufacturing footprint.

What are the key objectives for Piramal over the next few years?

VS: Our key strategy is to support customers as best as we can. We want to continue expanding our capacity in current areas of operation, and also add capabilities to our portfolio. As integrated service needs continue to grow, we are well positioned to serve our client base as a trusted partner to reduce the burden of disease, by focusing on the three pillars that serve as the foundation for Piramal: Customer Centricity, Quality, and Innovative Science.

Outsourcing partners playing a more active role

As drugs become more complex, novel solutions are often required, for which many pharmaceutical companies do not have internal capabilities. By outsourcing, these companies can gain access to state-of-the-art technologies and the most advanced solutions on the market. Key considerations are safety, efficacy and bioavailability. Particularly as development timelines are condensed, either through fast-track designations or an internal drive, any increase in efficiency is welcomed.

When it comes to implementation of new technology, the industry remains surprisingly risk averse for one built on innovation. However, risk appetite is increasing with added cost pressure as advantages are perceived and better results are realized.

Hitting the Target

Driven by a lack of bioavailability, a notable area of growth is drug delivery technologies. Whilst contract service organizations may not be considered innovators, many CMOs and CDMOs have developed proprietary technologies and made vast progress in this pertinent area. New treatments only go so far if the molecule cannot be deployed into the bloodstream or reach the right target.

Companies such as Catalent, 3M and Patheon go much further than simply manufacturing dosages; they help pharmaceutical companies better formulate the drugs they have. Catalent's Drug Delivery Institute advocates a more effective use of delivery technologies, particularly focused on non-invasive delivery, and made progress in patient-focused drug design. The company also has a very broad platform for oral drug delivery, focused on solubility and bioavailability. "Solubility, one of the biggest challenges in the oral pipeline, reflects somewhere between 60% and 90% of the problems," commented Cornell Stamoran, vice president, strategy and corporate development at Catalent. "We have built a whole toolkit of solutions such as particle size reduction for increased absorption; we acquired a company specializing in soft gels, the most commercially-proven dose form to do that, called Micron."

Process innovation

Although there is demand for high-throughput facilities, the general trend falls towards smaller batch and product sizes, demanding greater flexibility and a reduction of capital cost. These requirements have led to an uptake in single-use technologies at large companies, such as Catalent and Therapure, and smaller players alike. "This also allows high-product changeover and smaller throughput, or multiple-product changeover in one facility," explained Sean Sommer, vice president at Jacobs. "Additionally, plastic bags eliminate the need to clean (CIP) and steam (SIP) the vessels, a regulatory requirement for traditional vessels, because the bags are thrown away. These bags are mainly used for products that have a short lifetime with a smaller population demand, and they allow the company to change the facility quickly to introduce a new product."

The other facility type uses the traditional stainless steel piping and large tankage because the disposable equipment cannot handle the high-throughput.

An early adopter of single-use bioreactors and one of the first to adopt the technology for biomanufacturing in the United States is CMC Biologics. "In the biologics CDMO industry the use of single-use systems is becoming much more widely accepted and this will become a more common approach to manufacturing," said Mahler.

CMC Biologics has made investments at its Seattle and Copenhagen facilities for

six 2,000L bioreactors, named its Bioreactor 6PACK™ Facility. "This provides a modular platform, all single-use, so turnarounds are very quick, at eight hours instead of several days. We are also able to lower the price for the customer and obtain several extra batches per year, lowering our break-even point and increasing our profitability. Additionally, this model reduces a lot of ancillary work on maintenance, and the capital investment is 40% to 50% lower. Project timelines are also much shorter due to the fact that the equipment can just be rolled in. We are currently also looking at implementing this platform further in the downstream process."

Other advantages include low failure rates and highly scalable operations.

CMOs and CDMOs will continue to expand capabilities and specialize in niche areas in equal measures, likely seeking collaboration to maintain a balance of each. As the recently booming startup landscape begins to grow through investment, contract services should be well positioned to offer services beyond the existing capabilities of the biotechs, whilst offering specialized expertise to larger companies that lack the in-house capabilities. —

> "One of the main biotech developments is the need for larger-scale high-throughput facilities to accommodate high demand for one or two products, while adapting to the demand for smaller, more highly-flexible facilities - it presents an interesting dichotomy. The latter uses disposable equipment, reducing capital cost and increasing the operating cost, and allowing for flexibility in the scale of the process."
>
> - Sean Sommer, Vice President, Jacobs

Michael Quirmbach

Vice President, Global Marketing & Sales
CORDENPHARMA INTERNATIONAL

Formed as a pharmaceutical branch of International Chemical Investors Group in 2006, CordenPharma provides specialized technologies for the development and manufacturing of oral, sterile, highly potent and antibiotic pharmaceutical Drug Products, their Active Pharmaceutical Ingredients, and associated Global Supply Chain and Packaging Services.

Could you start with a brief introduction to CordenPharma and its U.S. operations?
CordenPharma was created by the International Chemicals Investors Group (ICIG), which was founded in 2006 with the vision to build a global industrial conglomerate covering non-GMP chemical production and activities (WeylChem), and pharmaceutical cGMP manufacturing activities (among other businesses) under the CordenPharma umbrella. We have structured our business into five Technology Platforms: Peptides, Oligonucleotides, Lipids & Carbohydrates; Injectables; Small Molecules; Antibiotics; and Highly Potent & Oncology. With these platforms, CordenPharma is able to uniquely offer truly integrated supply solutions, encompassing a full spectrum from API manufacturing in the early clinical phase, all the way to commercial manufacturing for drug substances and drug product finished dosage forms, including pharma logistics.
Today, we have ten manufacturing facilities, including eight cGMP plants, and two R&D labs. Our business is currently split at about 60% in the United States, 35% in Europe and 5% in Japan. In the United States, we operate out of our CordenPharma Colorado facility in Boulder, Colorado, which focuses on drug-substance manufacturing for three Technology Platforms (Peptides/Oligonucleotides, Highly Potent & Oncology and Small Molecules). We also have a state-of-the-art R&D lab in Boston which focuses on non-GMP production of carbohydrates and lipids.

Many of the large API manufacturers supplying the United States manufacture in India. What are the advantages to manufacturing in the United States?
We do not see Indian manufacturers as competition to our offering due to our top quality products and services. Customers value our excellent FDA track records, especially at our U.S. facility. We are also one of the few large CDMOs that is truly back-integrated. Whilst we might buy certain raw materials from India or China, CordenPharma has the advantage of access to the other companies owned by ICIG, so we are unique in the sense that we can back-integrate raw materials through our sister company WeylChem, which allows for further manufacturing to take place in Europe and the United States.

