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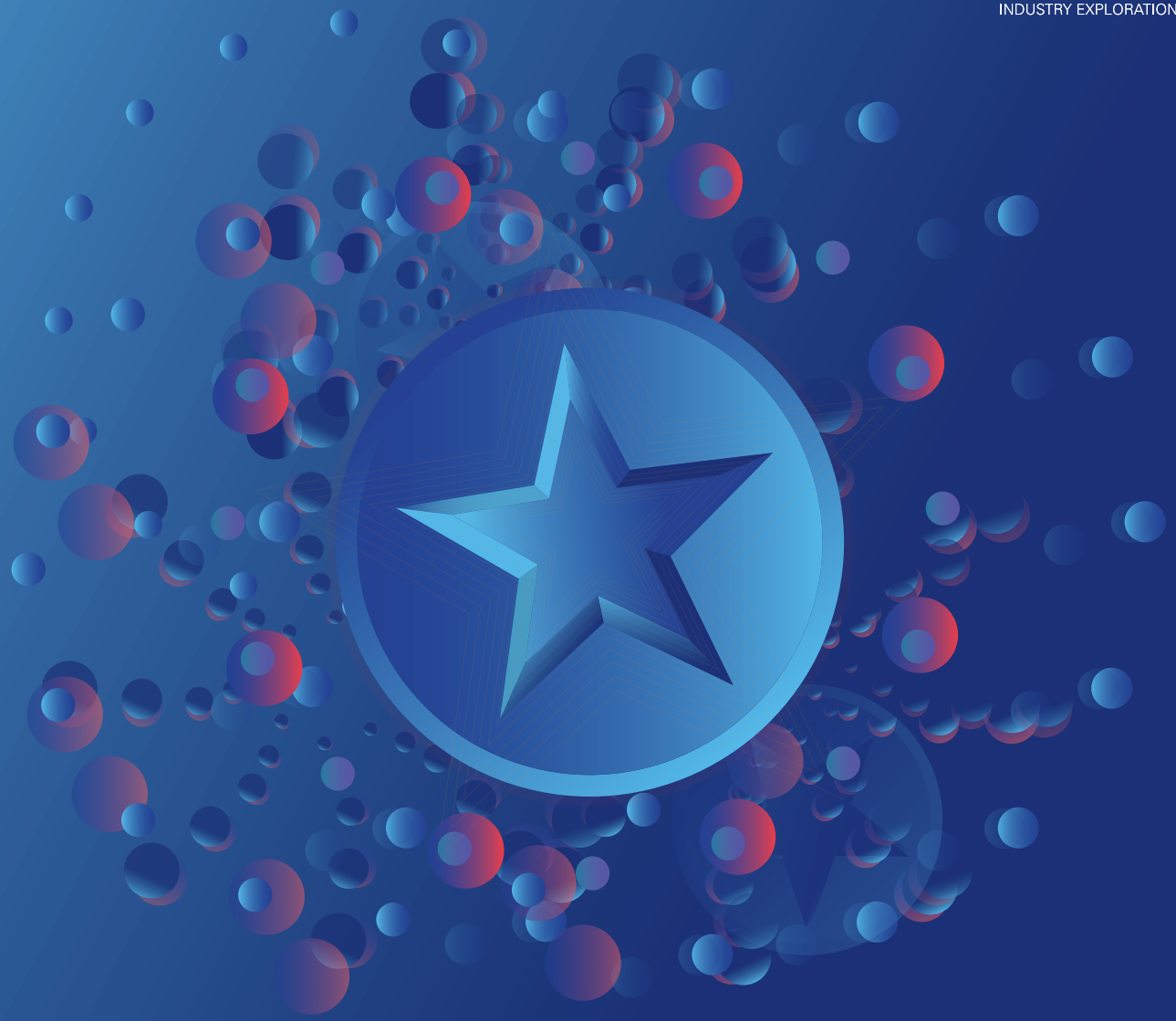
INDUSTRY EXPLORATIONS



UNITED STATES BIOPHARMACEUTICALS 2019

Biopharma Superclusters - Research and Development - Contract Services - Drug Discovery - Academic Research
Regulations and Compliance - East Coast - West Coast - Logistics and Distribution

Dear Reader,

Welcome to the 2019 edition of the United States Biopharmaceutical Industry Report, a joint CPhI-GBR analysis launched at CPhI North America.

The United States continues to hold its position as the global capital for innovation and an important market for companies worldwide, maintaining significant year-on-year growth despite external pressures and shifting global dynamics. 2018 was a record year for generic drug approvals, exceeding the FDA's previous record set in 2017. Meanwhile, innovation is being driven across therapeutic areas, with companies incorporating precision medicine approaches into their discovery and development efforts. As we move through 2019 and into the 2020 presidential election, the pressure already seen on drug pricing and the United States' relationship with China have the potential to be highly impactful, but the U.S. life sciences sector has proven itself to be resilient and its strength as a global powerhouse is unlikely to be called into question.

Biotechs continue to be an increasingly important segment of the sector as a focus for large pharma in their external innovation strategies and also for contract service providers, which are adapting their business models in line with the opportunities they see in working with biotech companies at earlier stages in their development timelines. Because of this, biotech hubs continue to garner the highest levels of attention from the various stakeholders across the industry, which is reflected in our 2019 research for this publication.

The following pages bring together insights collected from interviews conducted with over 150 of the biopharmaceutical industry's most insightful and authoritative executives across all areas of the sector. We would like to warmly thank our association partners at BIO, Biocom, BioNJ, MassBio and Life Sciences Pennsylvania for their continued support, as well as all the executives and researchers who shared their valuable insights.

Joseph Marks
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Alice Pascoletti
General Manager
Global Business Reports (GBR)

Editorial Analysis

GBR journalists provide unique and first hand analysis and insights into all aspects of the U.S. biopharma industry after months on the ground

8, 30, 56, 64, 72...

Exclusive Interviews

Leading industry figures from biopharma hubs across the country share their insights and their pipelines with GBR

12, 35, 59, 74, 82...

Data, Maps and Infographics

Maps, charts and graphs illustrate industry trends

9, 28, 35, 45, 48...

Industry Thoughts

The ideas shared with GBR during our encounters with over 120 of the leading players in the U.S. biopharma industry

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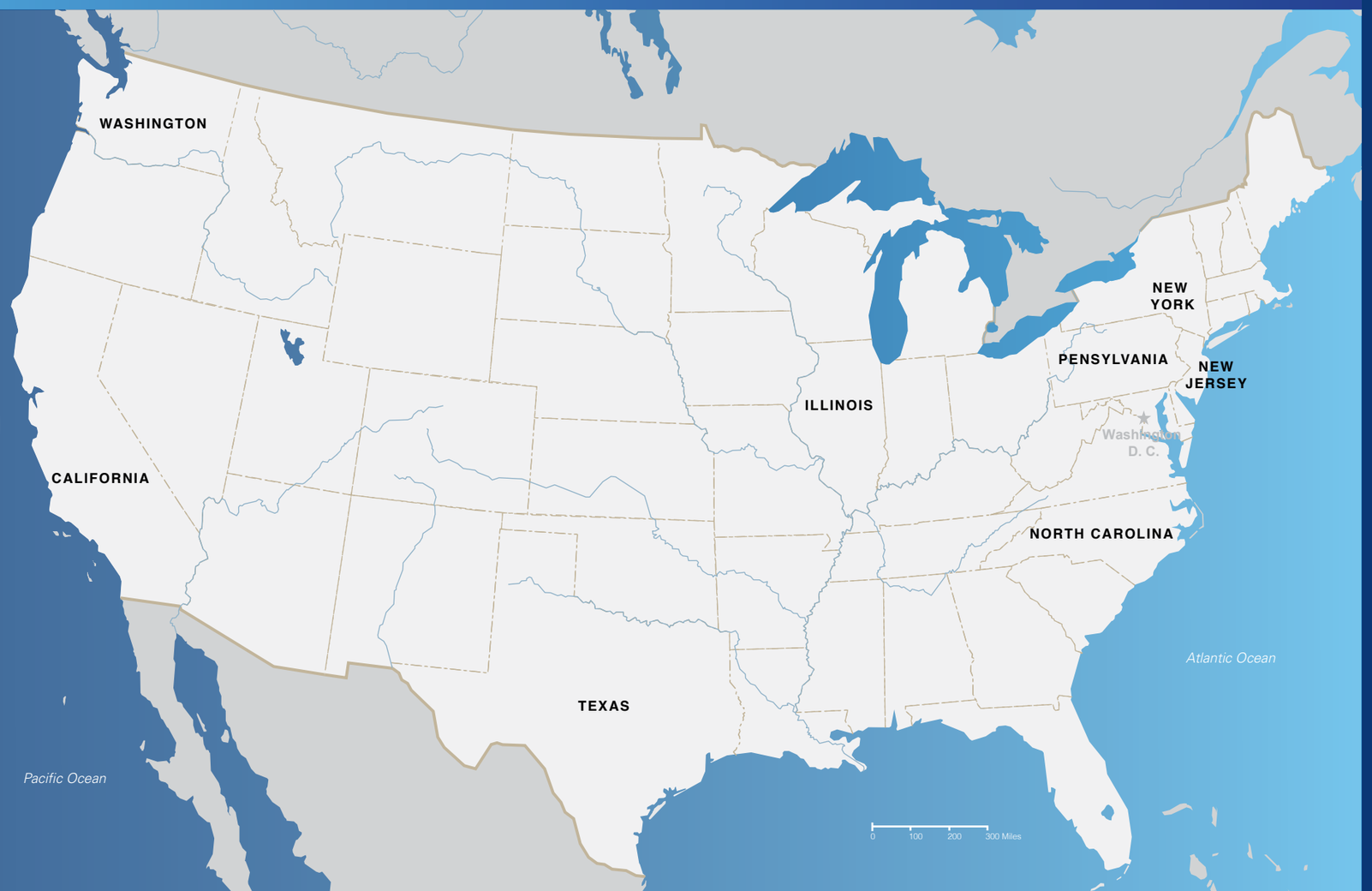

United States of America

International Boundary
State Boundary
National Capital

UNITED STATES BIOPHARMACEUTICALS 2019
Industry Explorations
CPhI & Global Business Reports

This research has been conducted by Catherine Howe and Julian Issa

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A Global Business Reports Publication
For updated industry news from our on-the-ground teams around the world, please visit our website at gbreports.com, subscribe to our newsletter by signing up to our VIP list through our website, or follow us on Twitter: @GBReports

The U.S. Biopharma Industry

"Medical innovation is simultaneously at both its moment of greatest hope and under the greatest political pressure we have seen."

- James Greenwood,
President & CEO,
Biotechnology Innovation Organization

Image courtesy of Evonik

A Solid Foundation for Success

The U.S. biopharmaceuticals industry remains resolute

The U.S. biopharmaceuticals industry is unparalleled across the globe. From New Jersey – the historic base of large pharma with the epithet of 'the medicine chest of the world' – to the biotech superclusters of the Bay Area and Boston-Cambridge, and the smaller biotech hubs strung across the country, stakeholders in the U.S. biopharmaceuticals industry have consistently shown a mutual desire to collaborate, evolve and innovate. However, following what was a dynamic and volatile 2018, domestic and international factors have led to an uncertain outlook for the U.S. economy and raised questions over what advancements the biopharma industry could be expected to make this year.

Pressure continues to increase for companies across the board with the Trump administration's concerted efforts to lower drug prices. On the one hand, generic companies are already battling for market share in an increasingly crowded space where margins are already low and price advantage is key, while innovator companies are in jeopardy of having their business models undermined altogether. The 2018 to 2019 government shutdown has presented its challenges for biotechs looking to go public and new regulations put in place by the U.S. Department of the Treasury in October 2018 have meant that foreign investment resulting in a non-controlling equity stake in a biotech will be subject to review by the Committee on Foreign Investment (CFIUS). This could be bad news for U.S. biotechs, since over the first eight months of 2018, US$2.85 billion of investment came from Chinese investors, representing nearly a third of overall VC investment, according to Pitchbook. "Feedback indicates that Chinese investors are becoming tentative when deploying capital into the United States due to the current trade war and the future consequences U.S. investment may have for them," remarked Louis Lehot, managing partner at DLA Piper's Silicon Valley practice.

Despite growing concerns over the aforementioned political and geopolitical factors, the U.S. biopharmaceutical industry's strong foundation and diverse base across multiple cities and states means it is unlikely to be shaken in the medium to long-term. The U.S. biopharma industry reached US$2 trillion in annual economic impact for the first time in 2018, according to the Biotechnology Innovation Organization (BIO), a figure larger than the entire GDP of all but eight countries. Other promising signs include accelerated venture capital investment and job growth in the life sciences industry across the nation. Top academic and research institutions remain the key driver for developing a successful biotech hub, something that has increased in relevance as more opportunities – both through greater early-stage VC investment and an increasing number of incubators/accelerators – are being afforded to researchers and early-stage biotechs to help bridge the often problematic 'Valley of Death.' Boston-Cambridge, home to more than 500 biotech companies, five of the top six hospitals in the United States, and 48 colleges, continues to cement itself as one of the top biotech superclusters. The hub attracted US$2.155 billion in VC Investment in 2017, as well as attracting 48% of all U.S.-based biotech IPOs the same year, according to MassBio. Moreover, the Bay Area – the birthplace of biotechnology – continues to underline its status as the biotech powerhouse, adding to the well-intentioned East –West rivalry between the two hubs.

Total spending on medicines and growth

Source: IQVA, National Sales Perspectives, IQVA Institute, Dec 2017

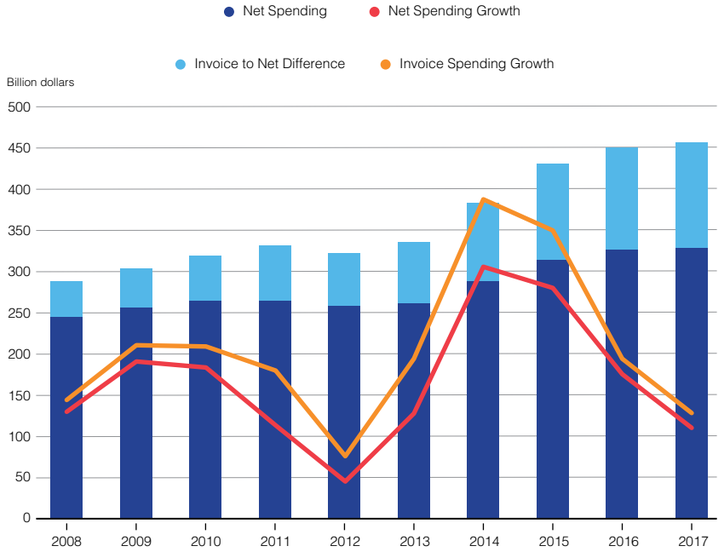
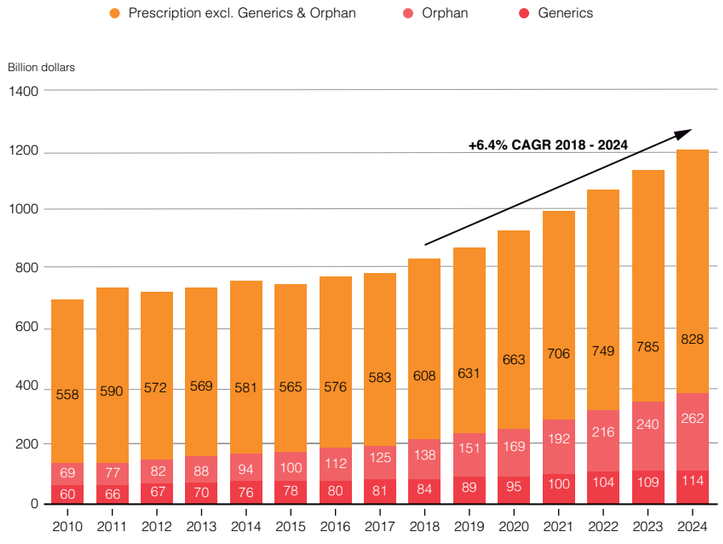


Image courtesy of Ajinomoto Bio-Pharma Services

Worldwide prescription drug sales, 2018–2024

Source: EvaluatePharma, 2018



Although these superclusters often take the limelight, the U.S. biopharmaceuticals industry is by no means concentrated between the two. San Diego, where 48,430 people were employed in the life sciences sector in 2017, ranks third in VC investment in the United States according to EY, garnering more investment than any other country, including China and the United Kingdom.

Rising Stars of the U.S. Biopharmaceuticals Industry

Away from the broadly recognized biotech hubs of California and Massachusetts, a number of cities are aiming to learn from the success of the superclusters. New York City has set plans to become a leader in life sciences innovation and R&D with a US$500 million investment plan. The De Blasio administration's Ten Point Plan, as part of LifeSci NYC, aims to create 16,000 new jobs, with a US$100 million new Applied Life Sciences Hub and US$300 million in tax incentives to attract investment in commercial lab space for life sciences businesses. Next door, New Jersey is also trying to reinvent itself. Long respected as the epicenter for the biopharmaceutical and medical device industry, as well as being home to 13 of the world's 20 largest pharmaceutical companies, a New Jersey Biotechnology Task Force has been set up to foster and evolve the New Jersey biotech ecosystem. North Carolina's life sciences industry, built around its Research Triangle Park – the largest research park in the United States with the highest density of Tier 1 universities in the country – continues to increase in relevance. Although unable to attract the same level of capital investment as the superclusters, the state is home to more than 700 biopharma companies that directly employ more than 63,000 people, according to NCBIO.

Los Angeles has a burgeoning and ever-growing life sciences sector. In 2018, the University of California, Los Angeles (UCLA) and University of Southern California received a combined total of US$636 million in NIH funding, and the county had the second largest employment numbers for life sciences in California. "L.A. County's bioscience industry currently generates more than US$40 billion in economic activity and supports more than 70,000 direct jobs and 160,000 indirect jobs, but it still has tremendous potential for growth," highlighted Mark Ridley-Thomas, supervisor on the L.A. County Board of Supervisors.

The United States has multiple biotech clusters that rival any across the globe. Its biopharmaceuticals industry has been built through its unparalleled research institutions, strong IP protection, collaborative ecosystems, stream of domestic and international investment dollars, and an insatiable desire to keep innovating. Whilst other industries would be heavily affected by macro-economic and geopolitical factors, the U.S. biopharmaceuticals industry is unlikely to be held back in the interim. ■

James Greenwood

President & CEO
BIOTECHNOLOGY INNOVATION ORGANIZATION

The Biotechnology Innovation Organization (BIO) represents biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations

What are BIO's mandate and core areas of focus in driving innovation?
BIO is reaching its 26th year of operation and today we represent about 1,000 members, 85% of which are in the biopharmaceutical space and the remaining 15% in areas such as the agricultural side of biotechnology, biomaterials and biofuels and bioterrorism. Our activities are twofold. Firstly, there is the advocacy side, which involves developing the policies we believe are conducive to the success of innovative companies and working hard against policies we believe will be detrimental. Secondly, we hold conferences and events through which companies can connect with investors.
At the moment, drug pricing is at the epicenter of our focus. The criticism directed at drug companies over pricing has been ongoing for several years but is currently at its most intense due to a number of factors. We see this criticism coming from the media, policy makers, some patient groups and healthcare providers.

To what extent is the criticism around drug pricing justified, and what is at the root of the challenges around patient access and affordability?
Many drugs today are quite expensive. This is because 90% of clinical programs to develop new drugs fail – the basic economics of our industry are high risk, high reward. In the period that the drug is under patent, the price point must be high enough to attract the initial interest from investors and cover reimbursement. Pressure is also mounting because about half of all out-of-pocket spending today occurs when patients are in their deductible. It is the design of the insurance plan that drives the patient's financial experience. In addition, when Obamacare began, the health insurers low-balled their premiums to capture market share. They then realized they set these premiums too low and had to raise them, and blamed drug pricing as the root cause.
In fact, net drug price increases have been on the decline and in single digits for the last five or six years. This includes innovative as well as generic drugs, despite the outliers we see from time to time.

How great a threat is the current rhetoric around drug pricing to medical innovation?
Medical innovation is simultaneously at both its moment of greatest hope and under the greatest political pressure we have seen. By nature, science is always advancing, so our capacity to provide treatments and cures has never been better. However, the potential policies following on from President Trump's emphasis on high drug prices over the course of his 2016 campaign and ever since could be very detrimental to that progress and innovation. We have 100 new members of Congress that were elected in a climate where drug pricing was a major factor. The threat is very real, and we are busy figuring out how to explain our business model – it is often not understood that the private sector contributes the lion's share of R&D money while taking on all of the risk. Some policy makers now even believe that IP and patenting is a bad thing, without understanding that without this protection companies will not be able to find investment for their innovation. 100 members of Congress have signed onto a bill that would enable the Secretary of Health and Human Services to compulsorily license a company's IP to generic companies if that company does not accept the pricing negotiated in the Medicare Part D program.
We believe that a big part of the solution is to focus on patients' out-of-pocket cost, because this is what drives the pricing conversation. Even in the Federal Medicare Part D drug program, one million patients pay more than US$2,000 per year out of pocket, and some pay up to five times as much.

What is BIO doing to educate both the public and policy makers?
Three years ago, we started a "Time is Precious" campaign, based on the premise that our industry enables quality time with loved ones beyond what would otherwise be possible. Nevertheless, the industry cannot communicate itself out of the current negative perception. We have tried highlighting that we consistently only account for 14% of the healthcare spend; we have tried communicating that our prices are not sky-rocketing; we have tried saying that our drugs development programs fail 90% of the time and that price controls would curb investment; we have made TV and radio ads and presented all around the world. But when a patient enters a pharmacy and cannot afford to pay for their medicine, none of that matters. This is why focusing on the out-of-pocket cost is essential.

As some companies look towards a "direct-to-patient" supply chain, do you expect to see major changes with respect to the "middle-men"?
The original notion of Pharmacy Benefit Managers (PBMs) was to negotiate with the drug manufacturers to secure benefits for employees on behalf of the employers. This made sense, since group purchasing organizations offer leverage. What they have evolved into, however, is something quite different. When companies have roughly equivalent drugs to sell, the PBM no longer looks for the best price to benefit the people it represents. Instead, it asks for the biggest rebate, sometimes even requesting that the company raise the price of their drug to offer a bigger rebate. The PBMs therefore tend to cover the drug that includes the biggest rebate rather than the one that is least expensive for the people they are working on behalf of. This has become increasingly recognized, and the PBMs are very much under the gun.
Kick-backs are frequently against the law, but there has been a safe harbor whereby a rebate is not considered a kick-back. The Secretary of Health and Human Services has just announced the abolishment of that safe harbor, taking the rebate system out of Medicare Part D entirely. This is a very positive step.

What work is BIO doing to raise the visibility of companies across the country to the investment community and ensure innovation gets the best chance of reaching the market regardless of geography?
Notably, the most widely-recognized hubs of activity have grown around great universities. These universities tend to attract significant NIH funding and will license great technology to industry under the Bayh-Dole Act. At the BIO International Convention each year, almost all states have a pavilion – they all want to have biotech hubs because the industry is seen as the future for economic strength and an area in which the United States dominates. We have an almost infinite amount to learn about biology and an infinite number of applications within healthcare.
States can encourage and support technology transfer from universities and company formation and retention through initiatives and incentives. The hardest part is attracting venture capital, since venture capital firms tend to want to place an executive on the company board and that executive is likely to want to keep their portfolio companies close to each other geographically. However, we are seeing some firms consider their opportunities more stealthily and starting to identify prospects in lesser-known areas. We also see differing areas of specialization between states, causing some to garner greater attention.