What are the main areas of focus within CordenPharma's portfolio?
Peptides is a niche area, but has big potential, and many biotech and large pharmaceutical companies today are very active in peptide research. Another area that has seen a huge demand with very limited competition is the oligonucleotide field, which is part of our Peptides, Oligonucleotides, Lipids & Carbohydrates platform. We also see injectables as a very interesting, top-notch area. By offering end-to-end solutions across APIs and fill-and-finish, we are uniquely positioned. In addition we have strong service offerings within our Highly Potent & Oncology platform supplying integrated services for API and Drug Product manufacturing, both for oral solid dosage and sterile fill & finish.

What steps are CordenPharma taking towards the implementation of serialization?
Serialization is a very complex topic, especially as every country seems to have different standards for installations, regulations, and requirements. However, due to a strategic decision to invest in serialization quite early, we are well-prepared to support the various demands of customers that will arise. Having started in our CordenPharma Latina facility near Rome, Italy, where we are supplying to Eastern markets, we are now preparing our CordenPharma Plankstadt (Germany) and CordenPharma Caponago (Milan, Italy) facilities to meet those requirements. It is a very complex target which requires a lot of IT know-how, with infrastructure that is not straightforward.

Are there any other innovative areas in which CordenPharma is working?
We manufacture highly potent oncology drug products in CordenPharma Latina and CordenPharma Plankstadt. In addition, CordenPharma Colorado is well-equipped to manufacture cytotoxic drug payloads, which are being used in the manufacturing of antibody-drug conjugates. The manufacturing of highly potent drug products and API payloads, including how to handle them, requires well-designed infrastructure which meets the highest HSE standards and the ability to handle very complex chemistry. Our entrance into the oligonucleotide manufacturing market is also very innovative, where we recently made a $15 million investment into this area. We are also expanding our injectables production line, having invested more than $10 million. Because injectable medications go directly to the bloodstream, it is paramount we manufacture according to the highest possible standards, and we have gained a lot of experience in this area over the years.

What are the objectives for CordenPharma going forward, both globally and in the United States?
We want to achieve greater critical mass by adding additional capabilities and capacities to our five current Technology Platforms, and are considering adding in the near future a new platform in biologics, an area in which we are currently inactive. This can be achieved either through further acquisition of assets or by investments in existing facilities, as discussed above. We also want to continue growing in the U.S. market, where we are actively seeking the right opportunity. In terms of geographic expansion, we are evaluating different markets, including a planned entrance into South America.

Cornell Stamoran

VP Strategy and Corporate Development
CATALENT

Catalent is a leading a global leader in drug development, delivery and supply

Catalent has grown a great deal through a number of acquisitions over the last two years. What are some of the recent landmark developments?

Having been purchased from Cardinal Health by Blackstone Private Equity and a few others in 2015, Catalent is now a fully-public company traded on the New York Stock Exchange (NYSE), following Blackstone's sale of its last remaining interests in September 2016. Whilst this does not change how the company operates, the move has been an educational experience for the market, and built the visibility of the CDMO sector in North America.

The second evolution point for Catalent has been through continued business growth and reinvestment into new technology capacity. Over the last five years, we have invested over $1 billion back into the company, including over $600 million of CAPEX, and more than $400 million in M&A. A major development has been a $15 million expansion at our Winchester-Kentucky control-release facility, doubling capacity to meet an anticipated increase in customer pipeline needs. The facility deals with almost all aspects of complex oral solid doses, including a lot of coding work alongside the production of tablets and hard capsules containing that technology. We have also fully acquired a company called Redwood Bioscience, which brought us an antibody drug conjugate technology called SMARTag.

How has Catalent developed its biologics business area?

We continue to invest heavily in our biologics business area along several fronts–one is the biomanufacturing area, producing bulk biologics on a small to medium scale. There is a significant need for the production of biologics at a specific batch scale of less than 5,000 liters. Today, roughly 40% of the pipeline into active development is biologics, and 70% of that pipeline is likely to need less than 5,000 liters of capacity annually. Demand currently exceeds supply for this scale of capacity, and we have spent some time setting up single-use bioreactors. We were the first outsource plant to comprise solely single-use bioreactors in North America at least. Since then, we have completed a second expansion and broken ground on a third. Further to this, we have actually brought a great deal of our biologics work across the business under a singular leadership group, entering the market as Catalent Biologics. This has added further focus through a combination of disciplines, and this segment has now become the fastest growing area within Catalent, almost doubling in revenue over an 18-month period.

In what ways is Catalent addressing and overcoming solubility and bioavailability challenges?

We have built a very broad platform for oral drug delivery in terms of solving problems such as solubility or bioavailability. Solubility, one of the biggest challenges in the oral pipeline, reflects somewhere between 60% and 90% of the problems. We have built a whole toolkit of solutions such as particle size reduction for increased absorption; we acquired a company specializing in soft gels, the most commercially-proven does form to do that, called Micron. In addition, we added capabilities in hot melt extrusion, which is a different processing technique for the active ingredients. The last technology platform is a technique called spray drying, which is used to enhance solubility and bioavailability. At the same time, we began to develop an offering that could help companies better predict which formulation technology would be relevant to them, launching a platform called Optiform Solution Suite to do just that.

How can Optiform technology benefit Catalent's customers?

Optiform is one of the key evolutions of our business strategy, which is focused on extending our capabilities further into early development, including preclinical development and preformulation. Our customers told us that the lack of good predictive technologies was one of their biggest barriers because experimentation was expensive and took too long within the development cycle. Using very little active ingredient, which companies typically do not have much of at early stage development, and in a very fast way, the idea was to find and fix problems before later-stage testing. We started with a focus on solubility, but are now using a similar approach for peptides. Our recent acquisition of the Pharmatek business in San Diego ties in well to the Optiform strategy, and also added spray-drying capabilities. The other acquisition is the Accucaps acquisition, which is two Canadian softgel facilities, mostly focused in consumer health.

What is Catalent's strategy for continued growth?

Catalent is a global, organic-growth company. We have over 600 customer compounds and active development which in theory will be reaching the market over the next five to seven years, and are continuing to bring more new molecules to our network. We are actively focusing on the United States, Europe, Asia Pacific and Asia, and are starting to shift our focus slightly within Africa, too. Despite changes around the world, we are staying focused on trying to help our customers develop the best products for patients, and ensuring a consistent supply of those products.

Dr. Stephan Kutzer

CEO, President and Chairman
ALCAMI CORPORATION

Alcami is a contract development and manufacturing organization (CDMO) headquartered in Wilmington, North Carolina

Whilst Alcami's new brand identity was only announced in March 2016, the roots of the company can be traced back through its four parent companies: Cambridge Major Laboratories, AAIPharma, ChemShop B.V. and Celsis. How extensive is Alcami's service offering?

The result of combining and growing these four companies is a robust end-to-end offering from development of preclinical drug substance to final dosage form packaging of drug product. Alcami today has six sites in the United States and one in the Netherlands, offering a fully integrated service package, providing detailed attention to small- and mid-sized pharmaceutical companies that may lack the in-house capacity and expertise for navigating the clinical and regulatory paths. Our focus is not only on developing the process design and the manufacturing path, but also on developing a regulatory strategy for a successful pathway through the clinic and the launch.