What are your expectations for the role China will play in advancing biotech innovation?
For some time, biotech has been one of China's seven pillars of focus within its plan for economic growth. In the past, there have been a number of inhibiting factors. For example, the CFDA was terribly understaffed – a challenge we have helped to address. Historically, IP protection has also been a great challenge, but this is also improving.
China is a huge market, and there is also a tremendous amount of money coming from Chinese investors into the U.S. biotech industry. While we understand the administration's concern around IP protection due to previous occurrences, we are very troubled by the potential impact that increasing scrutiny would have on the ability of U.S. biotechs to access this important source of funding. We are working with the administration to find our way through this.

Taking into account the current challenges faced by U.S. biopharmaceutical companies, how robust is the industry likely to remain through 2019 and 2020?
The reason U.S.-based companies produce such a high percentage of the world's new molecules is that the United States is close to a free market. While the industry has to yield about US$90 billion according to federal requirements, such as the state rebates in the Medicaid program and 70% discounts in the donut hole in Medicare Part D, before paying corporate taxes, operating closely to a free market drives innovation not only in the United States but also in Europe and Asia since companies in these jurisdictions often look to the U.S. market to recover their investments.
Our major focus at the moment is policy. We are likely to face some tough legislation and proposals from the administration as policy makers respond to the outcry against drug pricing due to the perception that the drug developers are to blame. We have our own policy ideas focused on protecting patients' out-of-pocket costs, and we will focus on getting policymakers to understand the real problem.

What would your message to the industry be as we move through 2019 and towards 2020's presidential election?
Be not disenchanted in challenging times. At BIO, we are very hard at work to protect innovation, and we will ultimately succeed in the policy arena. We want to encourage companies to be part of the solution and to be thoughtful about their pricing. Everyone in this industry has to be politically involved, from the bench scientists to the CEOs – we are facing a strong headwind and must act together to drive the industry forward. ■

Global Business Reports

INTERVIEW

A Balancing Act

Innovators and generics

Under the guidance of Scott Gottlieb, who left as commissioner of the FDA in April 2019, the FDA has fast-tracked drug approval timelines. 2018 was a record year for FDA approvals with 59 novel drugs – new molecular entities – being approved by the FDA's Center for Drug Evaluation and Research (CDER) and two recombinant therapies from the Center for Biologics Evaluation and Research (CBER), as well as a record 971 generic drug approvals.

The CDER approved its first drug ever to treat smallpox, as well as a first of a new class of drugs to treat patients with HIV-1 infection who have not responded to other treatments. Moreover, 34 novel approvals were for rare diseases, including rickets, Fabry disease and phenylketonuria. Of the 61 drug approvals, four were from Pfizer, while Array, AstraZeneca, Eli Lilly, Shionogi and Shire had two approvals each.

Novel drugs entering the market are addressing a range of unmet medical needs, whilst generics are helping to keep costs down for patients. In fact, 90% of all prescriptions in the United States are now generics, compared with 20% 30 years ago. "The FDA has improved their timeline in terms of drug approval," highlighted Jay Shukla, president and CEO at Nivagen. "Previously it could take up to 15 months for approval, which has now decreased to be between eight to 11 months."

> The cost of commercializing an IP has increased tenfold as the cost of API, components, testing and of course the fees have gone up significantly, which has been a great burden. We hope the FDA will provide faster approval rates and hence we will be able to get to market faster.
>
> - Himanshu Brahmbhatt, VP - Business Development and Sales, Sunrise Pharmaceutical

Innovator and generic business model approaches vary quite significantly. The innovators are taking on far greater risk over a much longer time frame with potentially high rewards at the end. On the other hand, generics pharma companies are more cost conscious. Due to record FDA-approved generic drugs entering the market, their margins are becoming increasingly tighter. "It is no secret that the U.S. generic drug market is significantly crowded, so we are looking at multiple avenues for opportunities," remarked Himanshu Brahmbhatt, VP for business development and sales at Sunrise Pharmaceutical. "Our strategy has been to look at scenarios where there may be a pathway to faster approval or to tackle a complex molecule or drugs with unmet market needs."

Indeed, there are a number of different routes generic companies can take in order to seek value in the market. For example, Teligent, under its Topical, Injectable, Complex and Ophthalmic (TICO) strategy, has focused on specific areas of the market where there is less competition. "We chose to develop products that did not require clinical end point studies, had a high chance of obtaining FDA approval and were in relatively small, stable markets," underlined Damian Finio, CFO at Teligent. "Topicals were an obvious choice and, over the course of the next couple of years, approximately 50 ANDA's were filed."

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>
> - Damian Finio, CFO, Teligent

With a clearer pathway for generic drugs to enter the market than ever before, a fine balance needs to be kept where drugs remain affordable for patients through generic approvals, but there is also incentive for universities, biotechs and pharma seeking IP to pursue innovative, novel molecules with the high financial risks associated with them to address the range of unmet medical needs.

IP protection has been essential in helping to promote the development and availability of novel drugs, allowing authorities the opportunity to assess the quality of drug products as well as preventing counterfeit copies. This is also set to change in the coming years as a high volume of patents are filed as a result of more scrutiny due to post-grant proceedings. "In terms of strategies in biologics, pharma companies will likely try to patent all different aspects of their technologies," remarked Vishal Gupta, partner at Steptoe & Johnson. "These include dosage forms, formulations, methods of treatment and manufacturing processes in addition to the main therapy itself. Companies may also seek to claim biologics in various ways (e.g. by sequence, binding properties and competition) as patent laws in this area continue to evolve.

Moving forward, retaining a balance between the innovator and generics market will remain key to the health of innovation for the biopharma industry, especially as the rhetoric around drug pricing grows in the coming year. ■

Doug Giordano

Senior VP, Business Development
PFIZER

Pfizer is the world's second-largest independent biotech company by market capitalization.

Could you share Pfizer's approach to business development, as well as its key objectives for 2019?
Pfizer's approach to business development is to seek out opportunities that advance our breakthrough science and business strategies. This has been our overall approach in recent years, and will continue to be in 2019. While our general approach has not changed, we are increasing our focus on opportunities that can provide early-stage pipeline assets that can provide potential for long-term growth, rather than later-stage assets that can provide near-term revenue.
We have a particular focus on continuing to find the right partnerships and investments that focus on accessing cutting-edge science and breakthrough biology for novel targets, technology platforms and old and new modalities to generate true first-in-class therapies in areas of high unmet medical need. Additionally, we will look for those opportunities across all stages of drug development to enhance growth mid- to long-term, and do so globally, regardless of geographic location. In addition, nontraditional partnerships – such as those with technology companies – are becoming increasingly interesting to us. It's still somewhat early to determine exactly how our core capabilities can truly complement each other to advance scientific research, but we are excited about future possibilities in this space.

Oncology continues to be a hot area for investment and R&D. How integral will this therapeutic area be for Pfizer?
Pfizer invests in areas where we see the greatest opportunity and where we believe we can deliver the best value. While oncology is a core therapeutic area for Pfizer, we have a diverse pipeline and product portfolio, and we continue to invest in each of those areas. For our R&D efforts specifically, our core therapeutic areas are: inflammation and immunology, internal medicine, oncology, rare disease and vaccines. We look to business development to enhance our pipeline with programs that are approaching or already in the clinic. We also seek partnering opportunities to gain access to specific technologies within Pfizer's core therapeutic areas and platforms to enable drug discovery and development.

What is Pfizer's attitude toward "external innovation" versus acquisition and building out internal capabilities and capacity?
It's always important to find the right mix of external innovation versus internal innovation, but the lines are not always clear-cut. While we certainly focus on building internal capabilities, we also seek early-stage platforms and technologies externally that we can bring in-house and then continue to build internally to suit any specific needs. Traditionally, business development in the pharmaceutical industry was generally confined to M&A and in-licensing assets or technologies. But in recent years, our focus on true research partnerships – where we work collaboratively with a partner to achieve shared goals, building on the unique strengths of each partner – is often where we can unlock the most potential. And that blurs the lines a bit between innovation that is purely internal or purely external.
We believe this is what has been key to our success and will continue to be in the future: sourcing the best assets, capabilities and talent from within our walls, while creatively tapping into the rich external environment. Ultimately, our goal is always to bring forward the best science to help us deliver transformative therapies to patients.

Could you outline the strategy driving Pfizer Ventures' fund allocation?
Pfizer Ventures was founded in 2004 with the goal of investing in emerging companies that are advancing innovative breakthrough science across all stages of development. Today, Pfizer Ventures actively manages an investment portfolio of more than 40 companies with more than US$1 billion of total assets. Pfizer Ventures only invests in areas of current or future strategic interest to Pfizer. In June 2018, Pfizer announced an expansion in venture investing with US$600 million commitment to Pfizer Ventures, and up to approximately 25% of new funding will be dedicated to neuroscience. In 2018, Pfizer Ventures made seven investments, three in neuroscience.

Could you share a final message to Global Business Reports' national and international readers?
When it comes to our partnering philosophy, we seek partners who share our goal of bringing highly differentiated therapies to patients faster and more efficiently than would otherwise happen in isolation. We recognize that each partnership is unique, and over the years our teams have become more and more creative and resourceful in creating deal structures that share in the risks and opportunities so that each party and its respective stakeholders are positioned for success. ■

Eric Falcand

Vice President, Head of Business Development and Licensing
SERVIER GROUP

Servier is a privately owned global French pharmaceutical company that manufactures and markets pharmaceuticals and conducts pharmaceutical research and development

As one of the leading privately-owned pharmaceutical companies, where does Servier position itself in the market?
Servier is a unique pharmaceutical company in the sense that we have no shareholders and are controlled by a non-profit foundation. We have been committed to therapeutic progress to serve patient needs, and we strive to create a world where quality healthcare is available and accessible to all. Servier provides branded and generic drugs used to treat nearly 100 million patients daily. Servier reinvests approximately 25% of our revenue into R&D, and we have over 2,900 employees worldwide committed to R&D activities. Our growth is driven by innovation in five therapeutic areas, including: cancer, cardiovascular diseases, diabetes, immune-inflammatory diseases and neuropsychiatric disorders. We are a leader in cardiology - ranked second in Europe and eighth worldwide. Oncology has also become a top priority for Servier in recent years, highlighted by our recent acquisition of Shire's oncology branch, and the decision has been made to focus our R&D spend to reach 50% on oncology in 2020. We have a commercial presence in 149 countries and employ approximately 22,000 people worldwide.

Historically, Servier has had a focus in cardiology and rheumatology. How has your US$2.4 billion acquisition of Shire's oncology branch changed your overall therapeutic focus?
Servier is a research organization focused on serving the needs of patients, and therefore, the oncology space is an obvious area that we wanted to focus on. The company is not reducing its activities in other domains such as cardiology or diabetes, but only adding another priority field to balance its portfolio.
In 2018, Servier acquired Shire's oncology branch for US$2.4 billion, which enabled the company to establish a direct commercial presence in the United States and strengthen our oncology drug portfolio. The objective is to continue expanding our presence and research activities within the field of oncology. The acquisition included two in-market products: ONCASPAR - a treatment for acute lymphoblastic leukemia (ALL) - and the rights for ONIVYDE - a treatment for metastatic pancreatic cancer post-gemcitabine based therapy – the last one outside of the United States. Moreover, the portfolio also included two early stage immuno-oncology pipeline collaborations.

Servier also launched Servier BioInnovation in Cambridge, Massachusetts in 2018. What was the importance for Servier in establishing a presence in the United States?
Servier opened the BioInnovation office in Cambridge, Massachusetts in February 2018, at the core of this world-class innovation cluster. The United States is a key market for us, especially in the field of oncology, and we intend to establish a long-lasting position in this field with the objectives to treat even more patients with innovative medicines and to become a leading global player in the oncology domain. Servier has several research alliances with U.S. biotechs, pharmaceutical laboratories, startup companies, scientific organizations and prestigious academic centers with our active partnership policy in the field, which includes Novartis, Amgen, Cellectis, Allogene Therapeutics, Macrogenics, Pieris, Miragen, LabCentral, MIT and Harvard University. Together we are committed to therapeutic progress to serve unmet patient needs.

What are Servier's key objectives moving forward as you continue to establish the company's U.S. presence?
Servier's key objective is to continue serving the need of the patients. We want to ensure with existing drugs that there is enough supply, that patients have access to drugs and that lives will be saved. Another objective is to add products to our portfolio and increase our footprint in the oncology space. We have the ambition to be a strong player in the U.S. market and a leader in each of the domains where we have a presence. Servier is focused on innovation and progress in the pharmaceutical industry. We aim to be a partner of choice in the life sciences industry as we believe that multiple collaborations will increase the probabilities of success of our programs and the chances to discover new therapeutics for the benefit of patients. ■

Jay Shukla

President & CEO
NIVAGEN PHARMACEUTICALS, INC.

Nivagen is engaged in the development, acquisition and sales of 505(b)(2)s, injectables, and specialty generic prescription drugs for the North American market

Could you provide an overview and an update on the recent developments at Nivagen since its founding in 2009?
We are currently focused on the development of 505(b)(2) drugs, injectables and specialty generic prescription drugs for the North American market. We also provide our existing commercialization platform to other manufacturers seeking to break into the U.S. market. The company has been growing significantly since our inception, and we are currently in the process of scaling up. We expanded our laboratory facilities in Davis, CA, and we now have in-house capabilities to offer formulation development of injectable and ophthalmic products and to develop and validate stability-indicating analytical methods.
Since establishment, we have achieved substantial growth and now hold a significant market share. In approximately one year, Nivagen has managed to grow its revenue ten-fold. We expect to see competition in the generics space in the near future, but believe that we will still have a competitive edge and will continue to hold our market share despite a decrease in margins. We plan to expand our product portfolio to compensate for this anticipated decrease in margins.

2018 has been a record year for FDA approved generic drugs for commercial use. How has this impacted Nivagen?
The FDA has improved their timeline in terms of drug approval. Previously it could take up to 15 months for approval, which has now decreased to be between eight to eleven months. Despite this, the FDA has increased the generic drug user fee amendments (GDUFA), maintenance fees, facilities fees and drug master files (DMFs) fees. Accumulated fees are now almost US$200,000, as compared to US$80,000 in 2017. This has impacted the pharma industry in such a way that companies are more mindful of which molecules and drugs they dedicate for approval. Increases in the approval of generic drugs is not a result of the FDA being more lenient, but rather the result of companies approaching the FDA with higher quality research and data. Nivagen's approach is to be more mindful and add more 505(b)(2) programs. From a portfolio perspective, we aim to have niche products with good margins, high volume products with lower margins and products that are unique in their fields.

What is Nivagen's market proposition for companies wanting to launch a product in the United States?
There are four key elements to entering the market: the product, the supply, the quality and the cost structure. If one does not have the right product to fill a market need, one will struggle to succeed. If there is a need for a product, it will need to have a solid, robust and consistent supply. The product must be at the highest quality, FDA certified and offered to the market at the right price. Our sales and marketing personnel are among the best in the world. Nivagen can offer instant access to the U.S. market. We also offer reporting and auditing services to companies wanting to enter the U.S. market. We provide transparency by creating online portals for our clients so that they have access to all the information related to their products, such as inventory and daily sales information.
It can be challenging for a foreign company to launch a product in the United States, as it is time consuming, capital intensive and their product is not known to the U.S. market. As Nivagen is already set up as a vendor in the United States, we can provide complete turnkey solutions and cost-effective delivery on an accelerated timeline. We have been in the industry for over nine years and thus have experience in moving through the commercialization process in a timely and cost-effective way.

What are Nivagen's key objectives for 2019?
Nivagen aims to build its own manufacturing unit in 2019. We are in the process of raising funds for the project, which will require approximately US$40 million. Our goal is to establish the facility on the West Coast; we believe that this area holds significant opportunities for manufacturing. Another objective is to spin off our 505(b)(2) group to create a company solely focused on our 505(b)(2) programs. We are also actively looking to partner with a CRO and CRAM to co-develop products. ■

Breaking Down Drug Pricing

A look at the U.S biopharmaceuticals industry would be incomplete without approaching the elephant in the room – drug pricing. The 2020 presidential election campaign will no doubt be one of the hardest fought, both in the primaries and the election itself. Record numbers of funds have already been raised by the candidates and possibly the only thing in common between the Trump administration and the Democrat hopefuls is their desire to lower drug pricing. In his 2019 State of the Union speech, Trump appealed to Congress to pass legislation to deliver fairness and price transparency for American patients: "We should also require drug companies, insurance companies and hospitals to disclose real prices to foster competition and bring costs way down," remarked Trump.
Undeniably, Americans spend a lot on their healthcare and, justifiably, the majority of the population want this to change. U.S. healthcare spending accounted for 17.9% of overall GDP, reaching an astonishing US$3.5 trillion, or US$10,739 per person in 2017, according to the National Health Expenditure Accounts (NHEA). The 2017 figure represented a 3.9% year-on-year growth in healthcare spending. When breaking the spending figures down, from 2017 to 2026, payments to hospitals and doctors are expected to grow by US$1.1 trillion, more than four times the growth in prescription drug spending, according to CMS – National Health Expenditure Projections. Moreover, U.S. spending on prescription drugs as a share of total healthcare dollars in 2017 was at 12%, lower than in Germany, France (both 13%) and Canada (14%) in 2015, according to the Organisation for Economic Co-operation and Development. When taking into account that 2018 was yet another record year for FDA drug approvals with 59 novel drugs and biologics, and that the United States regularly approves more than half of the world's new drugs despite having one of the most stringent approval systems, blaming the biopharmaceuticals industry for healthcare costs sets a dangerous precedent. "Medical innovation is simultaneously both at its moment of greatest hope and under the greatest political pressure we have seen," underlined James Greenwood, president and CEO of the Biotechnology Innovation Organization. "By nature, science is always advancing, so our capacity to provide treatments and cures has never been better. However, the potential policies following on from President Trump's emphasis on high drug prices over the course of his 2016 campaign and ever since could be very detrimental to that progress and innovation. We have 100 new members of Congress that were elected in a climate where drug pricing was a major factor. The threat is very real, and we are busy figuring out how to explain our business model – it is often not

National Security Changes Impact Biotechnology Industry

By: Laura Fraedrich, Justin Huff and Sara Rafferty

Executive Summary

In August 2018, the President signed two transformative bills impacting the biotechnology industry. Rooted in the idea of protecting U.S. national security, the Export Control Reform Act of 2018 (ECRA) and the Foreign Investment Risk Review Modernization Act of 2018 (FIRRMA) share the dual goals of enhancing U.S. export controls and expanding the United States' ability to review foreign direct investment in U.S. businesses. ECRA modernizes U.S. export control regulation of commercial and dual use-items and mandates additional export controls on "emerging and foundational technologies"—terms yet to be defined. FIRRMA expands the authority and oversight of the Committee on Foreign Investment in the United States (CFIUS). FIRRMA also requires the notification to CFIUS of certain foreign investments, including noncontrolling investments, in U.S. "critical infrastructure" and "critical technology" companies, as well as companies that maintain or collect sensitive data of U.S. citizens (collectively "Sensitive U.S. Businesses").

ECRA - Impact on the Biotech Industry

Congress passed ECRA with three primary goals: establish permanent statutory authority for U.S. export controls on commercial, dual-use and less sensitive material items; mandate a formal interagency process for identifying "emerging and foundational technologies" essential to U.S. national security; and increase controls on countries subject to U.S. arms embargoes.

The process for identifying emerging and foundational technologies will have the largest impact on the biotechnology industry. Under §1758 of ECRA, the President has established an interagency process involving the departments of Commerce, Defense, Energy and State to institute export controls on "emerging and foundational" technologies to restrict sensitive technologies from foreign access. Emerging and foundational technologies are not defined terms in ECRA.

As part of the process, the U.S. Department of Commerce's Bureau of Industry and Security (BIS) published an advance notice of proposed rulemaking (ANPRM) in November 2018 to seek public commentary before releasing a definition of emerging and foundational technology. This public comment process was slated to last 30 days but was later extended, reflecting the difficulty of establishing the proper contours of this important new concept for export controls.

The ANPRM outlined 14 general sectors of technology being considered for tighter regulations, and BIS specifically sought input on named sub-categories to determine whether they contain emerging technologies. Biotechnology was highlighted as potentially warranting an increase in export controls, and BIS highlighted four subsectors of particular interest: nanobiology; synthetic biology; genomic and genetic engineering; and neurotech.

Currently BIS is reviewing the nearly 300 comments received related to its ANPRM. BIS received less than 25 public comments specific to the biotech industry. Most of the comments call for BIS to allow for continued global collaboration in the biotechnology industry.

BIS is also examining publicly available information; classified information; information relating to reviews and investigations of transactions by CFIUS; and input from certain advisory committees. Once defined, companies with emerging and foundational technologies in the biotech arena may need a license to export these technologies. In some cases, the licensing requirement may be subject to a policy of denial, thus effectively making the license requirement a prohibition on exports.

FIRRMA – Impact on Biotech Industry

In addition to potentially needing a license from BIS to export emerging and foundational technologies in biotechnology, a U.S. company with emerging and foundational technology may trigger a mandatory CFIUS notification before closing when the subject of a foreign investment or acquisition.

FIRRMA expands CFIUS's authority and oversight through a mandate that foreign investors notify CFIUS prior to making certain investments, including noncontrolling investments, in what are considered Sensitive U.S. Businesses. Specifically, effective November 10, 2018, CFIUS began requiring filings for investments in "critical technology" companies through the implementation of a mandatory pilot program.

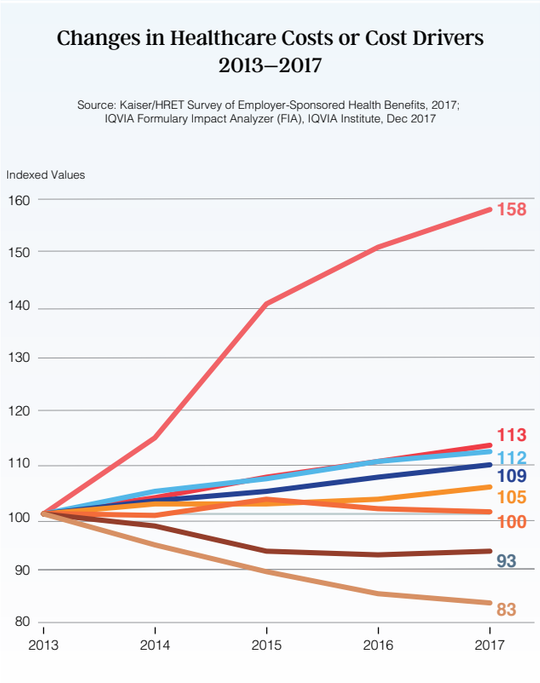
Any investment by a foreign person in a U.S. company that produces a "critical technology" must notify CFIUS 45 days before closing if the technology is used in connection with one of 27 identified pilot program industries. These industries are defined by the North American Industry Classification System (NAICS) and include research and development in nanotechnology (NAICS Code: 541713) and research and development in biotechnology (except nanobiotechnology) (NAICS Code: 541714).

In our recent experience, most biotech companies do not possess the type of technology that is captured in the current definition of "critical technology." However, once the interagency process defines emerging and foundational technology, U.S. biotech companies may be subject to the mandatory CFIUS notification requirement when the subject of a foreign investment or acquisition. Due to the pilot program's global application, any foreign investment must comply with the regulations. Failure to do so may result in a fine up to the value of the transaction, attributable to both the investor and the U.S. company.

Summary

Through ECRA and FIRRMA, the U.S. government is focusing on policies that enhance U.S. export controls while expanding the United States' ability to review foreign investment in U.S. businesses. As the scope of these laws is clearly defined in the coming months, there will be major implications for the biotechnology industry. The definition of "emerging and foundational" technologies may restrict sensitive technologies from foreign access and the added layer of the mandatory CFIUS pilot program may deter foreign investment and limit U.S. biotechnology businesses' access to foreign capital. ■

Ms. Fraedrich, Mr. Huff and Ms. Rafferty are attorneys at the global law firm Jones Day, based in its Washington office and part of the Firm's Government Regulation practice.



understood that the private sector contributes to the lion's share of R&D money while taking on all of the risk."

Indeed, there is money to be made in the biopharmaceuticals industry, but this is what drives innovation in a high-risk industry. Tufts Center for the Study of Drug Development put the cost of getting a drug to approval at US$2.6 billion in 2014, a colossal increase of 145% from their 2003 figure. Despite this, net drug price increases have been in decline and in single digits for the past six years. The industry needs to come together in this precarious moment to help educate Congress and the population about drug discovery and development. When a system is broken, as the U.S. healthcare system seems to be, it is easy to want to point fingers. However, when an innovative drug or technology has the capability to become a treatment, or even a cure, and subsequently prevent decades worth of healthcare costs, it puts the price of drugs into perspective. Gilead's series of drugs – Sovaldi®, Harvoni® and Epclusa® – have cured Hepatitis C. When taking into account the significant healthcare costs incurred by Hepatitis C patients, a virus that can necessitate a liver transplant through hospitalization and associated procedures, the long-term savings enabled by these drugs, or "costs avoided," are clear. ■

Thoughts on the Drug Pricing Debate

"We do not have a drug pricing issue, but rather a healthcare system issue. Politicians can continue to look at the costs of drugs as an issue, or they can try to really understand that even if drugs were free, we would still have a healthcare problem."

- Robert K. Coughlin, President & CEO, MassBio

"Both the Trump Administration and Democrats are committed to reduce drug pricing. This concurrence puts an emphasis on new and innovative technologies, which means that companies need to have cutting edge and novel technologies to get a premium in the market. Because of this, companies have the additional pressure to prove their "value add" to the market."

- Edward John Allera, Buchanan Ingersoll & Rooney

"We often hear the phrase "sky-rocketing drug prices" in the media and from policy makers, but all the data shows this is not the case. In fact, net drug price increases have been on the decline and in single digits for the last five or six years. This includes innovative as well as generic drugs, despite the outliers we see from time to time."

- James Greenwood, President & CEO, Biotechnology Innovation Organization

John Patrick Oroho

Executive Vice President and Chief Strategy Officer
PORZIO LIFE SCIENCES

Porzio Life Sciences is dedicated to helping pharmaceutical, medical device and biotechnology organizations master the evolving regulatory environment

Porzio Life Sciences offers a range of solutions to its clients, including the Porzio Compliance Digest, Porzio AggregateSpendID and Porzio GST®. What has been your key area of focus over the past year?

Porzio Life Sciences has continued to specialize across several avenues, but one area of particular interest has been transparency and transparency reporting – which is the reporting of financial interactions and transfers of value between life sciences companies, healthcare practitioners and healthcare organizations. Transparency reporting is multi-layered, affecting individuals and companies at the city, state and federal level. Under the Affordable Care Act, there is a law – the Physician Payment Sunshine Act (PPSA) – that requires companies to report their financial relationships with physicians and teaching hospitals. Moreover, there are states that require reporting on a broader group of healthcare practitioners, including nurse practitioners, physician assistants, certified midwives, registered nurses and pharmacies. Specified regulations have also trickled down to cities; for example, Chicago requires sales representatives to be licensed by the Department of Health and to maintain records in connection with interactions with physicians. This is a way to regulate the sales and marketing operations of life sciences companies and Porzio Life Sciences is increasingly assisting companies in this process.

Could you elaborate on Porzio Life Sciences' client base?

Our client base is mainly small to mid-sized companies that are looking to outsource reporting as they do not have the internal resources to do so themselves. Larger companies historically did the reporting in house, but also made use of our Porzio Compliance Digest and consulting services in order to stay abreast of regulatory changes and complexities. Now that vendors, most notably Porzio Life Sciences, have demonstrated the ability to handle large quantities of data and to report accurately and in a timely manner, large companies are looking to us to handle transparency reporting under our traditional model or new outsourced model. Our focus remains to assist our clients – small or large – to master the evolving regulatory environment for reporting purposes globally.

Could you introduce us to the Porzio Compliance Digest (PCD) and how the platform has evolved in recent years?

Porzio Compliance Digest (PCD) is the first interactive, internet-based compliance database on state and federal laws, regulations and pending legislation governing the distribution of trade and sample products, sampling to mid-level practitioners and marketing disclosures, restrictions and limitations. We are currently tracking the regulatory environment in all 50 U.S. states and globally. We have increased the number of areas that we track as a result of client demand. Clients are also demanding the distribution and regulatory requirements of products in certain geographic areas. We now also work with clients to compliantly sell, market and distribute their products. Our clients are spread across the entire United States, and we also service foreign companies establishing operations within the United States. We develop systems and processes and then wrap professional and regulatory consulting services around them.

Could you elaborate on Porzio GST®, Porzio Life Sciences' second expansion of services related to global transparency requirements?

Porzio GST® – a global spend transparency solution – provides an easy-to-use, configurable interface that enables companies to capture and manage data elements necessary for meeting their reporting obligations in 40 ex-U.S. jurisdictions. Almost 40 jurisdictions outside the United States have some type of transparency reporting requirement, each with significant and unique challenges. A successful solution must contemplate these challenges and provide practical and effective operational and compliance answers. Our clients rely on us to help them with not only the reports that need to be filed, but also the actual interactions with healthcare organizations and practitioners around the globe so that they can be mindful whether or not they should have concerns regarding compliance. We have a global risk management system, which allows us to service and offer solutions to our customers internationally.

What are Porzio Life Sciences' key objectives for 2019?

We will continue to build out our global transparency and global auditing and monitoring capabilities. The market is now looking for an effective global healthcare professional (HCP) Engagement Center, so we look to continue building out our capabilities and the ongoing evolution of our Global Spend Transparency (GST) ecosystem. ■

Vishal Gupta

Partner
STEPTOE & JOHNSON

Steptoe & Johnson is an international law firm specializing across all areas of IP

Does Steptoe expect to see significant changes in biologics laws in the near future?
Biologics implicate an interesting area of the law that is continuing to evolve. For example, there can be various ways to claim an antibody itself – whether it be by its sequence, its binding properties or competition properties, for example. As the law evolves, it is expected that one of the foregoing categories will eventually emerge as less susceptible to invalidity challenges than another. The outcome of currently hotly contested litigations will end up being a driver for future laws and the ways in which patents are filed in the first place. Further, as the number of biosimilars litigations continues to increase, we will see procedural law in the area continue to clarify.

What are the current major regulatory trends in the life sciences space?
With respect to biologics, the patent thickets continue to grow in size. It is not a surprise that there is an uptick in filings in post-grant proceedings such as IPRs in this space. In addition, we have noted that in biologics and biosimilars litigation, the numbers of patents asserted often far exceed the numbers common in the small molecule space.

How are companies likely to change the way they file for patents in the future?
We expect to see high volumes of patents filed in the life sciences arena, particularly as they are now under more scrutiny due to post-grant proceedings. In terms of strategies in biologics, pharma companies will likely try to patent all different aspects of their technologies. These include dosage forms, formulations, methods of treatment and manufacturing processes in addition to the main therapy itself.

What are Steptoe's key objectives moving forward?
We believe that the life sciences space will continue increasing in relevance for the firm, and we will continue to focus our efforts on this space. ■

Alan Seem

Partner
JONES DAY

Jones Day is a large law firm in the United States and one of the largest firms globally

What changes in cross-border investment activity have you been noticing in biotech, especially between China and the United States?
In terms of cross-border activities with China, there are now capital controls that limit the amount of foreign exchange that can be taken out of China. This can present a significant challenge to M&A activity and bring into question a Chinese buyer's source of funds, the process and approvals needed for getting the money out of China, and the effect on timing of the transaction.
From the U.S. side, there has been more scrutiny by the Committee on Foreign Investment in the United States (CFIUS) on foreign investment from certain countries, particularly China. In August 2018, a new piece of legislation - The Foreign Investment Risk Review Modernization Act of 2018 (FIRRMA) - was passed, which further expands the authority of CFIUS. There is therefore some concern in certain areas that export controls need to be further tightened to protect critical and sensitive technologies from falling under the control of foreign powers. CFIUS filings were previously voluntary, but after FIRRMA was passed, 27 industry "pilot programs" were announced, one of which was biotech R&D, and the new rules mandate filings with CFIUS for transactions that fall within the scope of the pilot program. CFIUS is now being used not only to protect national security, but also to protect industries that have critical economic and strategic importance to the United States, including biotech, and prevent such technologies from being transferred or sold to foreign countries.

What is your outlook for clients working in both the United States and China?
The relationship between China and the United States is currently not on good terms, and both sides seem unlikely to back down without some significant diplomatic breakthroughs. ■

Louis Lehot

Managing Partner
DLA PIPER

DLA Piper, one of the largest law firms in the world, has a footprint across 40 jurisdictions and an active life sciences team

How has the opening of the Stock Exchange of Hong Kong to biotech companies and trade tension between the United States and China impacted biotech companies?
The HK Exchange is trying to provide Chinese biotech companies with an IPO alternative to the NASDAQ, and while there was a rush of activity from biotech companies earlier this year, it is uncertain whether the HK Exchange can provide a viable alternative in the near term. In the United States, there is a great opportunity to attain capital investment from China to grow life sciences businesses and sell the products back into the Chinese market. However, feedback indicates that Chinese investors are becoming tentative when deploying capital into the United States due to the current trade war and the future consequences U.S. investment may have for them.

What result have the recent U.S. tax reforms had on the biotech industry?
The corporate tax rate decrease from 35% to 21% has been a great advantage for corporations and investors. The application of a tax on global offshore cash with no further repatriation tax into the United States has also allowed American companies to bring cash back into the country from offshore and invest it. This has resulted in a huge increase of shares purchased in the open market by American public companies.

In terms of IP protection, what key industry trends are you seeing?
Since the TC Heartland v. Kraft Foods Group, 137 S.Ct. 1514 (2017) case in the U.S. Supreme Court, there has been a significant decrease in the amount of patent litigation in the United States. At the same time, China has become much more serious about IP protection, especially in key sectors such as biotech and medtech, and this trend will continue as companies increase their local innovation activity. Another trend in the biotech sector relates to biosimilars; we are already seeing some patent litigation around the approval and marketing of biosimilars. ■

Edward John Allera

BUCHANAN INGERSOLL & ROONEY

Buchanan Ingersoll & Rooney is a national law firm providing legal, business, regulatory and government relations advice

In 2018, there was a record number of FDA generic drug approvals. Is the market becoming overly competitive?
Yes, with the record amount of approvals there is a significant amount of competition for market share. To that end, Buchanan has done extensive litigation in the life sciences space to assist our clients in achieving the best market share and value for their products. I believe that the generic industry is currently in a highly compromised position, and companies are struggling to find value within the deflationary generic market. In addition to the competition, FDA's strict enforcement of cGMP regulations also makes it very difficult to make money in the generic sector.

With the government shutdown potentially impacting IPOs for 2019, what are Buchanan's expectations for 2019 with regards to capital markets and public offerings?
Because the capital markets sector does not like uncertainty, the government shutdown has caused a significant amount of disruption and volatility with investors. However, the real issue on the table is drug pricing. Both the Trump administration and Democrats are committed to reducing drug pricing. This concurrence puts an emphasis on new and innovative technologies, which means that companies need to have cutting edge and novel technologies to get a premium in the market. Because of this, companies have the additional pressure to prove their "value add" to the market. The big challenge arises as investors are continuously evaluating risks. Companies attempting to bring new technologies to the market do not necessarily have proven track records to help eliminate that risk. This results in investors focusing only in the later stages of the development process. As such, approximately 95% of biotech companies are being developed with the end goal of being sold off to a trade partner. ■

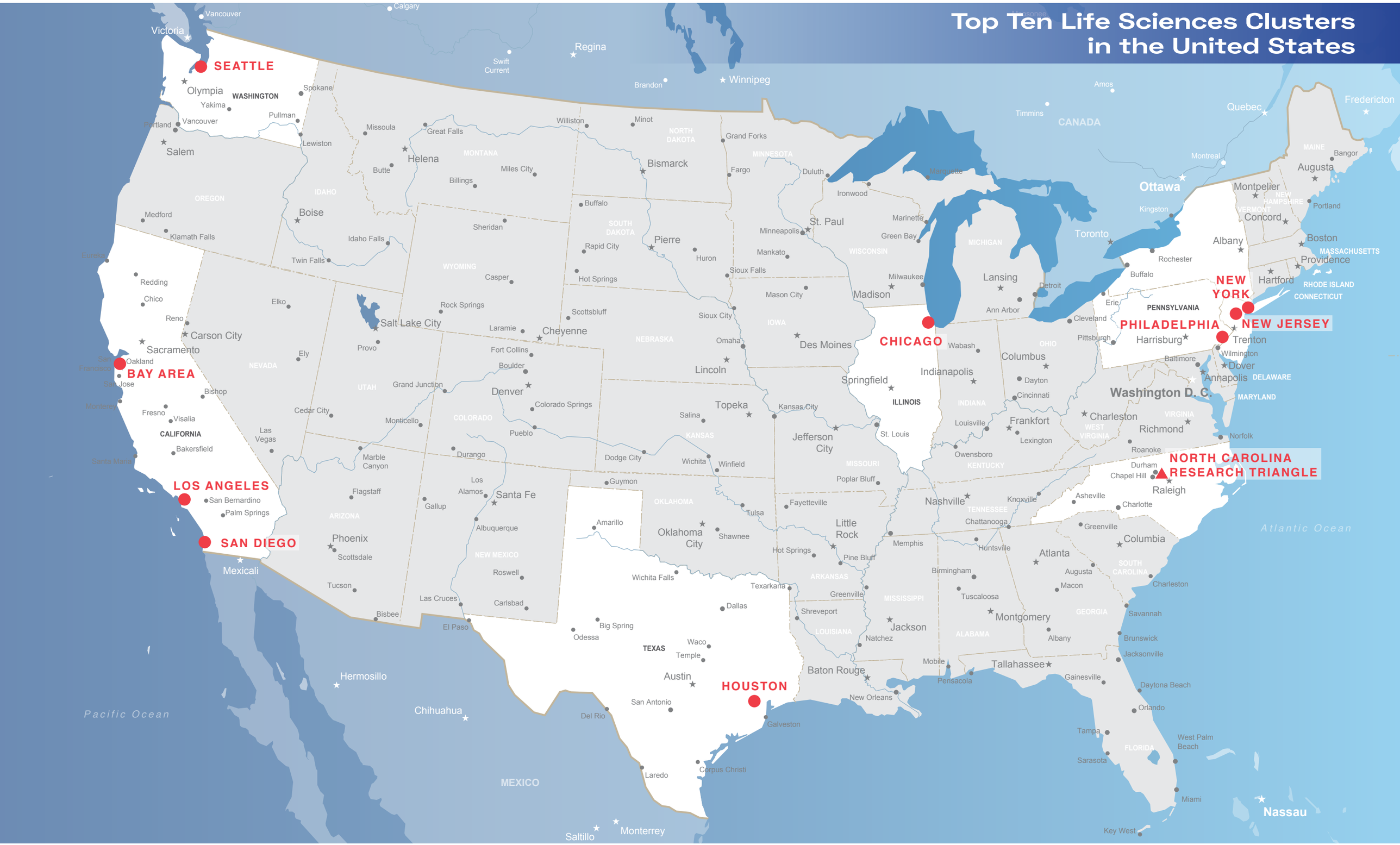
West vs East

"Healthy rivalry is a positive thing for the industry. The biotech community is very collaborative, but it also enjoys great competition, especially in California."

- Joe Panetta,
President and CEO,
Biocom

Image courtesy of CordenPharma

Top Ten Life Sciences Clusters in the United States



California

The golden state of opportunity

From the Gold Rush in 1848, to the creation of the motion picture industry in Hollywood in the early 1900s, and the tech boom of recent years, California has historically been an inventive state where dreams have been realized. Although some of the state's industries have declined in recent years, such as aerospace, California's economy is now the equivalent of the world's fifth-largest country, with a GDP nearing US$3 trillion. Home to 3,418 life sciences companies, including 1,570 biotech and pharma companies, the industry injects 958,000 direct, indirect and induced jobs into the state. Moreover, the state remains the national leader in NIH grants, attracting US$3.9 billion in 2018, as well as venture capital, which attracted US$7.6 billion the same year, US$1.5 billion higher than in 2017. California's life sciences industry has continued to evolve and is now incomparable across the globe in terms of size and investment.

What remains key to the growth of the state's life sciences sector is its research and academic institutions. Underpinned by the University of California (UC) system, which is comprised of more than 238,000 students, the state is home to 10 of the world's top 100 universities (Shanghai Index, 2018 Rankings). Spread across the state from Davis to Irvine, the depth and breadth of the region's academic excellence is unparalleled, igniting ecosystems through a combination of talent, technology transfer and company spin outs. California's institutions are the entry point feeding into the largest biotech network globally. This is in part helped by having the largest number of doctoral recipients (4,954) in science and engineering in the United States, much higher than the second largest (New York with 3,050), according to the California Life Sciences Association (CLSA).

Although attention is often reserved for the Bay Area, San Diego and more recently Los Angeles, it is California's entire network that contributes to an unsurpassable life sciences ecosystem. Sacramento – the state capital – which has 10,912 employees in life sciences, is an increasingly attractive choice for smaller biotechs and contract service providers due to its close proximity to the Bay Area and far lower living costs. Santa Cruz, roughly 70 miles south of downtown San Francisco, also offers similar opportunities. "Especially for young companies, setting up operations in Santa Cruz can be attractive as it is less expensive and with more square-footage available than most of the Bay Area," highlighted Andrea Pesce, industry alliances and licensing manager at UC Santa Cruz.

With so many hubs in California competing for investment dollars and talent, one would assume that the competition would be harmful. In fact, California has made a concerted effort to increase collaboration between the different hubs so that their strengths can be shared. Joe Panetta, president and CEO of Biocom, sees any sort of rivalry as a positive motivator for the hubs and state overall: "Healthy rivalry is a positive thing for the industry. The biotech community is very collaborative, but it also enjoys great competition, especially in California. I would not say the hubs are in competition with each other, but are constantly challenging each other in a healthy manner. It serves to move everybody forward and to grow the industry overall. The bottom line for all these companies is to launch products that improve human health."

CAPITAL
Sacramento

POPULATION
39,557,045
(United States Census Bureau, 2018)

Average annual life sciences wages by cluster

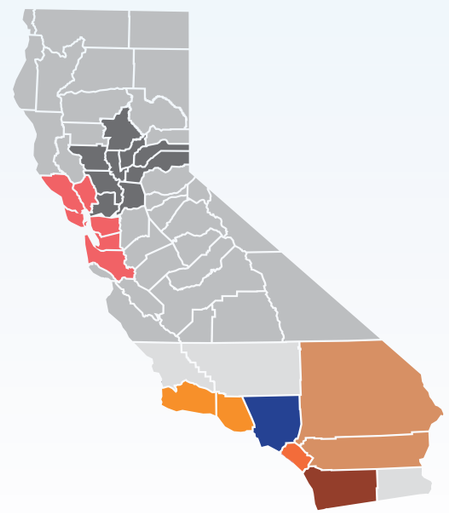
Source: Bureau of Labor Statistics Quarterly Census of Employment and Wages; 2012 Economic Census

Bay Area	$164,123
Santa Barbara & Ventura Counties	$155,711
Sacramento Area	$123,585
San Diego County	$118,719
Orange County	$91,523
Los Angeles County	$88,523
San Bernardino & Riverside Counties	$71,393
Other Southern California	$63,104
Other Northern California	$61,191

Total life sciences employment by cluster 2017

Source: Bureau of Labor Statistics Quarterly Census of Employment and Wages; 2012 Economic Census

Bay Area	82,568	27%
Los Angeles County	57,117	18%
San Diego County	48,430	16%
Orange County	44,957	14%
Santa Barbara & Ventura Counties	12,014	4%
San Bernardino & Riverside Counties	11,126	4%
Sacramento Area	10,912	4%
Other Northern California	6,084	2%
Other Southern California	2,807	1%
TOTAL	**311,226**	



STATS

Source: PwC, California Life Sciences Association

California state GDP per capita

US$58,821

Total estimated Revenue (2017)

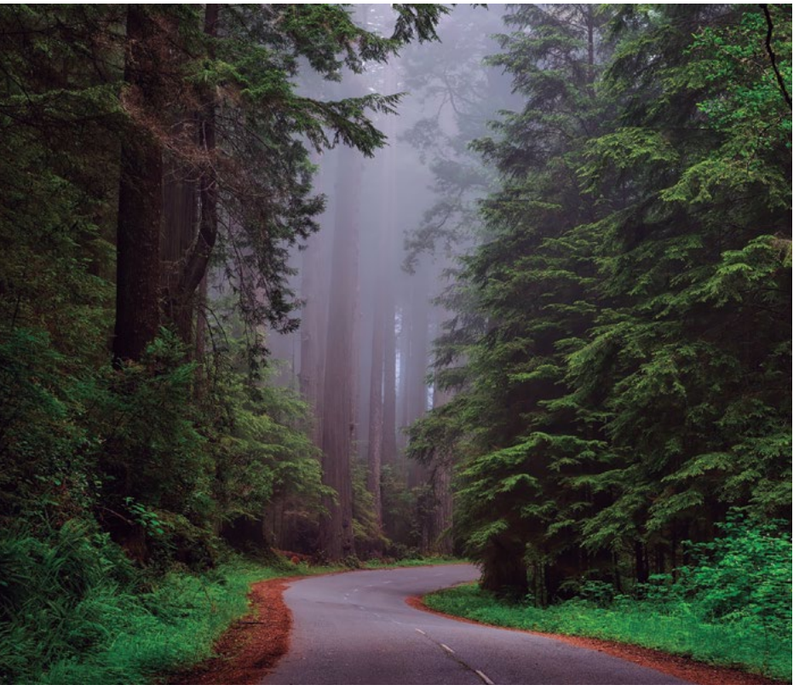
US$177.7bn

Total estimated Employment (2017)

311,226

985,000≈

total direct, indirect and induced employment



Unlike every other state and most countries, California must be viewed through its multiple life sciences clusters. Often singled out due to its status as a biotech powerhouse, the Bay Area is just one of a number of California biotech hubs vying for attention from companies, talent and investors.