Could you provide further insight into Alcami's Protect Your Brand™ offering and the advantages that it brings?

In our experience, the negotiation of commercial API contracts is a very lengthy and prejudiced experience. We frequently see companies dealing with supply constraints because of the FDA's issuance of warning letters to suppliers and shutting down their facilities. We want to offer a quick, flexible solution to these companies with a fast tech transfer. Our contractual setup and initial contracting can occur in less than two weeks whereas some larger providers take months to sign a service agreement. This allows for a quick and easy tech transfer process and less lost time for those customers needing to switch from another supplier. The value we offer with Protect Your Brand is that there are no strings attached to our arrangement with a client. We do not require any long-term commitments and are able to set up a project for short-term supply. This is the most flexible offering in the market today because it provides a flexible manufacturing solution to help drug makers protect their supply.

Many API manufacturers have their facilities in India, but Alcami manufactures solely in the United States and Europe. What are the motivations behind keeping manufacturing close at hand?

Our target market is the clinical space, and our clients want to keep their molecules and inventions as close to home as possible. About 75% to 80% of new molecules come out of U.S.-based laboratories. Therefore, having a local supplier and partner in the same time zone, communicating in the same language, that is also close to the FDA is very important. Overall, we have about six or seven full cGMP audits by the FDA every year at our facilities. Understanding the requirements of the FDA and EMA are best when done in close proximity. Since 90% of our market is the United States, we will remain a home-based player to support our local U.S. and European customers. We are not a low-cost, high-volume manufacturer; we are an innovative technology solution provider focused on bringing products to launch.

What are the next steps and main objectives for Alcami?

In the next two to three years, we will continue to grow organically across all of our business offerings. We are always looking at new technologies, and an expansion into a biologics technology platform is one obvious potential area of growth. We will be investing significantly into our Durham, North Carolina facility in the coming year to support biological, large-molecule, and microbial technology development. In this region in particular, there are many biotech companies needing support, and innovative solutions. These will be important milestones for 2017 and 2018, and a strong area of focus in the near future alongside a continued emphasis on meeting small-molecule demand in the marketplace.

Another area of focus for Alcami is the customer experience. We will launch a new Customer Portal application known as Alcami OnDemandTM, aimed at providing more seamless project tracking and management systems, and superior customer experience from the moment they are on-boarded. Beta testing will begin in April and the The Alcami OnDemand Mobile App will launch with Phase I of the portal, beginning in June.

Alcami is setting the industry standard for project management and transparency. Alcami OnDemandT allows Alcami clients and prospects unprecedented and rapid access and visualization into their ongoing projects. The portal will serve as a single source for customer project/order management with shared views to manage orders, libraries of compounds, test results and accounting information. This is just one example of the many ways we are focusing our attention and resources on optimizing the customer experience to provide world-class service that complements our existing scientific and technology expertise.

Trends in packaging

The North American market for packaging machinery is estimated to be worth $11 billion and represents 19% of the global market for packaging machinery according to PMMI, the Association for Packaging and Processing Technologies.

As the industry moves towards large-molecule biologics and personalized and targeted medicines, away from the blockbuster drugs selling hundreds of millions of units per year, quantity and value will correlate inversely. With an increase in value, the components and systems related to the drug come under increasing pressure and scrutiny. If they fail to maintain efficacy, or if delamination occurs causing a product recall, the company's ability to operate freely in the markets they serve and reach the patient population will be interrupted. Quality and performance are more important than ever.

Increasing emphasis on patient centricity also translates to providing patients with the best method to take their medication, which plays into compliance packaging. Particularly in areas of high value medicine, such as oncology, it is important to ensure that the patient is taking the medicine effectively. In line with this, FDA now requires human factor studies to ensure that the patient can safely handle the products. "Providing medicines to patients in well thought-out packaging that really helps facilitate effective administration of the medicine helps ensure it is taken as intended," noted Justin Schroeder, executive director marketing, business design and development at PCI Pharma Services. "Effective packaging can play a substantial role in patient health and wellness, which continues to be an area of heavy focus for PCI and our clients."

Efficiency, quality and flexibility remain the key drivers for packaging innovation. SCHOTT's adaptiQ vials embrace the trend of ready-to-use vials, which has picked up momentum in the last couple of years. "For smaller unit fills, companies are now able to acquire pre-washed, ready-to-use vials in tubs that can be fed directly into their filling lines, foregoing the washing and sterilizing process," explained Christopher Cassidy, SCHOTT's vice president of sales & marketing, North America. "This reduces a lot of their overall cost and becomes a very efficient process for them."

SCHOTT is also developing ready-to-use cartridges using exactly the same tubs.

Biosimilars, although generic, are still high value medicines and therefore handled like biologics. "In terms of procedure, they are similar to how we handle the general biologic category," said Schroeder. "Biologics are an increasingly higher proportion of the overall product mix these days, estimated

to comprise about 40% of all new pipeline products in development."

PCI is focused on market specialization in areas such as potent compounds and has developed a method of containment for the molecule. The company also recently announced an expansion of its serialization capability, partnering with Antares Vision, Marchesini and Domino.

Serialization is at the forefront of the pharmaceutical industry's minds in the lead up to the U.S. DSCSA and E.U. FMD implementation deadlines. On November 27, 2017 it will be illegal for non-serialized products to enter the supply chain in the United States and fines may be incurred for non-compliance.

Sharp Packaging is also at the forefront of serialization efforts, having serialized over two billion units of pharmaceutical products from its U.S. and E.U. packaging facilities. The company currently has 25 serialization programs in place and is undertaking a roll-out program with 16 packaging lines set up so far. According to Sharp Packaging, estimations are held that the impact of the new directives will increase the rate of outsourced pharma packaging from 15% to 17.5%.

Another advantage of serialization is that it supports automation, which in turn will increase quality standards whilst streamlining resource use. Although the benefits are clear, particularly when counterfeit drugs pose a threat to patient health and safety, a primary area of industry focus, PMMI estimates that the implementation of serialization at one manufacturing site can cost anywhere between $1 million and $4 million. —

"It is becoming increasingly important that packaging companies or systems organizations strive ever closer to a zero-defect result. Even low percentages of failures can result in very substantial losses and a failure to supply that critical drug to patients."

- Christopher Cassidy, VP sales & marketing North America, Schott Pharmaceutical Systems

Justin Schroeder

Executive Director-Marketing, Business Design & Development
PCI PHARMA SERVICES

A leader in pharmaceutical contract packaging, with a history dating back to 1967

How has the company developed over the last 50 years?
Recently, we made some acquisitions that have bolstered our company's suite of services, including the acquisition of Penn Pharma, which added drug development and manufacturing to our end-to-end services. We have also significantly invested in our clinical trials business, which includes an acquisition of Biotech Services International, bolstering our advanced specialization in Cold Chain and Ultra Cold Chain technologies for the emergence of exciting therapies in Biologics as well as Cell and Gene Therapy. Both of these acquisitions took place in 2014. Since that time, we have continued to invest in these areas to further expand capacity and capability. At a corporate level, the most recent activity is that we were acquired by Partners Group, a private equity firm, in mid 2016.

As the industry moves away from blockbuster drug models towards more specialized treatments with more targeted patient populations, how is the packaging sector impacted?
The major consideration from our perspective is that drugs are increasing in value, with a much higher percentage of new drugs in development designated as orphan drugs and other specialized medicines. This leads to a dynamic where batch sizes and patient populations are much smaller and the drugs are very high value. From an operational perspective, these trends have impacted how we typically handle a lot of these types of medicines, adapting to the new market conditions. We aim to provide our clients services that are nimble and responsive, cost effective, and truly scalable. Our investments have allowed us to continue stay in front of these changing market conditions.

Are there any particular considerations for biosimilars?
Biosimilars are really handled like a traditional biologics and, even though they are generic, they are still inherently high value medicines. In terms of procedure, they are similar to how we handle the general biologic category. Biologics are an increasingly higher proportion of the overall product mix these days, estimated to comprise about 40% of all new pipeline products in development. With the growth in injectable delivery forms, there is an evolution happening around patient convenience and patient self-administration. We are seeing a shift in delivery from traditional vials and prefilled syringes to auto injectors and multi-use pens, generally more focused patient-friendly systems. This substantially increases the complexity of the packaging due to the nature of these precision delivery forms, but very much appreciated by the patient. Also noteworthy is that a very high proportion of these medicines require end-to-end Cold Chain support, an area where we have invested significantly as that market segment grows.

Could you provide some insight into the importance of serialization?
The genesis of the serialization effort is to decrease counterfeiting and drug diversion. With the serialization initiative, every individual package will be identifiable by its own unique number and where it was packaged. We actually track all those numbers through the supply chain and the patient or pharmacy can verify its authenticity. This effort is consuming the pharmaceutical industry right now, as companies prepare for the U.S. November 2017 deadline. As the market leader in packaging, we have made some pretty significant investments into this area to prepare for the deadline and support our customers. In fact, in March we announced we had tripled our sterilization capacity in preparation for the demand created by the November DSCSA deadline in the US, which will be followed in 2019 by the E.U.'s FMD. We have really taken a leadership position in this industrywide effort focused on consumer safety.

What are the plans for PCI going forward?
We are pursuing continued growth and expansion, particularly through a suite of focused market specializations. Instead of trying to be the largest CMO, we prefer to focus our expertise in some very specific areas, such as potent compounds, which require very specialized facilities and technologies. Many companies deal with these molecules by gowning people in a certain way, but we feel like this is not the safest option from a risk perspective for the employee. With award winning facilities and procedures, we have developed a method of containment for the molecule, allowing us to work with companies focused in areas such as oncology and provide the both the expertise and infrastructure to develop these medicines without themselves investing heavily in the infrastructure. We are providing our clients a solution that is truly world class and cutting edge in this space.

Stephen L. Schweibenz & Benjamin W. Reed

SS: President
BR: Vice President Manufacturing
ALLIANCE CONTRACT PHARMA

ACP are expanding their contract manufacturing and laboratory services

SS

BR

How has the company developed since its establishment in 2008?

SS: We spent the first year getting established, building suites and investing in the company. Around 2011, the business really took off and we saw an upturn in our client base. We have always prided ourselves on the quality of our work and the ability to react quickly to our client's needs. That is one of the key areas that sets us apart from other CMOs. As a small company, we have had more success with small- to mid-sized pharma companies than the large CMOs, which do not have the same degree of flexibility.

BR: Over the past few years, we have been growing steadily, ensuring that we are controlling our growth to meet our client's needs. We have added a few key people every year, keeping the quality and the flexibility paramount in everything we do.

Could you elaborate on Alliance Contract Pharma's manufacturing capabilities and capacity?

BR: Currently, we have various types of dosage capabilities. Two of our main areas are liquid filled into hard shell capsules and ISO 7 suites that are capable of handling potent compounds. These ISO 7 suites are well suited for manufacturing terminally sterilized injectables, ophthalmic products or any product requiring higher classified rooms. Some of the procedures that we set up in-house for room clearance enable us to give our clients confidence that there is no carry-over of any products. Some of our other dosage capabilities include gels, creams, suspensions, capsules and powder processing.

Could you expand on some of the advantages and technical considerations with liquid formulations?

BR: There are a lot of benefits to liquid formulation, especially early in development. One of the advantages of liquid or semi-solid formulations is First in Man for clinical trials. This is possible because it foregoes extensive development work as is required for other formulations. This cuts down on early R&D time and discovery. Another advantage with liquid filled capsules is the accuracy of dosage weights and the ability to seal the capsules with a tamper evident band.

Is Alliance Contract Pharma working on any particularly innovative areas?

SS: A new niche market that we are currently operating in is nanomilling, which involves reducing the API dispersion to nanometer sized particles between 100 to 300 nanometers. The main advantage is the higher bioavailability and absorption speed within in the body.

What are the next steps for Alliance Contract Pharma?

BR: We have an upcoming expansion in 2017, which will add eight manufacturing suites to pave the way into tableting and larger kettles. We are looking at 1,000L kettles and higher efficiency machines for liquid filled into two-piece hard shell capsules. Four of the manufacturing suites will be for tableting, and include a roller-compacter, granulator, fluid bed dryer, tablet press, and coater. We plan to make this investment to broaden our offering and meet our client's demands.

SS: Many of our projects have reached the validation/commercialization stage of the product lifecycle. We feel it is important to continue to support our clients through this process and ensure all regulatory requirements are met. ACP remains committed on the highest of quality standard and performance.

Image courtesy of Mission Pharmacal

SUPPLY CHAIN, DISTRIBUTION AND LOGISTICS

"The logistics space is being driven by healthcare innovation, new technologies (think genomics and smart devices) and patient-centric trends that are shattering the status quo slowly but surely. The increase of temperature-sensitive pharmaceuticals entering the global marketplace is changing the game on how products are packaged, stored and shipped".

- Dirk van Peteghem,
Vice President of Global Healthcare Strategy,
UPS

Logistics and Distribution

From Factory to Patient

Although drug manufacturers have historically been disinclined to outsource logistics to third-party logistics (3PL) providers, the drive towards cost efficiency has made the option more appealing.

The logistics space has become highly consolidated, with key players such as DHL and UPS continuing to make acquisitions. For example, UPS' acquisition of Marken at the end of 2016 greatly extended capabilities into clinical trial services and biological sample shipments.