The Bay Area: The Innovation Capital of the World

The Bay Area has become an epicenter for the global biopharma industry. As the birthplace of biotechnology, it boasts top academic institutions, a host of the leading biotech companies, including Gilead Sciences and Genentech, and a plethora of VC investment opportunities. For example, VC investment in digital health alone in the Bay Area was at US$3.6 billion in 2018, according to the California Life Sciences Association, far greater than overall life sciences VC investment in every U.S. state apart from Massachusetts – even exceeding that of every country globally. Furthermore, UC San Francisco (UCSF) and Stanford University received the largest amount of NIH funding – US$599 million and US$473 million respectively – across the state. However, what has really set the biopharma industry apart in the Bay Area is how it is able to leverage the different opportunities within the entire ecosystem. "The Bay Area is a hotbed of innovation and, with the convergence of the Silicon Valley tech sector and the traditional biotech sector here, we are seeing amazing new technologies that leverage the strengths of both industries in digital health applications, computational biology, liquid biopsy technologies and AI/ML therapeutic applications," highlighted Michelle Nemits, senior director for business development in the Bay Area at Biocom. "The advances in personalized medicines, cell and gene therapy and synthetic biology applications are also proliferating. The participation of non-traditional investors, like Jeff Bezos, Bill Gates and Richard Branson, speak for the potential some of these technologies may have to be disruptive forces as we move forward."

As a global epicenter for both the tech and life sciences industries, the Bay Area continues to position itself as a strategic center for precision medicine, with the overall aim of increasing the success rate for drugs. UCSF has made precision medicine central to its overarching institutional vision ever since President Obama's Precision Medicine Initiative. The California Initiative to Advance Precision Medicine, hosted by UCSF, has been designated US$30 million for the current fiscal year. Increasing numbers of companies, specializing in bioinformatics or diagnostic tools for precision medicine, are finding their way to the Bay Area. DNAnexus – a spinout from Stanford University – has been developing a cloud-based data analysis and management platform for DNA sequence data, whilst Precision for Medicine's new Quartz Bio platform enables companies to manage biomarker data in a much more integrated way to help make sense of data in real time. Cytobank, located in Mountain View, has developed a SaaS platform for machine learning-based analysis of high-complexity life sciences data. It is furthering its technology by trying to better understand the needs of biotechs and pharma within the community. David Craford, president and CEO at Cyto-

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> Our vision is to help make Orange County a globally recognized entrepreneurial innovation region. Our key differentiator to other universities is that our vision is outwards facing: we opened the Cove to the community to create a center of gravity for the Orange County ecosystem and to break down barriers and build greater collaboration.
>
> **- Richard Sudek, Executive Director and Chief Innovation Officer, UC Irvine Applied Innovation**

Joe Panetta

President and CEO
BIOCOM

Could you update us on the recent developments at Biocom?

Biocom reached several milestones in 2018, including our geographic presence and our dynamic efforts to unite the life science community of California as a collaborative, unified, state-wide entity. Our strategy gained momentum in 2018, and Biocom is now the largest umbrella organization advocating for California's life sciences industry. We continue to accelerate success for our more than 1,100 members in terms of innovation, product development, product commercialization and manufacturing. We also leverage our expertise in cluster development by recognizing the economic prowess of California and the uniqueness of each of the major biotech hubs in the state.

One of the big changes to Biocom this year was a new allocation of staff resources in each of the three hubs – San Diego, Los Angeles and the Bay Area. This springs from Biocom's five key strategic objectives. First, we helped life science companies by advocating for public policies on a local, state and federal level. Second, we expanded our successful capital development program, helping members raise capital and find lucrative partnerships. We held many partnering days with large pharmaceutical companies, both from the United States and abroad, to facilitate this. Third, we offered programs to address the workforce development needs of our members. The California life sciences workforce has upwards of 350,000 employees, but there are different strengths and needs in San Francisco, San Diego and Los Angeles. In 2018, for the second year, we offered our marquee Human Resources Conferences in all three regions, and all were very well-received. Our final two pillars also continued to gain momentum in 2018: we had a record number of events across the state and milestone savings through our group purchasing organization.

Does rivalry reduce the opportunity for greater synergy between California's three major biotech hubs?

Healthy rivalry is a positive thing for the industry. The biotech community is very collaborative, but it also enjoys great competition, especially in California. I would not say the hubs are in competition with each other, but rather are constantly challenging each other in a healthy manner. The bottom line for all these companies is to launch products that improve human health. We are all in it together, and we compete for investment capital and talent – within California and across the country. One of the things Biocom aims to do is to communicate the vibrant message of California's life sciences industry whilst also underlining the individual strengths of each geographic hub. Moreover, we very much see ourselves as bridge builders not only in California, but also across the United States and the globe.

As questions surrounding drug pricing continue to lead to market volatility, what role is Biocom having to play as lobbyist?

With the fifth largest GDP in the world, California is a large enough entity that we behave as a country. The greater question is how can we fuel the R&D pipeline of innovative products so that they can get through a very-efficient FDA process and into the hand of patients? When Gilead's first hepatitis drug came out a few years ago, we looked at the comparative cost of the drug versus maintaining a patient with Hepatitis C. When looking at the cost of healthcare, the cost of prescription drugs is just one component. What we realize is that we are not doing a good enough job communicating the true long-term value of drugs and therapeutics to the general public. We need to challenge insurers and other healthcare players more as an industry. We need to find a way to work collectively to make the system fairer and bring down the cost of healthcare across the board.

What are Biocom's key objectives moving forward until the 2020 presidential election?

We still have a lot of work to do from a policy standpoint, especially in Washington D.C. We need to continue ensuring that the FDA receives the funding it needs. We will work to support the current Commissioner, who is doing an incredible job of creating efficient review processes for new technologies. Finally, we will advocate for funding the NIH, tax policies that spur innovation and growth in California and regulations that encourage investment in innovation for the foreseeable future. ■

> Biocom is the largest advocate for California's life science sector, serving members across industries in pharmaceuticals, medical devices, biotech and more

Richard Sudek

Chief Innovation Officer and Executive Director
UC IRVINE APPLIED INNOVATION

How does your vision at UCI Applied Innovation differentiate from other universities?
Our vision is to help make Orange County a globally recognized entrepreneurial innovation region. Our key differentiator to other universities is that our vision is outwards facing: we opened the Cove to the community to create a center of gravity for the Orange County ecosystem and to break down barriers and build greater collaboration.
We are evolving how translation is done at universities. The future of translation is going to be with startups, which will be aided by a more robust entrepreneurial ecosystem. To enable this, we have Proof of Product (POP) Grants to Bridge Innovation Gaps (BIG), supporting UCI projects in the early stages to effectively partner with industry to translate into commercially viable products.

How are you aiding the process of startup creation at UC Irvine?
Startup creation at UC Irvine is being facilitated by a number of avenues, including the Wayfinder program, POP Grants, the Student Startup Fund and the hundreds of events held at the Cove. Moreover, we have a number of mentors that we call "Experts in Residence" who are available to guide startups through their journey.

What will be your key objectives moving forward over the coming two years?
We plan on engaging in more industry collaboration, welcoming more startups from UCI and Orange County and increasing the funding flow for these startups. ■

Mark A. Wisniewski

Senior Director, Biopharmaceuticals – Business Development and Technology Transfer
UCLA TECHNOLOGY DEVELOPMENT GROUP

Could you highlight the type of research being carried out at UCLA and the start-ups being formed?
Recent success on the therapeutics side has been with successful prostate cancer drugs – XTANDI® of Pfizer and ERLEADATM of J&J – coming out of research at UCLA. Cancer, including CAR T-cell therapy, remains one of our strengths. Over the last few years, UCLA has established unified research themes across cardiovascular disease, metabolism, oncology, immunology, regenerative medicine, neuroscience and precision medicine to accelerate new medicines by facilitating collaborative translational research. The fact that the medical school, hospitals and engineering schools are located in proximity on one campus is very rare and beneficial so clinicians can collaborate with engineers, etc.

What are your key objectives for 2019, and what is your message to the various stakeholders of Los Angeles?
In 2019 will continue facilitating industry sponsored research, closing licensing deals and supporting new startups. We are also establishing a number of faculty training programs. Our overall goal is to support the commercialization of new therapies for patients. To ensure that the most promising technologies do translate and commercialize, collaboration is needed between the major stakeholders of faculty, investors, pharma, biotech and philanthropic donors. All stakeholders play a role, but we really need to align, collaborate and synergize because it "takes a village" to ensure that patients receive critical new therapies. ■

Paul Roben

Associate Vice Chancellor - Innovation & Technology Commercialization
UC SAN DIEGO

Could you provide a brief overview of the research being undertaken at the UCSD?
UC San Diego (UCSD) undertakes approximately US$1.3 billion of research per year across all sectors, with the largest portion within life sciences, which includes therapeutics, medical devices and healthcare delivery. Most recently, we started the Halicioglu Data Science Institute, which is a complete cross-campus and cross-disciplinary institute designed to address the challenges associated with data analytics and data management in all verticals, from healthcare to robotics and AI.

How is UCSD facilitating greater partnership between industry and researchers?
San Diego has the advantage of being more collaborative than anywhere else in the country. Across UCSD's scope of research, US$200 million is contributed annually by industry. We are the number one public institution in the country for industry dollars in research. We always try to understand what industry wants, and we structure deals to meet their needs.

Could you elaborate on how you help researchers spin out companies from UCSD?
UCSD has spun out between 50 and 60 companies per year, of which half are from faculty and the other half from students, both equally viable. The challenge is finding the right management team to make a success in the market. The reason for UCSD's success in terms of startup creation is that the entire university has a strong focus on streamlining technologies into the market. ■

Kevin Grimes

Co-Director
SPARK
Translational Research Program
STANFORD UNIVERSITY

The Stanford SPARK program was established in 2006 to advance new biomedical research discoveries into promising new treatments for patients

Since 2006, what has been the evolution of SPARK's therapeutic focus areas?
In the therapeutic space, we were initially involved with small molecule development. Over the years, we have gradually added antibody therapeutics, protein therapeutics, vaccines, gene therapeutics and nucleic acid therapeutics to our portfolio, and we have moved all the way into genomically modified stem cell therapies. The program is at a stage where we define therapeutics very broadly. Roughly 20% of what we do is in the oncology space and approximately a third of our work is in pediatric diseases. SPARK is a not-for-profit entity and, from the beginning, we wanted to focus on undervalued therapeutics such as those for children and the developing world.

SPARK's success rate of discoveries for commercial and in-clinic applications has continuously remained high. How does SPARK support its students and faculty to facilitate these rates?
We define success as either a hand-off to a commercial partner or bringing a project into the clinic ourselves. In 2017, approximately 50% of the projects that came through SPARK were licensed to a commercial partner, and at least half of these projects were going into clinical studies. Another 10% of the projects were brought into the clinic at Stanford. Our aim is to continue to keep the success rate of projects above 50%.

What are the key milestones for SPARK over the coming two to three years?
We have to start thinking about new models to fund our novel therapeutics. For example, new drug development is almost exclusively in the realm of the for-profit sector, but there are potential therapies that will provide immense benefit to patients that are not going to be profitable. We want to continue to fund projects that are going to improve patient outcomes, even if they will not be taken up by the commercial sector. SPARK is very open to industry partnerships to advance our projects and programs, but we are not able to take funding from commercial industry players with strings attached. ■

Andrea Pesce

Industry Alliances & Licensing Manager
UC SANTA CRUZ

UC Santa Cruz was founded in 1965 and was the first institution to map the human genome and make it publicly available—for free

Could you provide a brief overview of UC Santa Cruz's (UCSC) research capabilities, particularly the world-renowned Genomics Institute?
The Genomics Institute provides a framework for the next great leap in computational genomics and precision medicine, aiming to support the development of targeted disease treatments for even the rarest and most challenging of pathologies. The Institute's Genome Browser is an important catalyst in the success of their mission, and has exponentially contributed to the research impact. The Browser, which is currently used and operated by hundreds of thousands of scientists as well as commercial entities across the global biomedical research community, encompasses the largest collection of genomics data, assemblies and annotations, in addition to an enormous suite of tools for viewing, analyzing and downloading data. This is a unique resource that allows scientist and clinicians to come together to solve health issues with significant genomic components.

Could you elaborate on some of UCSC's recent collaborations with the industry?
Our Department of Chemistry and Biochemistry faculty are working in areas of commercial application, and we're aligning corporate partnerships here too. For example, we are collaborating with companies on developing membrane permeability assays for drug delivery, and potential drug-target cyclic peptide libraries derived from natural products that have favorable membrane permeability, metabolic stability as well as other pharmacokinetic behaviors. We're also working with companies to explore less understood molecular mechanisms that contribute to diseases like Alzheimer's and Parkinson's to identify novel treatment opportunities. From more effective and safer topical agent for poison oak, to safer alternatives to harmful phthalate plasticizers used to enhance flexibility and longevity in PVC plastics, we have a broad range of commercially relevant research supported by industry and opportunity for further collaboration. ■

Mark Ridley-Thomas

Supervisor
LOS ANGELES COUNTY BOARD OF SUPERVISORS

The Board of Supervisors is the governing body of the County of Los Angeles

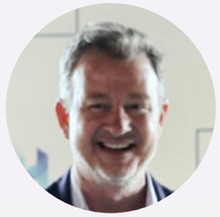
Could you introduce us to L.A. County's bioscience industry and underline the catalyst behind the increase in life sciences jobs over the past year?
L.A. County's bioscience industry currently generates more than US$40 billion in economic activity and supports more than 70,000 direct jobs and 160,000 indirect jobs, but it still has tremendous potential for growth.
Even during the Great Recession, when so many industry sectors plummeted, L.A. County's bioscience industry continued to expand by 12%. Last year, L.A. County overtook San Diego and moved into second place in California in terms of its number of life sciences jobs and amount of grant awards from the National Institutes of Health.
L.A. County is perfectly positioned to take the bioscience industry to the next level because it is the largest provider of public health services in California. As part of its Bioscience Initiative, L.A. County brings to the table not only financing but also real estate at its five medical campuses. It has invested in two bioscience incubators, the first at LA BioMed on the Harbor-UCLA Medical Campus, and the second at California State University Los Angeles. It is also working with LA BioMed to build a 15-acre biotech park on the Harbor-UCLA Medical Campus.
L.A. County has also allocated US$15 million to create a Bioscience Investment Fund for early-stage startups, partnered with community colleges and industry leaders such as Grifols and Bachem to implement life sciences apprenticeship programs. Options to expedite the permitting process for local companies wanting to expand are being explored, as well as for new companies looking to relocate to L.A. County.

L.A. County and Amgen have announced a collaboration to support the life sciences innovation hub – BioLA. Could you elaborate on the key focus of this organization?
A key component of L.A. County's bioscience initiative is BioLA, a nonprofit corporation intended to be an innovation catalyst and an entrepreneurial hub for government, research institutions and private investors to accelerate startup activity and amplify economic opportunity. Amgen is one of several entities that have stepped forward to help fund the initiative for the next three years.
Modeled after the Massachusetts Life Sciences Center, which catapulted Boston into becoming one of the world's leading bioscience hubs, BioLA will help coordinate academic institutions, research hospitals, investors, startups, mature companies, trade associations and public and quasi-public agencies to advance the pace of innovation and startup activity, as well as to facilitate local job creation.

How is the investment climate in L.A. currently set up to better facilitate partnerships between investors and the biotech industry?
After a 2014 Battelle Memorial Institute study affirmed L.A. County's potential to become a national bioscience leader, the L.A. County Economic Development Corporation released a Bioscience Industry Cluster Development Implementation Plan in 2016.
There is significant economic potential, scientific and research interest and opportunity for market penetration in L.A. County. Up until now, however, partnerships have happened organically due to interest from both investor and industry. With BioLA, we can ensure that the core elements of startup activity – infrastructure, capital and talent – exist in abundance for all early stage life science companies.

What are your key objectives for the life sciences space in your final two years in office?
We are taking the concept of public-private partnership to new heights with the goal of making L.A. County a world leader in bioscience. We want to contribute to advances in global health, drive economic development and create jobs.
Contrary to public perception, bioscience is not strictly a "lab coat" industry but one that provides well-paying jobs at all skill levels. In growing the industry, L.A. County is making a strategic investment to diversify the regional economy so that job losses can be kept at a minimum during economic downturns. ■

Allan Glass



Co-founder
HATCHSPACES LLC ®

HATCHspaces' HATCHlabs, located within the L.A. Bioscience Corridor, is a new multi-tenant lab and office space for life science companies

What was the rationale for creating the space?
The rationale for HATCHlabs was to make sure that when start-ups were ready to leave an incubator or an academic environment, they had a place to go in Los Angeles and that they were not forced to leave for one of the other key life sciences hubs. From the perspective of academia as well as the incubators, their business model is to bring in new researchers on a continual basis. If they cannot move out successful companies who have raised capital, a backlog is created. HATCHlabs creates a viable ecosystem for companies looking to take the next step, whilst also retaining companies within the L.A. ecosystem.

What sort of interest for HATCHlabs and the L.A. biotech ecosystem are you seeing from both domestic and international markets?
We have seen interest in HATCHlabs from Boston, the Research Triangle in North Carolina, Seattle, San Francisco and San Diego, with companies looking to increase their presence in Los Angeles. Mayor Eric Garcetti's office and the L.A. Economic Development Corporation have done a tremendous job of reaching out to the Chinese and South Korean markets, especially as Los Angeles has the second largest Korean population in the world, second to Seoul. As a result, we have been introduced to a number of international investors that are looking at opportunities to invest.

What is your vision for HATCHlabs in the L.A. life sciences hub?
Over the course of the next year we want to continue to build our pipeline of potential projects. We expect to double our capacity in 2019 as well as in 2020. In Los Angeles, we hope to become an integral part of the ecosystem, especially for companies leaving the incubator network or the academic environment. ■

> "The ability to identify well characterized – even rare – populations to demonstrate clinical proof of concept is paving the way for early approvals followed by expansion of indications. This approach is essentially replacing the 'traditional' phase 1/2/3. Contrast this with as recently as 10 years ago, where only a small handful of companies were proactively pursuing a personalized approach or forced into it by regulators or payers. Then, the general holy grail was the US$1billion+ blockbuster, despite high failure rates. The incorporation of diagnostic tools for applications like patient stratification or efficacy monitoring has played a major role in this change in mindset.
>
> - Rajiv Mahadevan, Managing Director, Precision For Medicine.

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bank, highlighted: "Recently the field has seen remarkable success with immunotherapies, especially in the area of oncology. This has driven pharma to generate and analyze higher complexity data to understand the immune system and the host-immune response, as they attempt to maximize the value of the information they can get from every clinical trial patient sample. Especially in early phase trials, pharma will run very high complexity technologies on their samples."
Undeniably, the Bay Area will remain at the forefront of the biopharmaceutical industry. With the region continuing to be central to the convergence of the life sciences and tech industries, there is true excitement as to what technologies will be developed here in the coming years.

San Diego: Biopharma in Motion

San Diego is home to one of the most collaborative and connected biotech hubs, not to mention the perfect climate and stunning scenery that attracts and retains talent. Although it has had to play second fiddle to the Bay Area for some time, the increased cost of living in the Bay Area and increased capital investment coming to San Diego – the city ranked third globally in venture investment ac-

> The Orange County area has been recognized as a hub for medical devices, optometry and aesthetic companies, but not for biotech in particular. There are challenges in attracting biotech companies to the area as there are a significant number of competing hubs in the country. The benefit for Bioniz is that, as one of the few biotech companies in the area, it is not difficult to attract and retain talent.
>
> **- Nazli Azimi, Founder and CEO, Bioniz Therapeutics**

cording to EY – are slowly turning the tide. San Diego is able to offer a depth of life science managerial expertise, a pool of the top biotech companies, including Illumina and Gossamer Bio, and even the benefits of Tijuana, Mexico on its doorstep as a top destination for biomedical manufacturing. "San Diego continues to have a robust biotech ecosystem, both on the financing and research and development side," said Steve Worland, president and CEO at eFFECTOR Therapeutics. "While we have comparatively fewer investors here than Boston or the Bay Area, San Diego has a very strong reputation for its research and early product development prowess, so we can attract VCs that are located in other geographies, thereby importing capital to the region."

However, what remains key to San Diego's biotech ecosystem is its academic and research institutions. UC San Diego and Scripps Research received significantly higher NIH funding in 2018 at US$438 million and US$190 million respectively, and of the 50 to 60 startups UC San Diego produces each year, 66% are in the life sciences. "San Diego has the advantage of being more collaborative than anywhere else in the country," remarked Paul Roben, associate vice chancellor for innovation & technology commercialization at UC San Diego. "Across UCSD's scope of research, US$200 million is contributed annually by industry. We are the number one public institution in the country for industry dollars in research. We always try to understand what industry wants and we structure deals to meet their needs."

San Diego has been named in some quarters as the Silicon Valley for early-stage biotechs due to the nurturing ground offered to researchers and early startups. From biotechs like Abreos Biosciences – a precision medicine company dedicated to improving the development and commercialization process for biotechs with its proprietary Veritope platform – to Agilinx Therapeutics – a biotech founded last year that is acquiring immuno-oncology and infectious disease molecules and taking them through to proof of concept in humans – there is a consistent stream of new biotechs entering the ecosystem.

Los Angeles: A New Phase of Growth

Los Angeles' desire to move further into the life sciences industry should not come as a surprise to anyone on the West Coast. In fact, its influence in the biopharmaceuticals industry has been subtly increasing for some time now. The county has the second highest number of life sciences employment at 57,117 and NIH funding grants in the state, and is home to a number of the top performing academic institutions, including UC Los Angeles, University of Southern California (USC) and California Institute of Technology (Caltech). It also has one of the most proactive public boards – the Los Angeles County Board of Supervisors – in the United States, which has identified the life sciences industry as a key growth industry for Los Angeles. "We are taking the concept of public-private partnership to new heights with the goal of making L.A. County a world leader in bioscience," said Mark Ridley-Thomas, supervisor for Los Angeles County. "We want to contribute to advances in global health, drive economic development and create jobs."

Over the past year, a number of initiatives have begun to help catalyze the county's growth. These have included the formation of BioLA – with Amgen as founding sponsors – a new bioscience organization that has been designed to strengthen the county's life sciences ecosystem and accelerate the pace of start-up activity. Moreover, L.A. County has allocated US$15 million to create the L.A. Bioscience Investment Fund for early-stage startups, and the county is working with LA BioMed to build a 15-acre biotech park on the Harbor-UCLA Medical Campus. The key emphasis for these initiatives is to instigate greater collaboration within Los Angeles, something that has historically held the county back given the fragmented nature of the city. "The geographical dispersion of Los Angeles does impact UCLA as many technologies and startups have traditionally relocated to Boston or the Bay Area after the initial research is licensed," underlined Mark A. Wisniewski, senior director of biopharmaceuticals, business development and technology transfer at UCLA Technology Development Group. "Critical components for creating an integrated biotech hub in Los Angeles include attracting seasoned management and smart capital from biotech venture capital firms. We are moving in the right direction in Los Angeles but need to accelerate this positive trend."

Bay Area and Boston-Cambridge-based companies have had the enviable benefit of not having to look elsewhere for venture investment, something not afforded to Los Angeles. However, in September 2018, Westlake Village BioPartners launched a US$320 million fund in committed capital to Los Angeles. With the funds set to be invested in pharma and biotechnology, especially around seed funding and series

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Image courtesy of Allergan

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A funding, promising research at UCLA, Caltech and USC a helping hand. Moreover, there has been a push by Mayor Eric Garcetti's office and the L.A. Economic Development Board to attract international investment from China and South Korea, especially given the city's strong Korean and Chinese communities.