Equally consolidated is the distribution and wholesale industry, with Amerisource Bergen, Cardinal Health and McKesson Corporation accounting for over 80% of drug distribution revenue in the United States. Other players include Morris & Dickson, H.D. Smith, Smith Drug and Rochester Drug Cooperative. The HDA Factbook for 2016 to 2017 marks an increase in sales through pharmaceutical distributors by 16% from $349.9 billion in 2014 to $407.6 billion in 2015. The report cites continued growth of specialty pharmaceuticals as the driver for this growth, alongside distributors capturing a greater share of chain drug store sales, also claiming that 94% of all U.S. pharmaceutical sales volume came to the market through pharmaceutical distributors.

> "The regulatory focus in the U.S. is tougher than in many countries. While there are similar framework regulations on CSR elsewhere, the U.S. is perhaps more highly regulated. There is a high level of investor interest and activity in CSR topics, but also that bottom line. There is a lot of uncertainty in the country right now, but PSCI's mission is very clear, and our Principles are based around what is right. We have a compass that guides the work we do and we are trying to future proof our supply chains, to bring those emerging issues to our members so that they are ready to address them."
>
> - Julie Brautigam, Chair, The Pharmaceutical Supply Chain Initiative (PSCI)

The Factbook is a product of the Healathcare Distribution Alliance (HDA) as it is now known, following a rebranding in 2016 to reflect the organization's growing role as a convener of the supply chain both domestically and globally. Founded in 1876 and today headquartered in Arlington, Virginia, the association represents 34 distribution companies alongside over 145 manufacturers and over 50 services providers.

In 2017, the life science logistics and distri-

bution space is marked by a consolidation of customers resulting from a high volume of M&A activity. This demands a great deal of flexibility as pharmaceutical companies subsequently realign their supply chains. Following a merger or acquisition, companies seek synergies to drive cost effectiveness, which generally translates into rationalizing supply chain activities. Consolidations or integration of supply chains also depress wholesalers' margins as buying power is diminished.

> We see a growth among drug store chains and pharmaceutical brands to evaluate the supply chain not only in terms of the quality and the origin of the raw materials that they are purchasing, but also in terms of the ethical sourcing practices that are utilized. This is an area that affects the entire supply chain from raw extracted materials all the way to process ingredients whether they be active or components of a product, it's about the supply chains ability to meet and uphold ethical standards.
>
> - Joshua Grauso,
> Sales Manager,
> UL Consumer & Retail Services

Keeping a watchful eye

Whether due to regulatory requirement or best practice, supply chains are coming under much greater scrutiny, with reliability and safety at the epicenter. "The residing challenge will be around the trust of consumers, which eventually reaches the ears of legislators; there are important defined regulations that are in most cases intended to ensure the safety of the consumer," stated Joshua Grauso, Sales Manager, UL Consumer & Retail Services. "On the other hand, there are other industry-wide initiatives that help to ensure that the trust of the consumer is intact. At UL, we encourage a cross-section between the two: self-governance by the industry, as long as it is transparent and evaluated by independent parties such as UL, plus the use of regulators to ensure that the products are safe before they reach consumers."

A primary area of industry focus is the stemming of counterfeit drugs entering the supply chain. According to UL, an estimated 10% of all medicines and high-tech products sold worldwide are counterfeits. UL is able to monitor counterfeit products sold with a counterfeit UL mark, working closely with Interpol and other agencies.

Fragmentation of regulatory requirements poses a challenge to many companies. "Responding to increasingly complex regulatory environments spanning multiple geographies and business activities is extremely challenging," commented Steven Atcheson, senior vice president, sales & marketing, Kuehne + Nagel. "Kuehne + Nagel's standards set a benchmark in the industry. All of our KN PharmaChain facilities are audited to the highest standards and are given KN PharmaChain status when they have been audited and documented to exceed GxP standards. In 2015, the International Air Transport Association (IATA) introduced the CEIV Pharma Standard and in February 2017, the complete KN PharmaChain airfreight network was certified IATA CEIV Pharma. In reaching this landmark, we became the first freight forwarder to be globally network certified."

In order to be compliant across all facets, companies often have to contend with various regulatory agencies internationally alongside external customers, for which there are often separate audits. Differentiations exist at an international level and also between states, many of which are still trying to define 3PLs and their implications for example. However, the general trend is towards greater global harmonization. —

Larry Doud

CEO
ROCHESTER DRUG COOPERATIVE (RDC)

A leading regional pharmaceutical wholesaler

RDC is ranked the sixth largest wholesaler in the United States. In an environment dominated by three companies, where has RDC found its niche?

Our niche is with the independent pharmacies. We are an independent wholesale cooperative, so stores can buy stock and own a part of us. Then, we share the profits at the end of the year with all of our shareholders equally, which is very appetizing to the independent pharmacist. We are also less rigid than the big players, which is necessary for independent pharmacies that all have different needs.

How does RDC compete against shortliners sometimes offering cheaper alternatives?

The main challenge right now is the reimbursements–the third-party payments to stores from insurance companies such as Caremark, Express Scripts, Optum, Aetna and Humana are so low that they cannot survive on what they are receiving. In turn, the only thing they can do is lower the cost of their acquisitions. Although they can lower their overhead, they cannot do anything else to increase their return, because it is restricted by what the third party tells them they have to accept for it. That is why they are looking to buy cheap.

At RDC, we operate a cradle-to-the-grave concept. From the setup and fixtures to the computer system and merchandise, we provide everything, even allowing companies to pay us back over a period of time. We also send a sales rep into the store once every three to four weeks and have a customer service department to help the stores identify products that they need, and then source these for them. Stores that recognize our value-added service and the extent of support will choose to work with us over other wholesalers able to sell their drugs at below-market cost because they got their supply from a government contract or hospital; places they should not get it from.

Transparency across the supply chain is a hot topic at the moment. Where do wholesalers fit into the discussion?

Unfortunately, there is a perception in the industry that wholesalers add a significant margin, but we do not make any margin at all. Even the big wholesalers have incredibly lean cost structures. The key focus should be transparency amongst the insurance companies, the payers. Nobody understands how much the Pharmacy Benefit Managers (PBMs) are making on the backside, and yet they control everything and receive a significant rebate on reimbursements. Whilst only managing the benefit, they make more than any pharmacy that we service, also receiving money from the manufacturers to make sure their product is on the formulary versus another product; this is what they call a slotting allowance.

The NCPA, the Independent Pharmacy Association, is fighting to force the PBMs to become transparent. There used to be 55,000 independent pharmacies in the United States, and we are down to about 21,000 because of the attrition caused, first-off, by CVS and all the chains buying independents, but also because they cannot afford to stay in the business. On this note, RDC also offers a buyout fund to help our stores acquire exiting independent pharmacies so that the independent does not go out of business. If there is another independent that is interested in buying them, we will help them.

Could you shed some light on RDC's cost structure and revenue model?

Although RDC made about $2 billion in revenue in 2016, which is incredible for a company with only 220 employees, it does not make anything on what it sells. As a matter of fact, through January of this year, we only made $16 million on $1.735 billion worth of sales–not even 1%. We make everything on backend rebates, with price increases accounting for a large part of our profit structure. We get paid on the back of manufacturer agreements to limit our inventory, on-time payments, and to supply information on every place to which we sell the product. We also finance some of our pharmacies that need the help, on which we charge interest and add a service charge, so we make money on that.

All of us are experiencing the same challenge because generic pricing is going down. The deflation is significant, running at about 13% to 15%. Price increases, through which both we and our stores make money, are running behind.

Matt Thiel, Melissa Authelet & Charles Dodds

MT: Vice President
MA: Director, Regulatory & Compliance
CD: Executive Vice President
ROCHEM

Rochem is a global manufacturer of ingredients for human and animal health products

MT

MA

Could you give a brief introduction to Rochem and any developments since we last met in 2015?

MT: Rochem has continued to invest heavily in regulated human health products and the veterinary side of the business, leveraging on our expertise in regulatory and compliance, developing DMFs for human health products and VMFs for Animal Health products. We have also worked our way much further into the development side; partnering with manufacturers in China, we are now developing products that are not coming off patent for up to seven years or more.

Rochem is focusing heavily on the peptide area. What are some of the particular challenges and barriers to entry?

CD: Peptides can be very complex; it is not just a question of the technology, but ensuring the right sources for all the amino acids and a large amount of investment is required. The biggest of all the peptides by far is liraglutide, which is a very difficult product to make.

MA: Generics are generally considered cheaper to develop and get to market, facing fewer barriers by far than the innovator. With peptides, however, demand can be as little as 2g to 3g per year but they cost as much to develop as far bigger products.

Rochem distributes products in both the oral and injectable areas. What trends have you seen since we last spoke in 2015?

CD: The overriding factor for both is that there are fewer products coming off patent, because we are now on the downward slope of the patent cliff. There are a much great proportion of biologics coming off patent in the next decade, for which the barrier to entry is much higher even than peptides. As the space is becoming more crowded, companies are looking into more innovative ways of collaborating.

We are looking at where we can add value for our customers and it will be very difficult to find that in mass-market, oral, regular-release products.

On the regulatory side, are there any disparities from a compliance perspective across different regions?

MA: Across the board, there have been more inspections, more warning letters, more import alerts, and more zero-notice inspections. The FDA's presence in India and China has greatly increased and seemingly every month a major player gets knocked out with a warning letter or import alert. This can have huge repercussions throughout the supply chain, with manufacturers in the United States experiencing drug shortages, and so on.

MT: China's increase in environmental regulation has also had a major impact over the last two years, affecting the supply chain significantly as manufacturers are removed from the market place because they are unable to invest further into waste management, or have their capacities reduced to manage waste.

With the increasing emphasis on regulatory harmonization, how will the framework be shaped going forward?

MT: In the last few years, we have seen improved communication among the regulatory authorities, including the EMA, FDA and Health Canada; information from negative inspections seems to be passed very quickly. We are starting to see some synergy, but it is more focused on the negatives and identified problems.

CD: It is a binary game: companies have to be right 100% of the time. If a customer loses a major product because they are single-sourced or even dual-sourced, the supplier is out. The higher number of inspections in Asia is something that U.S. and European suppliers have requested for years and, whilst the playing field is not yet level, it is much more so than previously.

What are the next steps for Rochem?

MT: We will continue to invest in developing niche products, getting away from commodity areas with a large number of companies offering the same thing. We plan to work more closely with our manufacturers, in some instances entering joint ventures to act as a selling and marketing arm and provide regulatory resources.

The supply challenges stemming from regulatory issues over the last few years have translated into a trend for manufacturers of finished dosages to look at their supply chains much more critically than in the past. Whilst single sourcing heightens regulatory risk and has huge potential cost impacts if that source is lost or price increases are passed down, it is still the more common option. We need to rethink our strategies so as not to be tied to one source.

Scott Cubbler

COO Life Sciences & Healthcare, Global
DHL SUPPLY CHAIN

DHL Supply Chain is the leader in contract logistics in the Americas and part of DHL Group, headquartered in Germany.

How far has the company progressed along its 2020 strategy as outlined in 2015?

Our Strategy 2020 remains our complete focus, and has been since 2015. We have been working towards increasing our ability to react and respond, especially in healthcare logistics. Within life sciences, we have nine key initiatives in support of Strategy 2020, of which the most important is to be number one in quality and compliance. Ultimately, our goal is to have a positive impact on patient health, which, at the end of the day, is what drives each and every DHL Supply Chain employee. DHL Supply Chain's Life Sciences sector continues to be our fastest growing sector within DHL Supply Chain North America.

What are some of the key trends and developments in the logistics space?

The recurring theme is simply change. The consolidation of customers is critical in the Life Sciences industry, with the high volume of M&A activity in both the pharmaceutical and medical device space. It is driving a lot of activity, with our customers trying to establish and align their new supply chains and striving to find synergies. There is also tremendous pressure to improve the reliability of drugs in the supply chain and to do so more efficiently and effectively to alleviate cost. Equally, there is great urgency and pressure to increase efficiency and add best practices and tools to ensure that the customer gets the medicines they need, when they need them. Maintaining cold-chain integrity through storage and delivery is another area that has been a focus for our customers.

How does DHL Supply Chain address challenges related to delivery?

First of all, we are moving further and further away from the big blockbuster drugs that used to be handled through wholesalers into pharmacies where the customer would pick them up. With biosimilars and personalized medicines, it is increasingly challenging. Many drugs coming into the market now require a different level of attention, with requirements such as home delivery. It is no longer a case of simply passing medicines to a wholesaler and into a pharmacy.

We are being asked to deliver not just to a single wholesaler but into a lot of metro and suburban networks. They have more demanding delivery windows; all of these products require specialized attention and special handling requirements. It is up to companies like ours to tackle our customers' challenges as efficiently and effectively as possible.

Last month, DHL Supply Chain announced that it will be using collaborative, autonomous robotics solutions within the life sciences area at its Tennessee facility. Could you comment on the growing role of automation and robotics in the industry and provide some further insight into LocusBots?

Again, the main challenge in the life sciences space is the degree of change. Flexibility is greatly limited by a reliance on pick-to-light, carousel picking, and other "bolts-in-the-ground" automation. For instance, when one manufacturer buys another, or sells off a business unit, the work content changes and suddenly the automation becomes antiquated. We are focused on improving efficiency whilst not negatively impacting flexibility. The use of LocusBots at one of our Tennessee sites is therefore very exciting: these are automatically-guided picking aids that travel with the employee, allowing the individual to pick and place products into the right shipping container rather than cart it back to a shipping area. The robot itself can be released and automatically head to a shipping area, and a new one follows right behind. We think it has the potential of improving our picking efficiency by about 30% at some of our right sites.