Next to Los Angeles County, Orange County has been historically known as a hub for medical device companies. With Edwards as a key anchor company, and Allergan, Medtronic and Abbot all operating in the county, the ecosystem has been developed through these multinationals. Well situated in the Southern California corridor between San Diego and Los Angeles, and home to a number of well-regarded academic institutions, including Chapman University and UC Irvine, Orange County also remains a relatively untapped opportunity for biotechs. Nazli Azimi, founder and CEO of Bioniz Therapeutics, an Irvine-based biotech focused on discovering and developing novel peptide therapeutics for the treatment of immune diseases and cancer, has many opportunities afforded to her for being based in Orange County, especially as the competition amongst biotechs still remains low. "Increasingly, investment firms are starting to open shop in the L.A. area, which is attracting more biotech companies to the region and will have a positive effect in terms of propelling the industry forward," highlighted Azimi. "There is also a significant number of universities in the area, including UC Irvine and Chapman University. Partnering and collaborating with these academic institutions is a great advantage for us."

For Los Angeles, moving forward, trying to connect all stakeholders together so that the 4,751 square mile county can work more effectively as a single unit will be the main challenge. However, there is a clear concerted effort to make this happen and to create a life sciences hub to rival San Diego and the Bay Area. ■

> Los Angeles has an enormous amount of unappreciated and hidden technology value as well as human talent, both on the research and the development side. There is great opportunity for investment in the area as there is currently little competition in what is a very dynamic space.
>
> **- Bassil Dahiyat, President and CEO, Xencor**

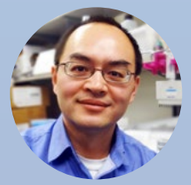
California's Biotechs Up Close

"Alkahest's breakthrough research has interrogated the plasma proteome to understand which plasma proteins are most impactful to the aging process. To do this, we investigated plasma samples from a range of ages to understand if the protein signatures were in fact different. About 10% to 20% of proteins on either end of the spectrum either increase or decrease with age, with the majority of proteins preserving their function over time. The proteins which change with age, which we call chronokines, can be either bene cial or detrimental. We then target these chronokines for potential therapeutic effect."

- Elizabeth Jeffords,
Chief Commercial & Strategy Officer, Alkahest

"Agilinx's strategy is focused on acquiring assets that are nearing human trial. We then rapidly take them into the clinic and look for proof of concept in Phase I and Phase II to prove efficacy. By doing this, a whole new world of opportunities opens. There is a very high failure rate in clinical trials but with smarter medicine and new ways of genomic mapping we can be much more deliberate about which compound we are bringing to clinical trial and how we select our patient group."

- Kevin Elliot,
CEO, Agilinx Therapeutics & Partner, Procela Consulting



"The company was developed for cancer patients who wanted effective, safe, and long-lasting treatment, without the use of drugs. But cancer is the smallest and first stage application of our approach, and Filtricine aims to be a next-generation therapy company for multiple diseases."

- Xiyan Li,
Co-Founder and CEO, Filtricine

"Rigel aims to discover key immune system processes, which we know are central to some diseases. IRAK, for example, is central to many immune-signaling processes. If we are able to block IRAK, we are able to block a large segment of downstream in ammatory cytokines that are activated. As a result, there are approximately 20 diseases where IRAK is potentially involved and we are excited to explore the broad potential of R835 in autoimmune and in ammatory diseases, such as psoriasis, lupus and others."

- Raul Rodriguez,
President and CEO, Rigel Pharmaceuticals

Mike Guerra

President & CEO
CALIFORNIA LIFE SCIENCES ASSOCIATION (CLSA)

California Life Sciences Association (CLSA) is the trade association representing California's life sciences sector, focused on prioritizing the advancement of California's world-leading life sciences innovation ecosystem

From San Diego, Orange County and Los Angeles, to the Bay Area, how are you able to create synergy and share strengths amongst California's life sciences hubs?

The growth in the key life sciences clusters of San Diego, Orange County, Los Angeles and the Bay Area continues to exceed that of other regions around the nation due to our ecosystem approach and CLSA's cultivation of it. The industry retains its strength because CLSA is constantly examining and evolving each piece of the ecosystem: education, infrastructure, corporate governance, investment, government regulation and other factors. CLSA plays a leading role in creating those synergies through our advocacy work, connection offerings and innovation services.

Drug pricing remains a hot topic in Washington D.C. especially as we enter the next presidential election cycle. What advocacy role is CLSA currently playing, especially in the United States Capitol?

Nothing about life sciences innovation is easy, and new therapies and technologies do not come cheap. To go from concept to reality, they require sweat equity and major investment. Drug development is an arduous process that can take 20 years, sometimes longer, and cost north of $2 billion. It's a long and difficult task, fraught with failures along the way. Policymakers must support, recognize and reward the value of drug discovery and life sciences innovation, and be on guard against ill-conceived, short-sighted proposals and policies that, in the name of "controlling prices," that could threaten patient care and undermine the promising research and investments into the miracle medicines and technologies of tomorrow.

What will be the number one challenge facing California and the United States' biopharmaceuticals industry in 2019?

As strong as California's life sciences ecosystem has become, we must always be aware of the growing communities in Europe, China and other regions that are also embracing biological innovation. Many Californians have worked hard to get the industry to the world-class innovation powerhouse it is today. CLSA is leading the way, ensuring that we maintain our leadership position on the world stage and being the center of innovation. ■

The East Coast

A rising tide lifts all boats

Whilst the volume of California's biotechnology network, from San Diego to the Bay Area, is difficult to match, the U.S. East Coast, comprising New England and the Mid-Atlantic states, encapsulates the entirety of the biopharmaceuticals value chain at its best. Giants, Patriots or Eagles fans would be quite displeased at the idea of collaborating with one other, but the same cannot be said for the East Coast life sciences hubs. Despite being in different states with differing policies and tax systems, much can be learnt from how the East Coast hubs have grown, collaborated and evolved over the course of time.

The Boston-Cambridge biotech supercluster and its development over the past decade is exemplary of what is needed to create a successful hub. Home to 120 academic institutions, Massachusetts already had the key ingredient for a top biotech hub and grew exponentially when MassBio – the state's premier life sciences trade association – began to attract large pharma before establishing a feeder system of small companies. With the high calibre of research institutions, a US$1 billion 10-year initiative implemented by the Massachusetts Life Sciences Center in 2008, and the ability to bring academia, industry and government together, the cluster transformed itself in a decade into an unrivalled global powerhouse. Achieving worldwide recognition, Massachusetts' life sciences industry continues to surpass expectations and go from strength to strength. "Venture investment in biopharma companies was over US$3 billion in 2017, which is more than triple what it was in 2012, and the IPO market has continued to exceed our expectations with Massachusetts having almost half of the U.S. life sciences IPOs. 20 in 2018," underlined Robert Coughlin, president and CEO at MassBio.

> "Servier opened the BioInnovation office in Cambridge, Massachusetts in February 2018, at the core of this world-class innovation cluster. The United States is a key market for us, especially in the field of oncology, and we intend to establish a long-lasting position in this field with the objectives to treat even more patients with innovative medicines and to become a leading global player in the oncology domain.
>
> **- Eric Falcand, Vice President, Head of Business Development and Licensing, Servier Group**

Proximity to New York City (NYC) has also been of value for Boston-Cambridge over the years, as accessing funds has never been in doubt. Headquarter to numerous VCs, private equity firms and investment banks, the Big Apple is also now putting greater emphasis on life sciences itself. "Both the Governor and the Mayor have initiated robust programs to increase the presence of life science companies in New York State and City," underlined Jennifer Hawks Bland, CEO at NewYorkBIO. "Together, these life sciences initiatives represent more than US$1 billion in investment. This includes tax incentives, direct investment and other programs focused on fostering an environment to grow New York into a world leader."

With its financial prowess, top academic institutions with world-class medical centers and US$1.8 billion in NIH awards — ranking second in the nation – NYC is a perfect environment for early-stage biotechs to develop. With a US$100-million new Applied Life Sciences Hub and US$300 million in tax incentives to attract investment in commercial lab space, NYC is making a concerted effort to become the next major life sciences cluster.

In its periphery, New Jersey is a state that characterizes the historic U.S. pharmaceuticals industry. As the 'medicine chest of the world,' and home to Johnson and Johnson, Merck and Celgene, to name a few, 35% of all new FDA approvals for novel drugs in 2018 came from companies with a footprint in the state. The traditional North American home to many large pharma companies, New Jersey is aiming to position itself at the forefront of biopharmaceutical innovation moving forward. The state has formed a Biotechnology Task Force focused on identifying strengths, weaknesses, opportunities and threats to the industry in New Jersey. Moreover, Princeton University, an Ivy League institution, recently opened its Princeton Innovation Center BioLabs, offering co-working lab and office space for high-tech startup companies. Celgene has also opened an incubator at its Summit West Research Facility. NYC's increased energy towards the life sciences space is also being recognized as an opportunity for New Jersey to leverage. "The NYC plan, coupled with the millions of dollars that New Jersey invests in the industry each year, will create tremendous synergy," underlined Debbie Hart, president and CEO at BioNJ. "Given the geographic proximity, it will create opportunities for both states. There are already a vast number of people who live in one state and commute to the other for work and that will continue. Furthermore, the concentration of venture dollars in NYC will benefit New Jersey given that we have no shortage of real estate in which to house these companies, so we can accommodate new ventures, and we are well connected to NYC by road and train."

Pennsylvania also benefits from its geographic positioning on the East Coast. With 2,800 life sciences companies in the state and 112,000 direct jobs within the life sciences industry, the state is benefiting from not only having two of the top five NIH funded research institutions in the United States – University of Pennsylvania and University of Pittsburgh – but also the legacy of large pharma.

Of no less importance, North Carolina's Research Triangle – a strong cluster of Tier 1 universities, including UNC Chapel Hill, NC State University, and Duke University – and Delaware with its strong manufacturing capabilities complete the interconnected life sciences network of the East Coast.

Large pharma and service providers have now spread themselves across the country. Biotech clusters are forming in far-reaching corners of the United States. Although there remains a concentration of biopharma companies within New Jersey and Pennsylvania, we can no longer limit by border. The biopharmaceutical East Coast corridor continues to take shape. Where there are top academic institutions with a motivated local government, there will be the opportunity for a city, or state, to get in on the action. ■

New Jersey

CAPITAL
Trenton

POPULATION
8,908,520
(United States Census Bureau, 2018)

Life Sciences Industry Employment

Source: Bureau of Labor Market Information. Winter 2018

177,260

nearly 3,200

total establishments in 2017

Source: New Jersey's Life Sciences Industry Cluster, New Jersey Department of Labor & Workforce Development Office of Research & Information Bureau of Labor Market Information, Fall 2018

50%

of 2017 FDA approvals came from companies with a footprint in NJ

Biopharma in New Jersey

Source: The New Jersey Biopharma Industry: A Prescription for Growth, BioNJ

3.7%

of GDP
2x U.S. average of 1.9%

25,088

life sciences papers published
in the NY-NJ innovation cluster in 2014

2,302

patents filled
in the NY-NJ innovation cluster in 2014

>350,000

direct, indirect and induced employment

29%

of drugs approved by the FDA
from 2015-2017 produced by New Jersey-HQ companies (33/113)

<$20

cost of lab space per square foot
compared to >$50 in NYC and San Francisco and >$70 in Boston

Debbie Hart

President & CEO
BIONJ

Founded in 1994, BioNJ's mission is to enhance the climate for the life sciences industry in the state

What is BioNJ's mandate within New Jersey's life sciences sector?
Our mandate is to make sure that New Jersey continues to be a robust life sciences ecosystem. Our key goals are to protect and facilitate innovation and to ensure that patient access to therapies and cures is protected at the state and federal levels. Our objective is to ensure that the overall climate is conducive to companies coming and prospering here and that the industry continues to grow here.

The issues surrounding drug pricing continue to be a major concern for large pharma and government, alike. Could you elaborate on the advocacy work being carried out in Trenton and in Washington D.C.?
At BioNJ, we want to make sure that policies, whether at the state or federal level, enable innovation and patient access. We believe that solutions should be focused on what patients pay at the pharmacy counter. We stand ready to work with policy makers and others to ensure that patients can access the therapies and cures they need and that innovation is enabled at every turn.

How is BioNJ helping to reinvent New Jersey as a destination for biotechnology?
At BioNJ, we are working every day to attract and retain companies and talent and to make sure that those in our ecosystem are connected and supported through our programs as well as by state government. One of the things that we are most proud of is our talent across the continuum, and, in particular, one of New Jersey's greatest strengths is our development and commercialization talent and capabilities. In fact, in 2018, 35% of all new FDA approvals for novel drugs came from companies with a footprint in New Jersey. Meanwhile, our academic institutions, including Princeton, Rutgers and NJIT are focused on increasing the number of technology spinouts. In addition, we are excited about a number of incubators that have opened in the last year. For example, Celgene opened an incubator at its Summit West Research Facility and Princeton University opened a life sciences incubator – the Princeton Innovation Center BioLabs incubator.

Is LifeSci NYC's ten-year, US$500 million investment plan to make New York City a biotech hub likely to detract from or facilitate interest in New Jersey?
The NYC plan, coupled with the millions of dollars that New Jersey invests in the industry each year, will create tremendous synergy. Given the geographic proximity, I believe it will create opportunities for both states. There are already a vast number of people who live in one state and commute to the other for work and that will continue. Furthermore, the concentration of venture dollars in New York City will benefit New Jersey given that we have no shortage of real estate in which to house these companies, so we can accommodate new ventures, and we are well connected to New York City by road and train.

What is your vision for New Jersey and the role it will play within the biopharmaceuticals industry?
Given our tremendous talent, large industry presence, desirable geographic locale, strong government support, proximity to Wall Street, the NIH, the FDA and leading academic centers – not to mention its quality of life – New Jersey is well positioned to continue its leadership in this sector. We see tremendous potential for New Jersey's continued growth in early-stage innovation. To help enable that potential, our governor is advancing an economic strategic plan including numerous programs that directly benefit the Life Sciences industry.
Meanwhile at BioNJ, we currently liaise with other international hubs and companies, and have agreements with several geographies around the world to facilitate collaboration. Governor Murphy talks about innovation at every turn, and has fostered several international relationships as well to facilitate innovation with countries, including Germany and Israel. As a result of having hosted trade delegations in New Jersey, we have an increasing concentration of companies from Sweden, China, South Korea, Japan and other countries around the world. Overall, New Jersey is well positioned to build on its historic strength. ■

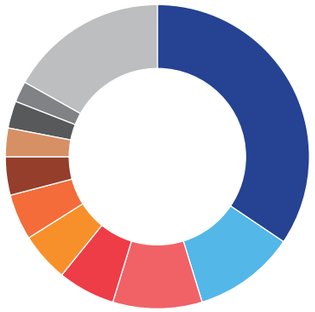
Massachusetts

CAPITAL
Boston

POPULATION
6,902,149
(United States Census Bureau, 2018)

Pipeline by therapeutic area

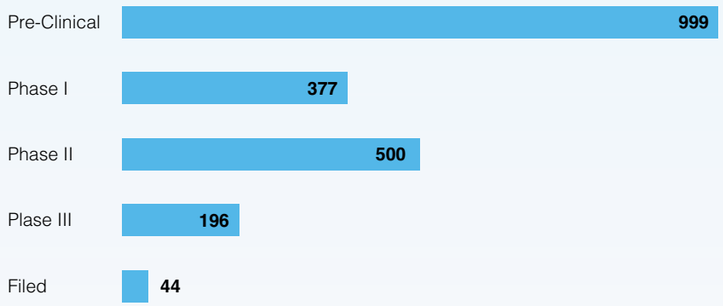
Source: EvaluatePharma, 2018



Cancer	35%	Respiratory	4%
Neurology	11%	Blood	3%
Infections	9%	Cardiovascular	3%
Immunology	6%	Skin	2%
Sensory organs	5%	All Others	17%
Musculoskeletal	5%		

Drug development pipeline and trials by phase

Source: EvaluatePharma, 2018



2,166
MA Drug Candidates

16%
of US Pipeline

6%
of Global Pipeline

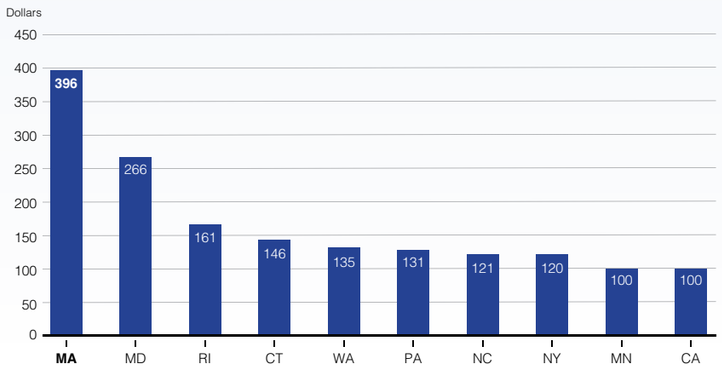
Total NIH funding

Source: NIH, Research Portfolio Online Reporting, U.S. Census Bureau

California	$3,946,354,973
Massachusetts	**$2,716,744,336**
New York	$2,386,044,645
Pennsylvania	$1,672,904,696
Maryland	$1,611,922,948
North Carolina	$1,245,779,004
Texas	$1,160,644,529
Washington	$998,183,675
Illinois	$805,534,710
Ohio	$754,319,250

Funding per capita

Source: NIH, Research Portfolio Online Reporting, U.S. Census Bureau



Robert K. Coughlin

President & CEO
MASSBIO

MassBio's mission is to advance Massachusetts' leadership in life sciences

How has MassBio and the Massachusetts life sciences ecosystem evolved under your tenure?
When joining MassBio in September 2007, the industry and ecosystem in Massachusetts was a completely different place than what it is today. We were facing an economic downturn, the IPO market was going to be diminished and the model for drug discovery needed to change. MassBio saw this as an opportunity to identify how to convince large pharma companies to come to the region and do licensing deals to make up for the billions of dollars that were not going to come from the public market. The region was forced to change, and it turned out to be a great opportunity.
In 2007, we were one of the top five clusters in the country, and our goal was to become the top cluster. To achieve this goal, our plan was to focus on company creation to establish a feeder system of small companies for big pharma. We also focused on collaboration with academic institutions. Having 120 academic institutions in a very small geographical area was already a differentiator that we could benefit from.
Looking at the industry and ecosystem today, we very much achieved our goal of becoming the number one life sciences hub in the world. Venture investment in biopharma companies was over US$3 billion in 2017, which is more than triple what it was in 2012, and the IPO market has continued to exceed our expectations with Massachusetts making up half of the U.S. life sciences IPOs – 12 in 2017.

What advocacy work are you having to do in both Boston and Washington D.C.?
Our aim in both Boston and Washington D.C. is to create an understanding of the value of a drug not only for the patient, but for society as a whole. From an economic standpoint, drugs can bring huge value to the healthcare system. My opinion is that we do not have a healthcare system, but rather a sick care system, which was designed in the 1950s and has not kept up with the innovations of our industry. We are not inventing pills that treat symptoms, but rather breakthrough therapies that change the course of disease, and in some cases cure disease. A sick care system is outdated and cannot absorb high value, higher price therapies, which avoid costs elsewhere such as reduced hospitalization or the need for fewer therapies and drugs. High value, high priced therapies have the ability to save patients money in the longer term.

With lowering drug pricing high on both President Trump and the Democrat candidates' agendas, what is key to solving the notion that pharmaceutical companies are at fault?
For change to happen, we need value-based contracts, systems and payment structures. We are focusing our efforts on bringing together the private payers, hospitals and manufacturers to come up with innovative payment models that are up to date with the current industry. We are also trying to change the way business is done within the healthcare space so that we can convince Congress to change certain laws that will allow for more flexibility in how drugs are accessed and reimbursed.

What is your strategy for workforce development in Massachusetts?
We have enough people in the region, but we need to get these people into our pipeline. It is a scientific fact that the more diverse an organization is, the better the outcome. MassBio has started a Diversity and Inclusion (D&I) initiative as we believe that in order for the life sciences industry in Massachusetts to continue its success, diversity and inclusion must be its backbone and this should be reflected in recruitment, retention and promotion strategies.

With over 1,250 members now, how do you aim to better connect your membership moving forward?
MassBio looks at acceleration and business development through three C's– convene, connect and catalyze. We need a space where we can encourage the industry to connect, and so we aim to build a conference center that will serve as a place to facilitate the three C's. The future of the healthcare system relies on interactions and collaboration between industry, academia and the government, and we want to create a space where collaboration is possible. ■

Olivier Safir

CEO
PACT AND PARTNERS, LLC

Headquartered in Boston, Pact and Partners services the life sciences industry across three continents. Why are you such an essential part of the biopharmaceutical value chain?

Pact and Partners was founded in 1987 and has a sphere of influence in the United States across Europe and South America. We have been advising and appointing senior talent since our inception, and these people have now become world leaders in the life sciences industry. Over the years, we have developed an expertise within the biotech and large pharma spaces, as well as in medtech, digital health and cell and gene therapy: all fields that serve the main purpose of servicing patients. Pact and Partners has become an expert leader in these sub-industries, whilst staying generalist in regard to the functions that we cover. We appoint professionals across R&D, manufacturing, sales and marketing, all the C-level executives and board members.

Over the last 32 years, there has been a major shift driven by globalization and internationalization. This has had a significant impact on the life sciences industry as well as Pact and Partners. Companies have gone global in terms of careers and education and have consolidated at a global level as well. We have also followed this trend and have become an international organization with multicultural diverse teams.

Could you elaborate on Pact and Partner's executive search process and how this differentiates from what is already in the market?

Since our establishment, we have added approximately 110,000 people to our database, resulting in one of the largest life sciences industry databases in the world. Our ability to source from this network gives us an edge in the market. We have access to a significant number of people and references, which helps us to operate much faster than other competitors in the market. We are also differentiated by being solely focused on the life sciences industry. Our main service is headhunting, but the process to succeed in doing so also includes some forms of market intelligence, risk management, strategic consulting and most of all understanding our client's challenges and business so we can introduce the perfect candidate.

Many stakeholders have highlighted that the leadership and management team is the key differentiator in a biotech rather than a product or technology. Does this present a significant opportunity for Pact and Partners?

Our domain of work is probably one of the riskiest in the world. It will take 5,000 to 10,000 medicinal candidates tested in drug discovery to achieve only one approved medicine. These numbers are unparalleled as there is not another industry with such a high level of failure yet with one of the highest concentrations of capital as well. Pact and Partners focuses on mitigating risks for our clients' organization so that they can build the best management and leadership teams to help them become that one company achieving success. Indeed, one of the most important elements of any company, especially biopharmaceuticals, should be the management team as they can easily be the difference between efficient thriving firms or failing ones. This puts even greater precedence on our work to deliver the right candidate to our clients.

Given that Boston is now Pact and Partner's global headquarters, what is your growth strategy and your longer-term vision for the United States?

The biopharmaceutical industry remains one of Pact and Partner's main targets for growth. The life sciences industries are booming, and we are happily surfing this wave. We have taken a leading position in transatlantic recruitment – United States to Europe – and this is one of the niches where we expect to continue seeing significant growth. Millennial entrepreneurs love working with Pact and Partners as we have a very startup feel to the way we work and our team members have almost all an entrepreneurial background. With respect to our longer-term vision, Pact and Partners aims to be the global leader in life sciences recruitment. ■

Pact and Partners is an executive search firm dedicated to the life sciences industry since 1987

Christopher Molineaux

President & CEO
LIFE SCIENCES PENNSYLVANIA

What is Life Sciences Pennsylvania's (LSPA) mandate and how has your membership evolved over the past two years?

Our mandate at Life Sciences Pennsylvania (LSPA) remains to develop and maintain a business and public policy climate that will make Pennsylvania the most attractive place to open and operate a life sciences company. LSPA maintains two core accountabilities – public policy advocacy, where we aim to shape legislation to establish a favorable business and policy climate at macro, federal and state levels for the life sciences industry, and facilitating strategic connections, which is why the size and diversification of our membership portfolio continues to be important. We can connect any business or scientific leader with the resources they need to grow their business or advance their technologies.

Life Sciences Pennsylvania's membership portfolio continues to grow and diversify and, as of the end of 2018, we have 817 members. Approximately 16% of our members are biotech, 11% medical device and diagnostics companies, 12% pharma, 6% research institutions and the remainders are made up of digital health companies, patient advocacy groups and contract service organizations. Our membership portfolio continues to represent the entire life sciences community of the entire state of Pennsylvania. We are unique and differentiated from our sister organizations in other states where there are multiple associations per state, in that we are the only statewide trade association for the industry. As there is increasing cross pollination and overlap within the industry, it is now even more important to represent the entire life sciences ecosystem in Pennsylvania.

How important is LSPA's advocacy work for the industry given that both macro-economic and geopolitical factors are impacting the biopharmaceutical value chain more than ever before?

Advocacy work and the education of elected officials and policymakers has always been paramount for LSPA. Of most importance is the drug pricing debate, which comes and goes but continues to be an issue for the industry, although it is largely driven by the insurance companies. An example when we have been able to successfully advocate was regarding the pharmaceutical price transparency bill. We agree with transparency, except when it jeopardizes intellectual property or the proprietary information of a company. The bill would have required pharmaceutical companies to disclose all of their pricing strategies, and if they did not, they would be excluded from state formularies. Fortunately, we defeated this bill, but it demonstrates there is a lot more behind the pricing discussion than meets the eye.

How is Pennsylvania trying to differentiate itself as a life sciences hub?

Pennsylvania is very attractive to life sciences companies as we have two of the top five NIH funded research institutions – University of Pennsylvania and University of Pittsburgh. We have an incredible talent pool as there is an abundance not only coming out of the university setting, but the legacy of large pharma. The diverse mix of resources that exist in Pennsylvania is unrivalled. Moreover, we have access to capital, our geographical location is a great advantage and the cost of living in the state is affordable. As an organization, we host various conferences where we bring in investors from around the country to create networking opportunities for our members.

At the end of 2017, there were 2,800 life sciences companies across Pennsylvania, including biotech companies, large pharma, medical device companies, academic research institutions, life sciences investment organizations, digital health companies and contract services, which all directly touch the lives of patients. These companies are responsible for 112,000 direct jobs, and there is a multiplier effect on the services community surrounding these companies. The life sciences sector in Pennsylvania is a vibrant, dynamic fast-growing community, but it is also very fragile as more than half of the 2,800 companies are made up of 10 employees or fewer. This makes our advocacy work and shaping the environment an even more important responsibility.

What will be LSPA's key objectives before we reach the presidential election cycle in 2020?

LSPA's key objectives are to continue to engage and educate. Pennsylvania has a rapidly growing community of startup companies, and currently the life sciences industry here is the largest it has ever been. We see this as a tremendous opportunity for the future to contribute to this fast-growing industry and to create a favorable business climate in Pennsylvania. ■

Founded in 1989, Life Sciences Pennsylvania (LSPA) is a statewide trade association for Pennsylvania's life sciences industry

Jennifer Hawks Bland

CEO
NEWYORKBIO

NewYorkBIO brings together more than 250 of New York's bioscience companies, universities, research institutions and others to advance life sciences research and commercialization

Could you outline NewYorkBIO's mandate?
Founded in 1990, NewYorkBIO is a trade association representing the life sciences industry in the state of New York. NewYorkBIO has a wide cross-section of members, including large pharmaceutical and small biotech companies, academic institutions, patient foundations and service providers. One of our key roles is to advocate for the interests of the industry with policymakers and other stakeholders. For example, NewYorkBIO works to encourage a policy landscape that allows New York-based companies to more easily bring their treatments to market.

Could you elaborate on the initiatives being put forward by Governor Cuomo and Mayor De Blasio to increase growth in New York's life sciences industry?
Both the Governor and the Mayor have initiated robust programs to increase the presence of life science companies in New York state and City. Together, these life sciences initiatives represent more than US$1 billion in investment. This includes tax incentives, direct investment and other programs focused on fostering an environment to grow New York into a world leader. The New York City Economic Development Corporation (NYCEDC) is incentivizing companies to locate and grow within the City.
With respect to upstate New York, in 2018 Governor Cuomo announced the formation of the Empire Discovery Institute (EDI), a groundbreaking partnership of the University at Buffalo, the University of Rochester and Roswell Park Comprehensive Cancer Center. This new entity will leverage academic and industry resources and expertise to accelerate life sciences research through early-phase drug development. EDI will expedite the pathway toward successful licensing and commercialization of early drug discovery research, creating new revenue, new companies and new jobs, while capitalizing on New York's leadership as a vibrant life sciences cluster and hub for early-stage discovery.

What will be a key factor in developing New York's life sciences industry moving forward?
Investment is key in facilitating industry growth. New York has seen tremendous growth in start-up and emerging biotech companies. New York is home to arguably, the world's best collection of academic medical centers, which provide tremendous support to building an ecosystem of biotech companies. New York is also home to capital markets and a significant collection of the nation's patient advocacy organizations, which therefore provide unique opportunities for companies to grow and develop and attract capital. While New York is not as mature a hub as a few other life science focused locations in the United States, we are making great strides in growing the New York presence in life sciences.

Could you tell us about your complementary membership for startups?
As a trade association, our goal is to support the industry and its development. We offer the Fellows Program for Life Science Entrepreneurs for companies with fewer than five employees and with less than US$5 million in funding. The membership is free for one year and renewable for a second year, with access to our discount purchasing program, which leverages the purchasing power of many biotech companies across the country. Fellows members enjoy all of the other benefits of membership in NewYorkBIO, such as networking opportunities and representation on policy issues.

What will be NewYorkBIO's key objectives moving forward?
In 2019, we have a series of meetings focused on our advocacy and policy work, which entails engaging in public policy discussions and working with legislators. We want to highlight the importance of the industry when we are in the New York State Capitol, because we are not only fostering the innovation of life-saving treatments, but also providing jobs within the state. A second key objective is providing a platform for networking and information for our members, and we host our NYBIO Annual Meeting in May.

Could you provide a final message to our readers on New York's biopharma industry?
The biopharma industry in New York is on the verge of explosive growth. We have investment from the state, the City, key institutions and stakeholders to grow the industry. We are on the cusp of a breakthrough in becoming one of the most important hubs within the United States for biotech drug development. ■

Sam Taylor

President
NCBIO

The North Carolina Biosciences Organization (NCBIO) is a trade association dedicated to promoting the future growth and development of North Carolina's bioscience industry

Could you introduce us to NCBIO and underline the role the association plays?
NCBIO is the trade association for the North Carolina (NC) life sciences industry. We represent the pharmaceutical, biologics, medical device, agricultural, biotechnology and contract research sectors within the state, and we are dedicated to promoting the future growth and development of NC's entire bioscience industry. We are primarily an advocacy organization that represents the industry before state and federal bodies, such as the North Carolina General Assembly and the North Carolina Delegation to Congress. Our aim is to motivate our legislators to build a policy environment that will encourage the growth of life sciences companies, support the development of a strong life science workforce and will promote research and technology transfer at universities and other institutions.
Our sister organization – the North Carolina Biotechnology Center is a state-funded economic development entity devoted to the life sciences industry. They receive approximately US$12.5 million from the state per annum to develop and operate programs that will promote the economic development of the life sciences industry. The programs include research grants to universities, loan programs for startup life science companies and recruitment programs for larger companies that are identifying locations to expand their existing facilities or to establish new facilities.

North Carolina's biotech cluster has increased by 31% since 2001. What have been the key factors driving this growth?
There are two components to NC's life sciences community. Firstly, the smaller companies that are just launching, and secondly, a large group of pharmaceutical and biopharmaceutical manufacturing companies. A key factor contributing to the growth and expansion of all these companies within the state is our extremely talented labor force due to a strong cluster Tier 1 universities, which includes UNC Chapel Hill, NC State University and Duke University in the Research Triangle area. There is also a major biomedical hub in Winston-Salem, which is built around the Wake Forest University, and we also have a teaching hospital in Greenville that is associated with East Carolina University.
In the manufacturing sector, we have had significant success around an initiative, launched in 2005, geared towards building training and education facilities dedicated to the life sciences industry. The state invested approximately US$75 million in a three-part project with the aim of growing the region's life sciences workforce, education and training capacity. The crown jewel of this initiative was the biotechnology training and education center at the NC State University where they provide hands-on experience to students and incumbent workers with commercial-scale biomanufacturing facilities, including fermentation, downstream filtration and purification. The facility operates a small simulated pilot scale manufacturing facility. The second element of the project was a US$20 million life science laboratory and undergraduate teaching facility at NC Central University, which has been very successful in the training of individuals that want to work in the drug discovery sector. Thirdly, approximately US$10 million was allocated to the community college system in NC for the purchase of equipment for biomanufacturing-related skills training and related curriculum development.

Apart from the collaborative emphasis of the Research Triangle, what are the key advantages for operating in NC?
NC has a low corporate tax rate as compared to most states in our country. The state has also been very cognizant of the impact of regulatory burdens that can be placed on industry, and has been amending its regulatory codes to make sure they are optimized for the current economy and business environment. NC also offers an excellent quality of life, which is very appealing to the community.

What role does NCBIO play as a lobbyist, both in Raleigh and Washington D.C.?
In NC, the core of our efforts is to keep the life sciences community in the minds of the legislators and to remind them that the industry can assist in the economic development of the state, especially with respect to job creation. We have a focus on rural development and we spend a significant amount of time reminding people that the life sciences industry can help in uplifting all communities within the state. We are also concerned with drug pricing, and NCBIO aims to keep informing Congress of the large costs and expenses associated with drug development. ■

The Biopharma Investment Climate

"There is certainly a lot of activity in the private and public capital markets. Over the past five years, with the run of a bull market from 2012, we have seen VC money increasing dramatically to record levels."

- Peter Meath,
Managing Director & Industry Head,
Life Sciences J.P. Morgan Commercial Banking

Image courtesy of Adents

Global Business Reports
EDITORIAL

Standing out in the biotech crowd

The VC investment climate

Image courtesy of Frontage Laboratories

The biopharmaceuticals industry has the highest percentage of R&D reinvestment in the United States. Recently, drug discovery has shifted away from large pharma, with biotechs now accounting for 70% of all clinical trials in the United States. Unlike large pharma, which will have commercialized products in the market and thereby have a revenue stream, many biotechs do not. It is therefore less surprising that 90% of biopharmaceutical companies are currently not making a profit, according to BIO. For an academic researcher or recently-spun out start-up, initial funding will likely come through grants. The NIH, for example, provides US$37.3 billion funding per annum. However, given that a 2016 Tufts Center for the Study of Drug Development report put the cost of developing a drug at US$2.7 billion, which includes cost associated with failed drugs, if a biotech does not receive private investment, strike a partnership with a large pharmaceutical company or a big biotech, or have an IPO, it is unlikely to sustain itself through the development period.

The beginning of 2018 featured a number of large M&A deals, including Celgene acquiring Juno Therapeutics for US$9 billion and Impact Biomedicines for US$7 billion, and Sanofi US acquiring Bioverativ for US$11.6 billion. However, it was VC private investment that took center stage, breaking numerous records, with US$13.5 billion in venture capital poured into biotechs in the first 10 months of 2018, far higher than all of 2017 (US$11 billion). Of note was Grail's oversubscribed US$300 million Series C round and Allogene Therapeutics – a biotech pioneering the development of allogeneic CAR T therapies for cancer – completing a US$120 million Series A, especially as both biotechs had substantial funding from Chinese VC firms. With CFIUS, as of October 2018, scrutinizing foreign transactions much more carefully, there could yet be implications for both biotechs and many other U.S. biotechs in the coming year.

Perfecting Due Diligence

Although there is increased capital pouring into biotechs across the nation, especially in California, which saw US$7.6 billion of VC investment in 2018, and Massachusetts, which saw US$6.2 billion the same year, hundreds of biotechs will struggle to raise capital each year. For every investment a VC fund or private equity firm makes, it will always carry with it long odds, given that drug-approval rates have dipped to 9.6%, according to BIO. Despite the monetary risks associated with drug research and development, large pharma, big biotechs and VCs are increasingly looking to invest in early-stage biotechs to capitalize on technology before more significant value inflection points. "There is a trend of investment capital moving into the market earlier in the cycle," remarked Thomas W. Chalberg, partner at Heroic Ventures. "In the biotech space, early capital is a requirement. There is also the recognition of how much value can be created early on in the cycle and investors now want to participate in this early stage value creation. Across the industry we are definitely seeing a trend towards investment at earlier stages, which is often related to partnerships with academic institutions."

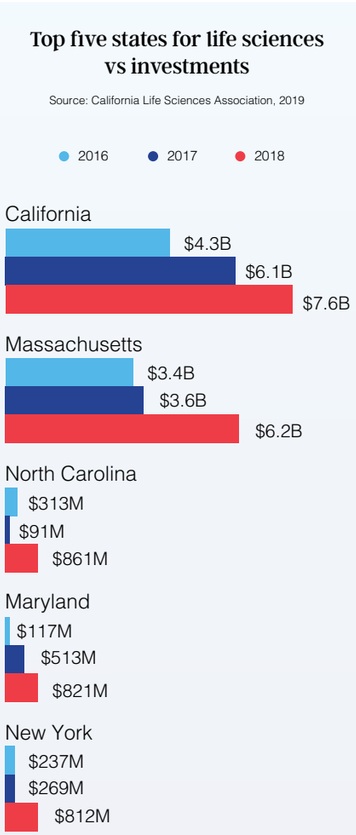
As investments are made earlier in the process, greater analysis will need to be undertaken to de-risk any transaction. "What is most important when doing a transaction with an early-stage company is that extensive due diligence is carried out as a result of higher potential risk. What we are seeing more of is a "build-to-buy" model, where companies put their money in with an option to purchase later," highlighted David H. Crean, managing director for investment banking at Objective Capital Partners.

Whilst certain early-stage biotech executives will travel the country searching for initial seed and Series A investment dollars, there are a handful of seasoned executives that understand exactly what investors are looking for. For example, Mirum Pharmaceuticals, a San Diego-based biotech, received US$120 million in its Series A funding round five weeks after its inception. "There are three key components for setting up a biotech: the science, which includes the technology or the molecule; the money; and the people," remarked Mike Grey, chairman and CEO at Mirum. "By far the most important component for any investor is the people. Mirum was a marriage between the previous leadership of

Top ten biotech venture investors by Overall round totals

Source: DealForma

INVESTOR	TOTAL ($M)
Arch Venture Partners	$3,919
Fidelity	$3,386
OrbiMed Advisors	$3,314
Celgene	$2,671
Comorant Asset Management	$2,571
Alexandria Venture Investments	$2,507
New Enterprise Associates	$2,368
RA Capital Management	$2,306
Foresite Capital Management	$2,210
GV	$1,805



Lumena and Tobira – a powerful group of minds. For the investors coming on board, the value proposition regarded the potential of getting to phase 3 clinical data in a relatively short period of time."

Indeed, when considering successful acquisitions, there is usually an executive with a strong track record behind the scenes of the fledgling biotech being bought up.

Therapeutic Focus for 2019

Oncology continues to be the key area for VC focus, although many others are venturing into therapeutic areas that are less crowded. Given that a third of Californian companies' pipelines were focused on cancer in 2018 according to CLSA (433 of the 1,332 total therapies in development), this should come as little surprise. For Arch Venture Partners and OrbiMed Advisors, the first and third largest venture investors globally, cancer therapeutic investments from January 2015 to October 2018 came to 35% and 43% respectively as a percentage of their overall pipelines.

However, VCs are now looking to diversify their investment pipelines into other therapeutic areas and different technologies. Areas of considerable interest for investors include stem cell therapy, gene therapy, orphan drugs, neurodegenerative diseases, regenerative medicine, precision medicine and digital health. "Even though the bulk of venture dollars are flowing into oncology, there are in fact opportunities across multiple therapeutic areas," highlighted Carolyn Ng, managing director of Vertex Ventures HC. "Hence, there is no good rationale for us to be pigeonholed into only one area of interest as we would then be missing out on good opportunities within other segments of the industry."

For oncology, a vast amount of funding is reserved for immuno-oncology, whilst other approaches do not receive as much attention despite presenting many opportunities. "Though it was identified, along with immuno-oncology, as one of the 10 areas of emphasis by Vice President Biden's Cancer Moonshot panel, side effect reduction is an under-appreciated field," remarked Brian Frenzel, CEO of Tosk, a biotech developing a family of inexpensive, small molecule drugs designed to prevent the toxic side effects of common cancer treatments. "Side effects not only adversely affect patients' quality of life, but can be costly to treat and can limit the effectiveness of cancer therapy. Our small molecule drugs are inexpensive to produce and fit easily into existing treatment regimens. They are intended not only to reduce the cost of treatment but to improve outcomes for cancer patients."

As well as looking at short-term value creation, VC firms must always understand the ultimate commercial viability in the long run. This has meant that certain therapeutics, especially in immuno-oncology, have taken precedence over the past decade. The Bill & Melinda Gates Foundation – the largest private foundation in the United States – through its US$2 billion Strategic Investment Fund (SIF) has had the opportunity to focus on meeting unmet patient needs that would not make monetary sense to a normal VC. SIF has the key goal of managing and even eradicating infectious diseases in the developing world. To capitalize on what is already being developed, the SIF has looked into the advancements being made in other therapeutic areas. "With so much investment going into areas like immuno-oncology, the Fund has looked to take advantage of this. Several companies in these spaces are focused on understanding the immune system and how we can manipulate it to fight such health conditions. Since the immune system is also critical in infectious diseases, a significant amount of the learnings and tools from other therapeutic areas can be applied to the foundation's priority diseases," highlighted Vidya Vasu-Devan, deputy director at the Bill & Melinda Gates Foundation's SIF. "As a result, the SIF team invests in these companies to leverage the products and technologies for diseases like HIV and TB. Additionally, we always look to support companies dedicated to eliminating infectious diseases."

As the public markets continue to reward biotechs earlier in their development timeline, the capital markets are also being more receptive to companies. The previous unwritten rule was that a biotech had to be in the clinic to have an IPO, which is not the case anymore. With such high valuations being given to biotechs going public, VCs have the opportunity to make an investment even earlier in the development process, including at academic institutions. This not only provides further options for researchers or startups to bridge the 'valley of death,' but also increases the odds of breakthrough technologies being noticed and eventually commercialized. In the end, all involved, including the researchers, biotechs, investors and most importantly, the patients, benefit. ■

Peter Meath

Managing Director &
Industry Head of Life Sciences
J.P. MORGAN COMMERCIAL BANKING

J.P. Morgan is a leading global financial services firm

Could you underline the bank's core expertise within the life sciences vertical?

J.P. Morgan's life sciences division is divided into biopharmaceuticals, medtech – devices and diagnostics tools – and service companies, which include CDMOs and CROs. Any company that develops or manufacturers a molecule falls under our purview. Commercial Banking's dedicated life sciences group was created in 2016 because we wanted to deliver the breadth of J.P. Morgan's services and institutional knowledge to companies in this industry vertical throughout their entire life cycle.

Given that the life sciences industry has been remarkably resilient, what has propelled the increase in banking activity within the space?

There is certainly a lot of activity in the private and public capital markets. Over the past five years, with the run of a bull market from 2012, we have seen VC money increasing dramatically to record levels. Moreover, the size of funds has grown significantly, and activity in the public markets has rapidly increased. When looking at all these ingredients, there is a robust private capital market that is helping fund early-stage opportunities and an active and receptive public market further enabling this development.

Do you foresee high-IPO valuations for biotechs continuing in 2019?

The public market for biotechs is interconnected with the private market. Pre-money valuations of biotech IPOs went up almost threefold in 2018. There is a preponderance of earlier-stage companies going public and getting the valuations they want from the public market. To get there, they are getting money from the private capital market. There is a robust venture and private capital market where more money is driving earlier, novel and transformative technologies, and the public market is being receptive in rewarding those technologies.

We are definitely in a unique time. Never before have we seen the pace of technological innovation in life sciences be as fast and as distinct. The markets are rewarding the ability for companies to transform medicine in innovative ways. The great thing about the life sciences space is there is a very specific construct by which we determine this – we can evaluate clinical progression with data results and definable milestones. The biopharmaceutical industry is unique in that there is reward for innovative technologies without a dollar of revenue being generated.

The life sciences industry has remained resilient in past economic slowdowns. Do you expect this to continue over the coming two years?

Every market in every industry is going to see bumps along the road as seen in Q4 2018, with the biotech space being no exception. However, when looking at the amount of capital that is still waiting to be deployed, the receptivity of the capital markets right now, the pace of technological change, the demographics in the United States as well as the international opportunities, all those line up for an industry that should be resilient regardless of what the macro economic factors are.

Away from J.P. Morgan's traditional banking offering, how are you looking to uniquely serve your client base?

We are very focused on companies in the innovation economy and the unique needs that come with that. The innovation economy is changing the face of business and disrupting industries. The pace of change is only getting faster, and high growth companies' banking needs can quickly turn complex as they scale and grow. We are leveraging our knowledge and global capabilities – including our US$11 billion spend on global technology at the bank – to help life sciences companies deliver medicine better, from opening an account on day 1 to expanding internationally, adopting new technologies like AI and all the way through to a potential exit.

How does J.P. Morgan aim to impact the biopharma value chain?

J.P. Morgan, given our history, size, capabilities and knowledge within the space, aims to positively impact companies of every size, be it a large biotech or a seed stage company that has just spun out of a university system. We aim to bring the full force of J.P. Morgan to bear to each of our clients. If we can do that successfully, which we know we can, and that seed stage company becomes the next large biotech company, then we have achieved our goal. This industry is about big ideas at early stages that grow fast and can significantly impact the healthcare market, our personal health and the capital markets. ■

Annette Grimaldi

Managing Director,
Life Sciences Investment Banking
BMO CAPITAL MARKETS

BMO Capital Markets is a leading North American financial services provider and the investment banking subsidiary of the Canadian Bank of Montreal

Where does the life sciences sector sit within BMO's offering?
BMO Capital Markets is the investment banking arm of BMO Financial Group. BMO Capital Markets has a number of industry specializations, but the healthcare group has been one of our rapidly growing industry sectors since a group of us joined BMO about 10 years ago. We grew from a team of five people at the end of 2008 to about 30 professionals across various areas of healthcare in 2019. In 2018, we were the number six bookrunner of life sciences IPOs.
We have driven our growth by bringing the resources of a bulge bracket bank to service offerings for growing and development-stage companies. We offer full services for public and private companies and their investors: IPOs, follow-on offerings, convertible and other types of debt financings and strategic advisory. We also lend to life sciences companies.

Despite great expectations for M&A in 2018, activity was relatively slow. What were the causal factors behind this lower-than-expected activity?
Many assume that strength in the capital markets and the new issue market is inversely correlated with M&A activity. But in fact, they tend to move in tandem. When capital markets are receptive to life sciences companies, like they were until the final quarter of 2018, companies that might otherwise be acquisition targets of big pharma had access to the capital needed to pursue standalone business models. Despite the downdraft that we saw at the end of 2018, this capital continues to be available.
Equally, life sciences companies tend to be bought rather than sold by pharma companies, meaning that pharma companies pursue acquisitions not merely because a company is for sale, but to plug a gap in their pipeline or arsenal of capabilities. In 2018, we didn't see much of this, but 2019 started out with a flurry of activity. The Bristol-Myers Squibb and Celgene transaction caught everybody's attention, and there was also a nice takeout of Loxo Oncology by Eli Lilly. Celgene is a widely-held stock and that acquisition will return a lot of capital to the market that can be redeployed in life sciences, which could be highly impactful for the market.