We are also excited about Augmented Reality. For some time, we have been testing vision picking, with the potential for picking aids to flash up on a pair of glasses, for example, and warn about certain parameters and offer safety advice. It can also direct our pickers to the next location and help them get there quickly. As with LocusBots, we think that Augmented Reality has the ability to help us with efficiency and accuracy without limiting us from a flexibility standpoint.

What are the next steps and key objectives for DHL Supply Chain in fulfilling the 2020 strategy?

We will continue to fully execute our nine key Life Sciences Initiatives in support of DHL Supply Chain's Strategy 2020. Our goal is to become a very trusted partner in helping to solve the healthcare challenge of providing phenomenal, world-class service as efficiently as possible. The Life Sciences space is a very challenging, dynamic and rapidly changing space – and our customers need partners like DHL Supply Chain that can help them be successful. In North America, or anywhere else worldwide – DHL Supply Chain is committed to improving patient health and doing so as flexibly and efficiently as possible.

Dirk van Peteghem

Vice President of
Global Healthcare Strategy
UPS

UPS is a Global Leader in Logistics

Could you start with a brief introduction to UPS and the significance of the Marken acquisition?

Healthcare logistics is a strategic priority within our company, and we are proud to provide best-in-class supply chain solutions and compliance expertise to pharmaceutical, biopharma and medical device companies. We have 60+ healthcare-dedicated facilities representing 7 million square feet of cGMP- or cGDP-compliant healthcare distribution space, and maintain the world's largest network of field stocking locations with 950 sites. For parcels requiring strict temperature environments, from controlled-room temperature (CRT) to cryogenic, and those requiring around-the-clock monitoring, UPS has solutions such as UPS Temperature True™ and UPS Proactive Response™ services.

UPS is committed to expanding our healthcare capabilities, with the recent acquisition of Marken being a good example, in order to meet the complex and evolving supply chain needs of the healthcare and life science sectors. Marken maintains the leading position for clinical trial services and biological sample shipments and offers a state-of-the-art GMP-compliant depot network and logistics hubs in 45 locations worldwide for clinical trial material storage and distribution. Marken's more than 720 staff members manage 50,000 drug and biological shipments every month at all temperature ranges in more than 150 countries. Services such as biological kit production, ancillary material sourcing, storage and distribution, shipment lane verification and qualifications, as well as GDP, regulatory and compliance consultancy add to Marken's unique position in the healthcare logistics industry.

What are some of the most notable current trends in the logistics space?

The logistics space is being driven by healthcare innovation, new technologies (think genomics and smart devices) and patient-centric trends that are shattering the status quo slowly but surely. The increase of temperature-sensitive pharmaceuticals entering the global marketplace is changing the game on how products are packaged, stored and shipped. We're seeing regulators around the world mandating a higher level of protection for all temperature-sensitive shipments, whether they require a 2-8°C degree temperature or a CRT environment. That is a challenge that calls for innovative solutions and is changing established practices across the industry.

Could you expand on the topic of supply chain visibility and any arising challenges?

The demand for greater supply chain visibility is being driven by manufacturers, distributors, healthcare providers and patients. With the increased incidence of high-value and temperature-sensitive products moving through the supply chain all stakeholders up and down the chain require a high level of assurance their products will be delivered uncompromised, safely and effectively. UPS offers a host of advanced visibility platforms, and leverages the latest (GPS/Bluetooth/data logger) technology to support our customers. To improve home healthcare and the patient delivery experience, we have developed tools specifically designed to support first delivery attempt success.

What technology trends help ensure stability of products and reliability of service?

New materials are being developed in cold chain packaging to improve insulation efficiency (vacuum insulated panels / thermal blankets) and to maintain temperature within a very precise range (phase change material). The temperature-controlled supply chain can benefit from better visibility through a wider use of data loggers that provide critical information sometimes on a real-time basis. We expect innovation to accelerate notably around the platforms to communicate and analyze the environmental information gathered by an increasing number of sensors. Expect to see ongoing cold chain technology enhancements across the healthcare and life science industries, and UPS is excited to be in the middle of these changes.

Do you have a final message regarding UPS's outlook and overall outlook on the industry?

While many supply chain best practices cross our priority industry segments — from retail, automotive, high tech, small business, industrial manufacturing and others — the healthcare sector requires a set of specialized services built around our mantra, "It's a patient, not a package." These services include healthcare-dedicated cGMP-compliant facilities, product security, monitoring and intervention solutions. UPS is committed to investing in services that add value for our healthcare customers.

For example, UPS recognized a need in the medical device industry to offer enhanced inventory control and visibility of surgical kits. To serve this need UPS recently opened a facility that offers comprehensive medical device inventory replenishment services. The ability to decontaminate surgical kits, replenish and repackage instruments, and respond quickly to urgent medical needs is pivotal to customers' market success. UPS will continue to stay focused on building and expanding innovative services and solutions that meet the specific transportation, warehousing, distribution and value-added needs of our healthcare customers.

Increasing sensitivity and innovation requirements

Reliability remains paramount to ensure the lasting efficacy and safety of products, particularly as those products increase in value. "First of all, we are moving further and further away from the big blockbuster drugs that used to be handled through wholesalers into pharmacies where the customer would pick them up," said Scott Cubbler, COO life sciences & healthcare, global at DHL. "With biosimilars and personalized medicines, it is increasingly challenging. Many drugs coming into the market now require a different level of attention, with requirements such as home delivery. It is no longer a case of simply passing medicines to a wholesaler and into a pharmacy."

Many drugs are very sensitive to temperature, and cold chain services have long been established, but demand is increasing as many new drugs have even higher requirements. "We are seeing regulators around the world mandating a higher level of protection for all temperature-sensitive shipments, whether they require a 2°C to 8°C degree temperature or a CRT environment," stated Dirk van Peteghem, president of global healthcare strategy at UPS. "That is a challenge that calls for innovative solutions and is changing established practices across the industry. Third-party logistics providers are being challenged more and more to keep pace as healthcare companies continue to innovate and push boundaries."

According to Pharmaceutical Commerce's 2016 Biopharma Cold Chain Sourcebook, cold chain will rise from representing 19% of a $12.6-billion industry to 22% of a $93.8-billion industry by 2020, valued at $16.7 billion. The bulk of spending is expected to be on refrigerated products at 2°C to 8°C.

The last year has seen a huge increase in capacity of cold chain capabilities. FedEx's new Cold Chain Center in Memphis, Tennessee, opened in 2016, adds 83,000 sq. ft. of space for frozen, refrigerated and controlled room-temperature storage. Other expansions include those of United Cargo in New Jersey and American Airlines Cargo in Texas.

Kuehne + Nagel took the prize at the BIFA Freight Service Awards for the 2015 Cool Award, and continuously adds to its multi-modal network, which spans 170 locations. KN PharmaChain Solutions include strategically-located stations, rigorous trade lane and carrier assessment with a specifically developed web-based risk management system, dedicated SOP generated for every single shipment, real-time temperature monitoring with active sensors and door-to-door track and trace.

In line with increased tracking requirements, Kuehne + Nagel is also working toward Blockchain implementation. Blockchain is a relatively new system, which maintains ever-increasing records and process transactions and removes the ability to alter information retrospectively. "Blockchain has been identified as a revolutionary step toward streamlining older logistics processes, providing the ease of convenience and flexibility through shortening downtime typically required for the verification of documentation," said Atcheson.

Emphasis on supply chain visibility and tracking measures will only increase as drugs become higher in value and more steps are taken to mitigate any sort of risk that could lead to disruption and loss of revenue. Logistics companies are therefore constantly innovating and adapting to ensure ultimate reliability, flexibility and effectiveness.

Image courtesy of Genomind

Image courtesy of Frontage

THE BIOPHARMACEUTICAL INDUSTRY'S OUTLOOK SEEN THROUGH A 2017 LENS

"Do not go gentle. Now is the time to put the accelerator to the floor. The best is yet to come – like groundbreaking advances in immunotherapy and personalized medicine – where the once impossible is now reality."

- PhRMA's GoBoldly campaign

Will the U.S. Biopharmaceutical Industries Continue to Thrive?

Image courtesy of Mission Pharmacal

Despite its leading global position, the U.S. industry faces a number of challenges that could shake up the playing field and demand a review of strategies at a national, state, and company level.

Political uncertainty and prospective changes to the framework, including healthcare and tax reform, will have repercussions globally, and companies will need to adapt to these shifts. Following criticism at a congressional level, the industry's image is currently somewhat negatively perceived, and increased awareness of its positive facets would be beneficial.

PhRMA's GoBoldly campaign seeks to offset this negative public perception by showcasing advances in medicine. With the accompanying slogan "Do not go gentle", the campaign states:

"Now is the time to put the accelerator to the floor. The best is yet to come – like groundbreaking advances in immunotherapy and personalized medicine – where the once impossible is now reality."

As new drugs gain in development cost and value whilst addressable market sizes shrink due to targeted treatments, companies will begin to reassess their pipelines

and market-entry strategies. Fast-track designations and streamlined pathways offered by the FDA will greatly facilitate new drugs entering the market that might otherwise fall by the wayside.

It is impossible to set the cost of time and quality of life, into which biopharmaceutical companies are essentially investing by extension of their products. However, affordability remains a key issue; one that the generics industry seeks to address. "When policymakers reference escalating drug prices without distinguishing between brands and generics, generics are perceived as equally blamable for the drug cost problem despite incontestable data showing that generics drive savings, not cost," argued Chip Davis, president and CEO at AAM. "This distortion presents significant danger for the generic industry because pricing policies that might be effective in controlling costs in a brand monopoly market can have the opposite effect in a commodity generic market. The unintended consequence would be fewer generic competitors and higher drug prices for patients and payers."

The importance of a competitive framework is clear, and must be balanced to ensure affordable alternatives and incentives for innovation in equal measures.

Dominating the playing field

Under the ruling hand of the FDA, the United States will continue to set the benchmark for quality, maintaining a competitive advantage for safety and efficacy over cheaper products that may follow more lenient regulations. Further steps towards global harmonization, coupled with rising labor costs in typically cheaper areas of operation, will also even the playing the field in these respects.

An emphasis from the new Administration on manufacturing in the United States could disrupt supply chains, particularly in the generic industry. However, drastic changes such as the implementation of the discussed Border Adjustment Tax are unlikely, particularly as the industry would not be able to respond so quickly. "Rapidly altering the supply chain would be difficult, in such a highly regulated environment," commented Robert Cunard, CEO at Aurobindo. "For example, it is not possible to simply increase manufacturing in the U.S.–there is a regulatory process that has to be followed. Examples include tech transfers, validation batches, and an approval process. This requires time, and the regulatory expertise to navigate those waters and do it efficiently."

Although far ahead on the innovation front when it comes to new products, the United States is lagging behind Europe in biosimilars. With only two products on the market so far and two further approved, the figure pales in comparison to Europe Union's approval of almost 30 products. Going forward, however, the United States is likely to rapidly close the gap, with the rhetoric around drug pricing and affordability presenting a key driver to push more biosimilar products into the market.

The U.S. industry landscape is shifting, and its internal dynamics will require the industry to remain highly adaptable. Through increasing collaboration towards a common goal–the advancement of medicine and its accessibility–the United States will continue to pave the way and lead by example. —

"Regulatory reform and corporate tax reform would encourage investment in this country. There are however some risks. For example, as an industry we are in favor of free trade, having one of the largest exporting sectors of the economy. Nonetheless, there would be a different set of challenges under another President. Corporate tax reform, which is an opportunity, would not have been on the table, and we probably would be fighting higher taxes in some areas."

- Kevin Swift,
chief economist and managing director,
American Chemistry Council

"We are not competing with other states; it is our responsibility to work together and get better at what we do collectively. Doing this will help make drugs more affordable because they will be less expensive to invent. The source of the treatment and cure is unimportant: our focus is on the result and the patient."

- Bob Coughlin,
president & CEO,
MassBio

"The industry needs to work together in a cross-functional manner to drive speed, efficiency and cost in trials. We have seen some fresh thinking in the industry at a leadership level, and companies are coming together to share their knowledge and experience to create industry standards across countries, like the TransCelerate initiative. These types of broad-reaching consortiums are well-poised to drive meaningful change in an industry which has historically been risk-averse and slow to implement new solutions."

- Valarie Higgins,
president & danaging Director,
Almac Clinical Technologies

"The market evolution is immense, and whilst cost optimization is still key, the discussion these days is all around improving outcomes, better effectiveness, variable capacity and agile innovation. Our focus is on end to end customer experience, while improving efficiency and effectiveness. We are able to make the most difference to our clients when we partner with them on their strategic agenda for their business."

- Manu Goel,
senior vice president,
Genpact

"HealthCare policy in the United States will quite clearly evolve, but the changes and their outcome are in early 2017 still uncertain and very much under active discussion. Ultimately, however, our companies have the capabilities and resilience to adapt because they will always continue to innovate. Innovation is our life blood and the industry will keep pushing, trying to find the next cure, the next treatment. We have had some real paradigm shifts; we are now seeing cures for diseases, in addition to treatments. In any event, the priority and focus must continue to be the welfare of the patient."

-

- Dean Paranicas,
president and CEO,
Healthcare Institute of New Jersey (HINJ)

"With so many changes happening in the U.S. and elsewhere, we are striving to keep our finger on the pulse. To do this, we are becoming more member-centric and learning more than ever before about what our member companies, both specialty chemical manufacturers and those in the pharmaceutical sector, need to thrive."

- Jennifer Abril,
president & CEO,
SOCMA

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This list intends to include just a representative sample of companies operating in the US Pharmaceutical sector, and as such it should not be considered a guide to take investment decisions.

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