Although there has been a strong track record of IPOs over the last few years, how great is the impact of the government shutdown likely to be?
It has been an extraordinary couple of years for life sciences IPOs, with an unprecedented rate of company creation. Since 2013, the number of publicly-traded biotech companies has more than doubled. I've been impressed that the capital markets have been able to absorb and fund this level of company creation.
The partial government shutdown has slowed the pace of life sciences IPOs in early 2019. Companies that were on file with the SEC, and would have otherwise launched their IPOs in January, were frozen for a period of time. We've since had a reprieve, with the federal government reopening for three weeks while border security and other negotiations continue and, in that window, a number of life sciences IPOs have been able to launch. But the number of deals is definitely less than it would have otherwise been.
The shutdown has also impacted public M&A transactions, which need to be reviewed by the SEC and the FTC. Similarly, the backlog is growing and the agencies cannot respond at the pace to which companies have become accustomed.

The increasing scrutiny of CFIUS on foreign investments has placed a question mark over future deal flow, particularly when it comes to China. What is your expectation for investment from China into the U.S. life sciences industry in 2019?
Venture capital investment from China has greatly increased, both in terms of the number of deals and capital deployed. We continue to see strong interest from Chinese investors, particularly in private life sciences companies. Since many of these private companies ultimately go public, these investors then hold ownership stakes in U.S. public companies. So far we haven't seen interventions from CFIUS prohibiting these investments, but we're monitoring the situation. ■

Christiana Goh Bardon

Managing Director
UBS ONCOLOGY IMPACT FUND MANAGED BY MPM CAPITAL
Portfolio Manager
BURRAGE CAPITAL FUND

UBS Oncology Impact Fund is an evergreen fund specializing in investments in early stage oncology and cancer therapeutics

At what stage of development would you look to invest in a biotech?
It used to be an unwritten rule that a biotech had to be in a clinical stage before having an IPO. However, today, there are more platform companies going public before their first clinical candidate. As a public investor, I tend to wait until there is early proof of concept in an indication, especially in oncology where pre-clinical models are notoriously unpredictable.

Apart from clinical data results, what attracts you to a make an investment in a biotech?
We invest when there is reasonable certainty based upon the scientific mechanism, the pre-clinical data and or clinical data. In fields like oncology, we feel very optimistic when we see early monotherapy efficacy in clinical studies, as this is drug activity.

What technological advancements have caught your attention in the oncology space?
We are active in cell therapy, which has demonstrated dramatic efficacy in several hematological cancers. One of our recent IPOs, TCR2 Therapeutics, is developing a T-cell therapy, which may be effective in solid tumors. We believe that solid tumors are the next unchartered territory within the cell therapy space and involve a much larger population of patients.

What is your long-term vision for the UBS Oncology Impact Fund and how do you expect the oncology space to transform?
The fundamentals of the industry continue to be strong for biotechnology and especially oncology. The over-65 patient population is set to double over the next twenty years, and as a result there will be a doubling of oncology patients. Innovation is at an all-time high where we are just scratching the surface of new modalities such as cell and gene therapy. We are very optimistic that our industry will be developing many new and important drugs and technologies to meet these growing unmet medical needs. ■

Thomas W. Chalberg

Partner
HEROIC VENTURES

Heroic Ventures is an early stage venture capital fund with key focus areas in gene and cell therapy and ophthalmology

Are you noticing a trend of VCs investing in biotechs at an earlier stage?
Heroic Ventures is specifically focused on seed and formation funding, after which companies will raise outside funding for their next stages. There is a trend of investment capital moving into the market earlier in the cycle. In the biotech space, early capital is a requirement. There is also the recognition of how much value can be created early on in the cycle. Across the industry, we are definitely seeing a trend towards investment at earlier stages, which is often related to partnerships with academic institutions.

Are academic researchers inclined to take on Heroic Ventures' value proposition?
Most university researches are hesitant to leave their full time jobs at the university, and are thus looking for entrepreneurs, investors and management that know how to build companies to help them commercialize their ideas. Universities understand innovation and creating intellectual property, but not necessarily the manufacturing or commercialization of a product. Consequently, there is a good opportunity for academic institutions to partner with Heroic Ventures. We will identify unmet need, market opportunities and match the opportunities with technologies from the academic institutions, which we can then license and commercialize.

What is Heroic Ventures' key objective moving forward?
Heroic Ventures is continuously looking for good opportunities for formation investments and seed investments. We are also spending our time forging partnerships and expanding our ecosystem, which will be helpful in understanding new investments and pursuing new opportunities. A critical step that we tackle in the beginning is to ensure we understand, very early in the lifecycle of the company and the product, what value that product can bring to patients. This helps us to target the right patient population that would benefit, which is crucial. ■

Carolyn Ng

Managing Director
VERTEX VENTURES HC

Vertex Ventures HC is a global life sciences focused venture capital fund investing in disruptive biopharmaceuticals, therapeutic medical devices and digital health companies of various stages

Could you provide a brief overview of Vertex Ventures HC?
Vertex Ventures HC is one of the pillars of the Vertex Ventures family of funds, a global platform that spans across the United States, Singapore, Southeast Asia, China and Israel. HC stands for "healthcare," and as the name suggests, we invest in various sectors of the healthcare industry. We invest in companies that are founded on breakthrough biological insights or technological innovations that are prime for translation to deliver therapeutic benefit in the clinical setting. With a focus on medical areas with significant unmet needs, we work with great teams to build transformational companies to improve the health and quality of human life. Our portfolio includes companies at all stages of development, from early-stage companies testing transformative technologies to commercial-stage companies seeking additional growth.

Is there a particular driver for Vertex Ventures HC diversifying its pipeline?
Even though the bulk of venture dollars are flowing into oncology, there are opportunities across multiple therapeutic areas. Hence, there is no good rationale to pigeonhole ourselves into only one area of interest as we would then be missing out on opportunities within other segments of the industry. We also seek to manage the overall portfolio by diversifying on stages, striking a balance between scientific, clinical and commercial risks across the entire portfolio.

Could you elaborate on Vertex Ventures HC's investment into Visterra and its acquisition by Otsuka Pharmaceuticals ?
We invested in Visterra in 2014, co-leading its US$30 million Series B funding round with Temasek and Merck Ventures. Other existing investors included Flagship Pioneering, Polaris Partners, Omega Funds, Alexandria Venture, CTI Life Sciences Fund and Cycad Group. Our investment thesis for Visterra was its disruptive platform approach in addressing difficult-to-drug targets. Its high precision antibodies-engineering platform enabled the development of multiple programs, ranging from infectious diseases to kidney diseases.
Visterra initially tried to go public but was not successful as their lead program in influenza was not considered attractive to public investors. They thus had to secure alternative financing options to move forward. Vertex Ventures HC and Temasek's involvement in the company lent a more global view to Visterra, which then started to explore opportunities for collaborations in geographies outside of the United States. One of Visterra's first OUS collaborations was with Singapore's A*Star (Agency of Science, Technology and Research) agency, which secured them a considerable sum of non-dilutive funding. This funding was used to develop Visterra's dengue fever asset, which in turn generated value for the company as it was out-licensed to the Serum Institute of India, who not only provided non-dilutive upfront capital for the company, but also came in as a Series C equity investor.

With every investment comes a certain level of risk. What are some of the key challenges Vertex Ventures HC is currently facing?
We find ourselves operating now in that phase of the cycle where there is a flood of venture funding, especially for the biotech sector. Many new players have entered the market, bringing in new sources of capital. However, with more capital available, it is easier for management teams to lose fiduciary discipline, which is a key risk we carefully watch. Biotech valuations are also reaching all-time highs, even for early unproven projects. One of the challenges we constantly have to face is how to strike a balance between being disciplined on the valuation front, and yet competitive enough to participate in high quality deals.

What is your exit strategy for your investment?
We do not believe in a "one size fits all" approach with regards to exits. Given the diversity of the investments we make, each one will have its own story to tell depending on the therapeutic areas of focus, sector-specific M&A dynamics, public market receptiveness and private sector's funding appetite. We keep a close relationship with the industry's top decision makers in both established and emerging markets to inform our strategy in creating optionality for our portfolio companies. Ultimately, we believe that when great people work on great science to do great things for the patients, an exciting exit outcome will eventually follow. ■

Vidya Vasu-Devan

Deputy Director
BILL & MELINDA GATES FOUNDATION'S STRATEGIC INVESTMENT FUND

The Bill & Melinda Gates Foundation is the largest private foundation in the United States. Its Strategic Investment Fund (SIF) works to leverage the private sector to achieve progress on the foundation's charitable objectives

Could you introduce us to the overall focus of the Strategic Investment Fund (SIF) and how it fits into the foundation?
The Bill & Melinda Gates Foundation's Strategic Investment Fund is analogous to a corporate venture arm that makes investments in support of the foundation's overall charitable objectives. The US$2 billion SIF is effectively a toolkit that can be used to partner with private-sector companies in any of our focus areas through financial tools such as equity investments, loans and volume guarantees.
The SIF's focus areas are aligned with the foundation's overall objectives. One of the key areas is global health, primarily the eradication or management of infectious diseases in the developing world, especially in South Asia and sub-Saharan Africa. We also focus on maternal and child health, which includes family planning and contraceptives. Additional targets of our global development efforts include financial inclusion, agricultural development, sanitation and nutrition. In the United States, our primary focus has been on education. We seek to ensure that all people, especially those with the fewest resources, can access the opportunities they need to succeed in life.
Over the last decade, the SIF team has made roughly 70 investments to support our mandate to leverage the foundation's technical and investment expertise to stimulate innovation and make markets work for the poor. Our investments are intended to further the foundation's programmatic goals – not to generate income. Any returns on investments are directed back to the foundation, ultimately furthering charitable impact.

With respect to the U.S. biotech space, what has been the foundation's strategy and thought process towards grants?
Right now, other therapeutic areas like oncology and neurodegenerative diseases are attracting significant amounts of venture funding. Several companies in these spaces are focused on understanding the immune system and how we can manipulate it to fight such health conditions. Since the immune system is also critical in infectious diseases, a significant amount of the learnings and tools from other therapeutic areas can be applied to the foundation's priority diseases. As a result, the SIF team invests in these companies to leverage the products and technologies for diseases like HIV and TB. Additionally, we always look to support companies dedicated to eliminating infectious diseases. For example, SIF made an investment in VIR Biotechnology, a San Francisco-based company focused on finding innovative solutions to unmet needs in infectious diseases. They have raised a substantial amount of capital and are a unique example of more capital moving into the infectious disease space.

Could you elaborate on the cross collaboration happening between different therapeutic segments and how the SIF is facilitating this?
In 2015, the foundation invested in the German company CureVac to accelerate mRNA vaccine technology development. CureVac manufactures unmodified mRNA as a drug product, which effectively gives the body instructions for creating its own proteins to fight cancer and infectious diseases. Although there were applications for its technology in infectious diseases, their primary focus was oncology. SIF made a US$52 million investment and attained a set of rights to work in partnership with CureVac to bring additional non-dilutive funding to the table to deploy its platform against infectious diseases. Our goal was to ensure that this breakthrough technology would be leveraged for getting low-cost vaccines that prevent infectious diseases to the people who needed them most.

Apart from the United States, in which geographic areas is the SIF focused on investing?
SIF is a concerted international investing effort. One of our long-standing team members is based out of London, and his team has spent the last two years building relationships and making investments in the European biotech community and developing our investment efforts in tech-enabled delivery of health, agriculture and financial services in India. We have also investigated opportunities in Israel and China, and have worked with large pharma companies in developing countries in South Asia and sub-Saharan Africa. A significant amount of our search efforts has been focused on Europe and India, and our aim is also to start focusing our investment search on sub-Saharan Africa. Additionally, we are working on further developing our market delivery strategy for the innovations in which we invest.
We want to encourage readers to point any private-sector innovations within the areas the foundation works towards SIF. ■

M&A Activity on the Rise

M&A activity in the biotech industry has been feverishly difficult to predict. There were hopes that 2018 would be a bumper year, but despite the US$62 billion Takeda acquisition of Shire, many were left disappointed. However, 2019 is already proving to be different with large pharma especially being busy. Eli Lilly has acquired Loxo Oncology for US$8 billion; Roche has acquired Spark Therapeutics for US4.8 billion; and Bristol-Myers Squibb took control of Celgene for US$74 billion in the largest pharmaceutical-company acquisition ever. Baker McKenzie has even predicted M&A activity will be over US$400 billion in 2019 for the healthcare industry, an increase from the US$308 billion in 2018.

It is now clear that high valuations in 2018, leading to an overvalued market, swayed companies away from M&A. Reduced valuations have been a key factor in the surge of acquisitions in Q1 2019. "In the biotech market, prices have now come down and are again a lot more attractive and, based on this fact, we expect to see more M&A bolt-on activity in 2019, particularly for small and mid-market 'bolt-on" deals,' remarked Adam Golden, head of the NY corporate practice group at Hogan Lovells. "When looking at potential private M&A, collaborations and partnering deals, there is a very strong demand from big pharmas and biotechs for new products and technologies, particularly in the areas of cell and gene therapies."

So, M&A activity is back, but megamerger deals have moved aside for now, with smaller bolt-on deals becoming the norm. "Companies are entering into bolt-on deals to augment their pipelines as opposed to combining two companies together," highlighted Geoff Meyerson, CEO and co-founder at Locust Walk. "Currently, the bolt-on deal climate is very dynamic, and we certainly see this type of deal playing a larger role in the future."

Undeniably, now is the ideal time for divestment and portfolio optimization. Whether it is large pharma identifying a molecule, or a CDMO looking to increase its capabilities with a new drug delivery technology, this is the opportune moment. "2019 is also a year for companies to look at portfolio optimization to create the most value possible by considering divestitures to fuel innovation internally through R&D investments, or externally through bolt-on acquisitions," underlined Arda Ural, partner and operational transaction services life sciences leader - transaction advisory services at EY.

2019 has already seen plenty of M&A activity, especially within the oncology space, but it remains difficult to predict whether this trajectory will continue. Nevertheless, with the amount of innovative breakthrough technologies being developed, large pharma will be constantly on the lookout to add to their portfolios, especially in the oncology and gene therapy spaces. According to EY, only 16% of life sciences companies' US$1.2 trillion worth of firepower, which includes debt, cash and other balance sheet items, was used in 2018. Taking this into account and despite M&A activity remaining difficult to predict, there is greater certainty that 2019 will be a more active year. ■

> We believe that the promise of the tax reform, with regards to M&A activity, did not completely disappoint in 2018, but it also did not live up to the broader market expectations. There was approximately US$198 billion in M&A activity across the life sciences sector, which is generally in line with 2016 and 2017 figures. We are entering 2019 with cautious optimism and do not anticipate a short-term recession that would derail this trend.
>
> - Arda Ural, Partner and Operational Transaction Services Life Sciences Leader - Transaction Advisory Services EY

Geoff Meyerson

CEO and Co-Founder
LOCUST WALK

Locust Walk is a global life science transaction firm

Large pharma is veering towards bolt-on acquisition deals. How is this impacting the transactions you are involved with?

Locust Walk has definitely seen a trend towards smaller deals as megamerger deals have declined. A significant number of the larger companies that were going to consolidate have already done so. There is a new crop of players coming into the market that will pick up some of the deals but cannot necessarily afford mega deals. The idea of a bolt-on deal is just a euphemism for a smaller transaction, and companies are entering into bolt-on deals to augment their pipelines as opposed to combining two companies together. Currently, the bolt-on deal climate is very dynamic, and we certainly see this type of deal playing a larger role in the future.

How do you see Locust Walk positioned in the market?

Locust Walk is unique in the market and our business has developed to help other companies realize their objectives. Our success relies on the success of our clients. We are involved in capital raising, IPO advisory, assisting companies that have non-traditional investors to attain institutional investors and regional or global partnering.

We've seen a significant increase in partnering deals as a way for companies to attain financing. Companies are struggling to attain equity, or they view partnering as more attractive than selling equity. Either way, companies are diluting something, and the question becomes: which is less costly? For some of the companies that do not have major institutions behind them, it might be potentially more advantageous to license their assets as opposed to selling equity.

Locust Walk is much more diversified than most banks or consulting firms, and whatever helps our clients achieve their objectives, we will navigate with them. We offer an integrated approach to deal making, and we integrate strategy and analytics with every deal execution. ■

Adam Golden

Partner,
Head of NY Corporate Practice Group
HOGAN LOVELLS

Hogan Lovells is an international law firm co-headquartered in London and Washington, D.C.

As biotechs look to attain funding, which avenue do you expect them to take in the current market?

Small biotech companies are always looking at an entire menu of options when it comes to attaining funds to move their products and technologies forward. They look at additional private financing, collaborations, M&A and the public markets as possible opportunities. It is always a balancing act based on the needs of the key programs, the company's expertise and financial capability to continue to advance those programs and how the relevant market values their business.

What is Hogan Lovells' expectations for M&A activity in 2019?

After a slow year in 2017, 2018 was expected to be a very robust year for M&A activity. However, after a strong start, we did not see that trend continue as significantly as anticipated. One of the reasons might have been due to increased prices as a result of the competition for deals. The valuations became so high that many dealmakers viewed the market as overvalued. In the biotech market, prices have now come down and are again a lot more attractive. Based on this fact, we expect to see more M&A activity in 2019, particularly for small and mid-market "bolt-on" deals. In fact, several significant transactions have already been announced, including the US$74 billion acquisition of Celgene by Bristol-Myers Squibb and Roche's US$5 billion acquisition of Spark Therapeutics.

When looking at potential private M&A, collaborations and partnering deals, there is a very strong demand from big pharma and biotechs for new products and technologies, particularly in the areas of cell and gene therapies. In addition to the demand for advanced technologies on the buy-side, a healthy venture capital market over the last few years has resulted in numerous early-stage biotech companies with products of interest to buyers. ■

David H. Crean

Managing Director – Investment Banking
OBJECTIVE CAPITAL PARTNERS

Objective Capital Partners, headquartered in Southern California, is a leading M&A investment banking firm

What due diligence process do you carry out when considering a potential client?
Our due diligence process is part art and part science. The science part entails detailed diligence on evaluating whether a company is ready to sell or be partnered with, who the management teams consists of, where their technology stands, their finances and whether they adopt proper accounting methods. Getting companies prepared to move from merely a cash management model to an accrual accounting system takes plenty of time. The art involves a softer approach, which includes sitting down with the owners and asking them about their goals and objectives, and then evaluating if they truly want to sell.

What advancements are you noticing within San Diego's biotech hub?
We are witnessing more capital being attracted into Southern California and more venture funds coming down to San Diego. There is a lot of great technology in Southern California, across Los Angeles, Orange County and San Diego, and we are starting to see a little bit of that momentum picking up.

Are cross-border transactions becoming more commonplace?
We are currently witnessing a lot of cross-border transcations, especially between Europe and India, China and/or Japan. This is a big area of focus for investment banks and financial service providers with cross-border transaction teams now being set up. We are also seeing a continued trend of investment from Asia Pacific, especially from Japan, South Korea and China, with companies looking to gain a foothold in the United States. Although the general market appears to be slowing down in some sectors and there are talks on Wall Street about a "potential" recession in the United States in the second half of 2019, I do not see it affecting the life sciences industry to a great degree. The life sciences and healthcare industry tends to be contra-cyclical. ■

John Bradley

Managing Director
TORREYA PARTNERS

Torreya is a global investment banking boutique providing mergers and acquisitions, capital markets and licensing advisory services to life sciences companies

From 2016 to 2017, 17.4% of all pharma transactions involved Torreya. What has differentiated Torreya as a partner of choice in the biopharma industry?
We are able to differentiate ourselves through our understanding and knowledge of the industry in terms of the science, products and networks. The company's management team has all been involved in the industry and so know what problems might arise and how to solve these problems, which can be helpful within the deal flow itself. As a team, we have the advantage of looking at deals from many different angles, and not only from a financing perspective. We collaborate with a significant number of industry leaders and focus on knowing who the key opinion leaders are and understanding their visions.

As trade tensions continue to bring uncertainty to global markets, what has been the impact to your service offering?
We have noticed that China has started to distance itself from the U.S. market, but we have found that, even in these uncertain circumstances, companies are still prepared to do business if it is going to help them achieve success.

Are you noticing increasing interest in a specific therapeutic area?
A substantial amount of investment has flowed into the oncology area, with stem cell therapy receiving a significant amount of interest. Orphan drugs is another area where companies are seeing the opportunity to capture a market. Despite being a small market in terms of size, there is a lot of financial opportunity.

What has been the company's main driver for growth?
Over the last 10 years, the sectors that have been contributing to Torreya's growth and market share include the generics industry, oncology and the orphan drug industry. Our drivers for growth change, depending on the market and the sectors receiving more attention at a given time. ■

Arda Ural

Partner & Operational Transaction Services Life Sciences Leader - Transaction Advisory Services
ERNST AND YOUNG (EY)

EY is a multinational professional services firm headquartered in London, United Kingdom

Where do you see the most opportunity for the biopharma industry to derive greater value and cost savings, and where does EY fit in driving this?
We believe that the value of consultancy and analytics lies within the prediction of population health and the deployment of interventions for patients before they have to go to the hospital. Approximately 4% of patients consume 45% of resources, which is a very skewed consumption pattern. If we can identify the 4% patients and take care of them before they need hospital services, healthcare costs can by decreased significantly.
We are just starting to scratch the surface on digital therapeutics, but we believe that it is going to be a huge market opportunity and transformative for patients. The industry has to embrace Pharma 4.0 to stay competitive as providing the personalized experience demanded by patients will require life sciences organizations to find new ways of working. Partnering with others in the industry to share data, medicine and resources while anticipating trends and regulatory changes will help ensure sustainability in this increasingly evidence-based, outcomes-focused sector.

With the new Committee on Foreign Investment in the United States (CFIUS) review process likely to impact cross-border transactions, is EY seeing more internal M&A activity between U.S. companies?
The expanded CFIUS review process of critical technologies has already started to affect incoming foreign capital into the United States from China since the signing of the mandate as a pilot in November 2018. This change is expected to delay closings of some deals and/or discourage some cross-border investors from investing in specifically biotechnology assets in the United States. It will also impose a compliance burden to Biotech CEOs since they have to declare and file qualifying investments under FIRRMA (Foreign Investment Risk Review Modernization Act), signed into law in August 2018.

After a slower-than-expected 2018, do you expect to see increased M&A activity in 2019?
We believe that the promise of the tax reform, with regards to M&A activity, did not completely disappoint in 2018, but it also did not live up to the broader market expectations. There was approximately US$198 billion in M&A activity across the life sciences sector, which is generally in line with 2016 and 2017 figures. We are entering 2019 with cautious optimism and do not anticipate a short-term recession that would derail this trend. We do, however, believe that now is the perfect time for divestment and portfolio optimization for a company on the selling side of the M&A space given favorable valuations within the life sciences, especially in the medical technology space that defied the market volatility we observed in the beginning of the year. Our research of 1,436 divestitures in the 2008-2019 period also supported the hypothesis that disciplined divestors created double the capital efficiency when compared to non-divestors and over 20% higher shareholder value.

How do you expect pricing structures within the biopharmaceutical space to evolve?
The headwind the biopharma industry has been experiencing for some time is to be able to show value, and ultimately price therapies in an outcomes-based modality. However, there is a multitude of confounding factors impacting patient outcomes outside of the potentially favorable impact of the medication, including compliance with therapy, behavior changes, adherence to prescribed medication, genetic risk factors or co-morbidities. The challenge for all stakeholders across the fragmented health ecosystem – payers, health care providers, hospitals and biopharma and med tech industry – is to recognize the need to move away from historic payment models based on product utilization and rebates towards value-based models that reward improvements in health outcomes. Sharing the longitudinal patient data across this ecosystem will be a key success factor for measuring outcomes to inform the contract reward and trigger points as well as identifying intervention types, timing and modes. Outcome-based contracts, which tie a product's performance to emerging evidence of improved patient outcomes, have the potential to reduce healthcare spending and change the healthcare price trajectory to more sustainable levels, while continuing to reward product makers for risky but important innovations. ■

The Bull Market is Set to Continue

IPOs within the life sciences space have been on an extraordinary run with the number of publicly-traded biotechs doubling over the past six years. 2018 was another blockbuster biotech IPO year with US$8.2 billion raised on Nasdaq, breaking 2014's record of US$6.5 billion. With strong expectations for 2019, the untimely U.S. federal government shutdown of 2018 to 2019 due to the disagreement between Congress and President Trump over the latter's demand for US$5.6 billion in federal funds for a U.S.–Mexico border wall introduced some doubts; as biotechs continued to file on the Securities and Exchange Commission's (SEC) EDGAR system, a bottleneck grew, leading to uncertainty over whether the public market could handle multiple IPOs at once.

The government shutdown has passed and biotech valuations for 2019 have exceeded expectations. The first two biotech IPOs in 2019, of Gossamer Bio and Alector, garnered valuations of over US$1 billion. Despite the distractions of the shutdown and a slower Q4 2018 – where the Nasdaq Biotechnology Index declined by 28% and the S&P Biotech Select Index by 36% – there is little doubt as to why the public markets continue to be so receptive.

An amalgam of factors is coming together to override the uncertainties that so often impact the public markets of other industries. Whether it has been due to rising interest rates or trade wars, the life sciences space has remained resilient despite market turbulence. With a record number of VC funding for biotechs in 2018 and expectation that this will continue through 2019, the public market is expected to remain healthy. "When looking at the amount of capital that is still waiting to be deployed, the receptivity of the capital markets right now, the pace of technological change, the demographics in the United States as well as the international opportunities, all those line up for an industry that should be resilient regardless of what the macro economic factors are. The U.S. population is getting older and they need to remain healthy," remarked Peter Meath, managing director and industry head of life sciences at JP Morgan Chase Commercial Banking.

Despite its relative immunity to external factors, the upcoming presidential election is likely to be a testing time for life sciences companies and biotechs in the public markets in 2020. The volatility will largely depend on the political campaigns and subsequently the election outcome. As a result, this has added greater gravitas on 2019 for biotech IPOs. ■

> "The decision for going public needs to be reflected on as it is easier to be private. Generally, one does not want to go public, but as we have six ongoing clinical trials, our expenditure is significant. As we had positive signals from our initial results and CD47 was present in every tumor we looked into, the breadth of opportunity was great. We did not want to focus on one indication but explore several simultaneously. Going public allowed for access to funds as well as maximizing the value of the company, not only to patients but to investors."
>
> - Mark McCamish, President and CEO, Forty Seven

The Hong Kong Stock Exchange: a viable alternative?

In April 2018, the Hong Kong Stock Exchange (SEHK) changed its listing rules allowing biotechs with no revenue stream to list. The rationale behind this move was to continue underlining the city's global financial status and establish itself as a viable alternative to the Nasdaq. However, U.S.-based biotechs choosing to list in Hong Kong instead of in New York, despite the potential for higher valuations, is unlikely. "The Hong Kong stock exchange is more targeted towards Chinese companies – Nasdaq or the NYSE are still likely the better options for most U.S. companies to list on," remarked Alan Seem, partner at Jones Day. "However, there are some situations in which it does make sense for U.S. companies to consider Hong Kong as a listing venue: if they are targeting the Chinese market for their products and are looking to raise their brand profile in China and Hong Kong, or if they have Chinese or Hong Kong investors looking for an Asian exit."

The new listing rules for pre-revenue biotechs has already attracted high-profile technology and biotech companies to list. Hong Kong's Main Market and Growth Enterprise Market witnessed a 120% increase in proceeds (US$35.4 billion) in 2018 compared with 2017. With geopolitical factors likely to play on the mind of Chinese biotechs, the SEHK, with its familiarity, proximity and potential for high valuations, is likely to be an attractive option from now on. ■

John Chambers

President & Head of Investment Banking
H.C. WAINWRIGHT & CO.

H.C. Wainwright & Co. is an investment bank providing corporate finance, strategic advisory, and related services in the biotech sector globally

What are your expectations for 2019 with respect to IPO and M&A activity?

The biotech sector used to be isolated from macro-economic factors, such as rising interest rates or a China trade war, and the broad healthcare sector was always a safe haven for investors when the market was turbulent. Biotech offered an interesting way to add a little more return to a one's portfolio while maintaining a defensive portfolio overall. From 2010 to 2018 the aggregate market cap of the sector grew from roughly $300 billion to in excess of $2 trillion by mid-2018. As a result of this strong growth, the sector is no longer insulated from macroeconomic events. We did witness a sell off more than likely triggered by generalist selling which caused more fundamental investors to seek to lock in their returns. As we entered 2019, valuations had pulled back so dramatically that the downside risk was mitigated.

The IPO market has been very resilient over the past 7 years and the expectation is that it will continue. The volume of IPOs will likely be down due to the government shutdown which caused a few months of delay. If the transaction market for existing public companies provides investors with an attractive after-market return that will bode well for the health of the IPO market. With respect to M&A activity, the pace of transactions is generally a function of public market sentiment – the stronger the valuations in the public markets typically will lead to a slowdown in M&A - and the inverse tends to be the case as well.

Do you expect the life sciences industry to remain resilient over the coming two years given the current political landscape?

The life sciences sector is currently very resilient, and I believe that it will prevail through a very high level of volatility. Given the maturity of the biotech space and the innovations that are being developed, we believe that investors will do their diligence and identify companies they think will continue to thrive even within a more volatile environment. ■

Drug Development and Delivery

"Ultimately, the gold standard for demonstrating clinical proof of concept is a clinical trial. There are many organizations that are developing more efficient ways to run clinical trials."

- Rajiv Mahadevan,
Managing Director,
Precision for Medicine

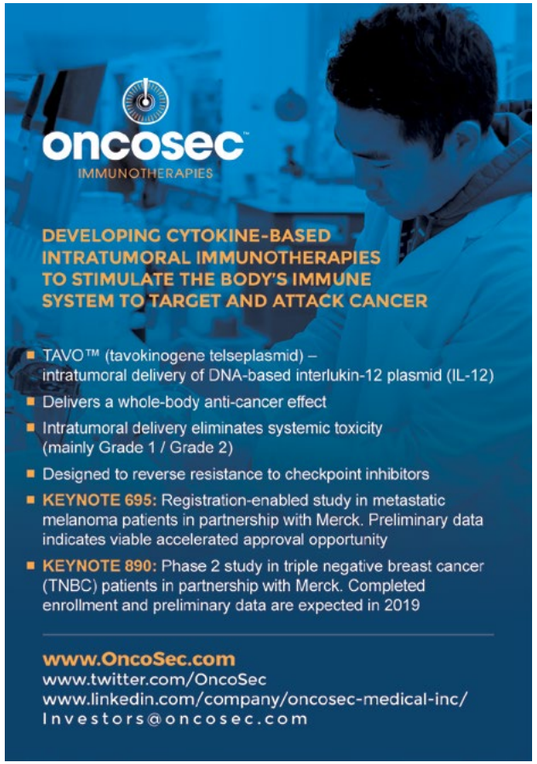
Image courtesy of Evonik Health Care

The Pipelines for Tomorrow

The current therapeutic focus of biotechs

The journey of a new drug will often begin in a research lab in one of the many academic institutions across the United States. Hundreds of biotechs spin out of universities every year, adding to the thousands of molecules currently in the development pipeline. Drug discovery has increasingly shifted away from large pharma towards biotechs, now accounting for over 70% of clinical trials.

Across the clusters, there are biotechs addressing a multitude of unmet needs across a variety of therapeutic areas. There are now nearly 7,000 medicines in development, 74% of which are potentially first-in-class, according to PhRMA.



Oncology continues to attract the most attention from researchers and investors alike. In 2018, an estimated US$50 billion was invested in oncology R&D, according to McKinsey & Company, and of the 1,332 total therapies in the pipeline from California companies, 433 – just under a third – were in the oncology space, according to the California Life Sciences Association. The oncology space has evolved tremendously over the past decade, and advancements continue to be made to find treatments and ultimately cures for a range of indications. There have been significant breakthroughs made in the immuno-oncology space. Merck's KEYTRUDA – a checkpoint inhibitor that blocks the PD-1 pathway and helps to prevent cancer cells from hiding – was the first breakthrough in immuno-oncology, but there are many instances of promising results as other therapies in this space move through the development pipeline and advancements continue to be made within the immuno-oncology space de-

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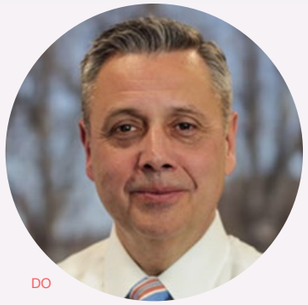
> We believe that novel small molecules can be active in the central nervous system (CNS). There are some big targets in CNS that have proteins associated with them, and we would like to address that unmet patient need. In almost 90% of diseases that are well known, there are dysfunctional proteins. As patients need all the components of the immune system to have an effective immune response, we believe we can adjust dysfunctional proteins back to where they need to be.
>
> - David Stirling, CEO, BioTheryX

Dan O'Connor & Sara Bonstein

DO: President, CEO & Director
SB: CFO & COO
ONCOSEC



DO

SB

OncoSec is a clinical-stage biotechnology company focused on developing plasmid IL-12 cytokine-based intratumoral immunotherapies with new technologies to stimulate the body's immune system to target and attack cancer

OncoSec has an extensive pipeline driven by a lead investigational product – TAVO. What were your key milestones in 2018?

DO: 2018 was an important year for OncoSec. Our Keynote 695 study – a TAVO + KEYTRUDA (pembrolizumab) registration-enabled study in R/R melanoma in partnership with Merck – has now enrolled one-third of the intended patients. We started enrolling in early 2018, opening sites in Australia, United States and Canada.

SB: 2018 was our first year of clean financing. In February 2018, we closed a US$23 million public offering of common stock led. Another important milestone was the extension of our collaboration with Merck. We entered into a second collaboration with Merck for triple-negative breast cancer (TNBC), which follows our first collaboration for melanoma.

Given Merck's status as a leader in immuno-oncology clinical research, what are the advantages of your partnership?

DO: The partnership with Merck was logical because of the potential to help patients who do not get a response to KEYTRUDA, most likely because their tumors are "cold." Since we believe that TAVO can turn an immunologically cold tumor hot, partnering with Merck is a perfect fit for us. KEYTRUDA only works with a minority of patients in most solid tumors, but when combined with TAVO, it opens an opportunity for the majority, again, under the premise that TAVO can convert a cold tumor into a hot tumor. As such, we believe that TAVO can be the key to unlocking KEYTRUDA.

What was the attraction around carrying out your Keynote-695 clinical trial in Australia?

DO: Firstly, there are high rates of melanoma in Australia and very few clinical trials taking place. Moreover, the government incentivizes companies to come to Australia. There are also a number of synergies between trials in the United States and Australia, including quality of data, the regulatory authority and demographics.

How is OncoSec able to differentiate itself in a crowded immuno-oncology space?

SB: A key factor is the safety and low levels of toxicity associated with TAVO; we generally have only grade 1/2 procedural pain or discomfort that readily resolves with any intervention. For a cancer treatment, this is very impressive. Moreover, TAVO is off the shelf, it is efficacious and works both as a monotherapy and in combination. There is a simplicity around the drug's administration as well as the cost associated with it. Pricing is an extremely important element – curing people is our goal, but we also need to think about what the overall cost is going to be.

What has OncoSec set out to achieve in 2019 and how do you expect the market to respond?

DO: There is interest in what we are doing and, if TAVO's tumor response data continues on its current trajectory, it is possible that we will see the interest continue to materialize and solidify into a transaction. TNBC is also very important for us. To date, several other companies have sought to find treatments for TNBC, but with very little success, which presents a significant opportunity, especially when you consider that TNBC tumors are seen as the coldest of the cold.

SB: Our underlying goal is to make people realize the true value of TAVO. For our melanoma target, we are opening sites in Europe this year and we will look to complete the enrollment of 100 patients with Keynote 695. Assuming the data holds as it is currently tracking, a response rate of ~20 %, we will look to file with the FDA in early 2020. For our cervical cancer indication - which is in partnership with the Gynecologic Oncology Group (GOG), the leading U.S. non-profit association of gynecological oncologists - we will look to start dosing patients in the first half of this year. We anticipate the enrollment will be 12 months, and we will then look to file for accelerated FDA approval in 2021. Our third indication is TNBC, which is an ongoing Phase II program of 25 patients. We plan to complete enrollment and provide preliminary data this year. The market today sees us as an under-the-radar. By mid-2019, we hope to surprise. ■

Brian Frenzel

CEO
TOSK

Tosk's TK-90, targeted at preventing mucositis, has been in human trials for a year. Could you provide an update on the latest developments?
We just completed a study of 25 head and neck cancer patients taking our Compan-ionTM drug TK-90 alongside methotrexate to determine safety and optimum dosage. We met the first objective – safety - and, giving patients four different doses of metho-trexate, found that the two highest doses were highly effective in preventing mucositis, a life-threatening side effect of many chemotherapies and radiation therapy. This far exceeds the 30% reduction needed for regulatory approval. Tosk is initiating a second phase of testing in 22 patients taking the optimal dose of TK-90. This study, which we anticipate will be completed in the first half of 2019, should fully establish TK-90 as an effective prophylaxis for mucositis. We call our drugs CompanionTM drugs because they are administered simultaneously with existing cancer therapies.

Is Tosk looking for partners to scale up and commercialize TK-90?
We have initiated a partner search to identify companies that would be a good fit with us on TK-90. We are also raising money through a mezzanine private offering that we anticipate will be our last round prior to an IPO. We will pursue these avenues with the goal of completing both by the end of next year. The company has plans to grow and scale-up our operations, but we do not anticipate taking a product to market ourselves, which would require greater infrastructure and global reach than we can real-istically put in place.

Apart from TK-90, what is the current status of Tosk's pipeline?
We have three other promising products in the pipeline. TK-39, Tosk's second patent-ed product, blocks the cardiotoxicity caused by a class of widely used cancer drugs known as anthracyclines. Their damage to heart tissue is permanent and limits the lifetime dose of these drugs. Anthracyclines are used to treat breast, bladder and lung cancers, as well as lymphomas and leukemias. We plan to put TK-39 into human trials next year. Our third drug discovery initiative, TK-88, is designed to block the damage that widely used platinum-based drugs, such as cisplatin and carboplatin, can cause. These adverse effects can be permanent and include kidney damage, peripheral neu-ropathy and hearing loss.

Tosk is partnering with Professor Jeff Thomas and the Texas Tech University Health Sciences Center on drugs to block the kRAS oncogene - a high priority for the National Cancer Institute (NCI). Could you elaborate on this effort?
Professor Thomas has been a member of our scientific advisory board for more than five years. Texas Tech's Health Sciences Center is the co-PI on our recent US$2 million Phase II SBIR kRAS grant. The U.S. National Institutes of Health's National Cancer Insti-tute has made this initiative a top priority because some 40% of all cancer patients are untreatable with an important class of cancer drugs - the EGFR inhibitors - due to the presence of a mutant kRAS gene. Using our approach, it may be possible to block the activity of this gene. This gene is also estimated to be present in 90% of pancreatic cancers, 45% of colon cancers, 35% of lung cancers and a smaller percentage in most other cancers as well.

What are the drivers behind Tosk's diverse pipeline?
Tosk's products are initially discovered using one of two different proprietary drug discovery technologies, both using the common fruit fly. These technology platforms use animals with a short life cycle to quickly and economically screen thousands of compounds to find hits. Hits are then optimized for safety and efficacy using more tra-ditional medicinal chemistry techniques to improve performance and are then formu-lated to become IND candidates. One of our two technologies – the 'side effect fly' – is a proprietary screening method to identify candidate compounds that selectively block drug side effects. Our second technology platform – the 'genetically modified fruit fly' – involves implanting a human cancer gene into the genome of a fruit fly to screen for drugs to block the activity of that cancer gene. We have selected the mutated kRAS gene, which is important in driving the propagation of many cancers, as our first target for this technology. ■

Tosk is developing a family of inexpensive, small molecule drugs designed to pre-vent the toxic side effects of common cancer treatments and has a program to dis-cover drugs that block cancer genes

Mark McCamish

President and CEO
FORTY SEVEN

Forty Seven, a clinical-stage immuno-oncology company, focuses on developing therapies to activate macrophages for the treatment of cancer

Forty Seven was founded in 2015 and had its IPO in July 2018. Could you outline the evolution of the company?
Although Forty Seven was founded in 2015, most of the research was carried out by Irving "Irv" Weissman and colleagues at Stanford University before. They determined that surviving cancer cells overexpress CD47 – a marker on normal cells – as a way of hiding their abnormality from the immune system. During his research, Irv was able to garner US$30 million of funding from the California Institute of Regenerative Medicine (CIRM). Over a ten-year period, they were able to evaluate which approach one should take to bind to CD47. Through animal models, they determined that the IgG4 type of monoclonal antibody (mAb) was the preferred approach. Subsequently, Forty Seven Inc was spun out from Stanford by raising an initial Series A of US$75 million. Since then, Forty Seven has started six trials, and we have raised a second Series B US$75 million, as well as additional funding from CIRM and Leukemia & Lymphoma Society. Our lead molecule is currently the F59 - IgG4 subclass mAb against CD47 - that is in Phase Ib/II clinical trials for a number of indications.

The immunotherapy market will be worth US$125 billion by 2024. What key advancement do you expect to see in the space over this time period?
Immuno-oncology is set to dramatically change, and we are hoping that chemotherapy will be archaic within ten years. The way this would happen is through a more personalized medicine approach to tumors. Questions to be answered will include whether we can coax our own immune system to attack the tumor. However, although we have seen innovation evolve rapidly in recent years, development can be slow. Another key consideration is how it will be funded and how the healthcare industry can cope.

How do you perceive the current immuno-oncology investment climate?
Immuno-oncology was very well perceived two years ago. At the time we went public, there was a major failure within the space, which raised a lot of questions. Right now, gene therapy is the darling of the investment community with high valuations and a lot of capital being raised. Immuno-oncology is on the downside in terms of perception and enthusiasm due to some recent failures.

Will there be space in the market for lots of different approaches to cancer or do you believe immuno-oncology will be the way forward?
There is always room for options when one is thinking about a patient, as long as patients can benefit. Immuno-oncology offers a lot in terms of harnessing the immune system but there is much remaining to understand. Moving forward, I believe there will be an emphasis on patient selection for specific treatments, perhaps using companion diagnostics and/or gene expression patterns.

What are your key objectives over the coming two to three years?
We have three compounds in our pipeline with the 5F9 being the most advanced. We have had initial discussions with FDA regarding what regulatory approach we should take with respect to our pipeline, and we have received fast track designation for two indications. For us, we must show that there is real benefit to patients through use of our product candidates, and that will continue to be our main priority. We are also excited to extend our expertise into using a combination of our anti-CD47 mAb along with an anti-cKit mAb for a non-radiation or chemotherapy approach to various bone marrow transplants. ■

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spite a number of failures over the past two years impacting the ease of biotechs' access to private and public funding.
Oncosec, who focused on developing plasmid IL-12 cytokine-based intratumoral immunotherapies with new technologies to stimulate the body's immune system to target and attack cancer, has partnered with Merck as the biotech's Keynote 695 study is a combination with its TAVO and Merck's KEYTRUDA. There is the potential within Oncosec's ongoing studies that patients who do not get a response from only KEYTRUDA will with the TAVO combination.
Moreover, Forty Seven, which went public in 2018, currently has six ongoing immuno-oncology clinical trials. The biotech's molecules are focused on blocking CD47 – a marker on normal cells – as surviving cancer cells overexpress it as a way of hiding their abnormality from the immune system. "Immuno-oncology is set to dramatically change and we are hoping that chemotherapy will be archaic within ten years," highlighted Mark McCamish, president and CEO at Forty Seven. "The way this would happen is through a more personalized medicine approach to tumors. Questions to be answered will include whether we can coax our own immune system to attack the tumor. However, although we have seen innovation evolve rapidly in recent years, development can be slow. Another key consideration is how will it be funded and how can the healthcare industry cope."
Whilst immuno-oncology is a hot area of research, there are many other areas in which novel research is being pursued in the oncology space. For example, eFFECTOR Therapeutics – based in San Diego – has focused its attention on pioneering the discovery and development of a new class of oncology drugs – selective translation regulators (STRs). "Most efforts to control gene expression have focused on the process of transcribing DNA into the mRNA that directs the synthesis of proteins," said Steve Worland, president and CEO at eFFECTOR Therapeutics. "eFFECTOR, on the other hand, is focusing on the translation of mRNA to protein. The importance of translation regulation in disease is becoming increasingly recognized in the pharmaceutical industry, and we believe we are at the forefront of discovering novel approaches to cancer therapy focused on STRs."
Novel approaches to drug discovery continue to take form across a number of

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Mike Grey

Chairman and CEO
MIRUM PHARMACEUTICALS

Mirum Pharmaceuticals is a clinical-stage therapeutics company developing drugs for treating cholestatic liver diseases.

What were the key reasons for choosing progressive familial intrahepatic cholestasis (PFIC) and Alagille syndrome (ALGS) as the two key indications for maralixibat?
We were particularly interested in pursuing these indications as they are progressive liver diseases. PFIC is very aggressive and patients may ultimately require a transplant. What patients show in common is incredibly intense pruritus. It is difficult to understand how disruptive and troubling it is for a patient, especially infants and their family. Typically what we try to do is reduce the level of bile acid by blocking the recycling and helping to alleviate this intense pruritus.

Regarding the mechanism of action, will maralixibat be a cure or a treatment?
With PFIC, the problem is a mutation in the transporter located in the liver. By blocking the recycling of bile acids through the drug, pressure is relieved on the liver. We now understand genetically which patient populations will respond to this - typically infants that are on the liver transplant list. They are able to be removed from the transplant list, but will need to keep taking the drug to maintain the benefit. With PFIC, it is difficult to claim that the drug is a cure because they need to keep taking it, but we do get a complete response with many of the subjects. Alagille syndrome is a more complex disease, and it is mainly focused on treating the pruritus, which is the most troubling symptom of the disease. There are no approved therapies for PFIC or Alagille syndrome.

How were you able to put together a series A round of funding of US$120 million in such a short space of time?
Mirum was a marriage between the previous leadership of Lumena and Tobira - a powerful group of minds. For the investors coming on board, the value proposition regarded the potential of getting to phase III clinical data in a relatively short period of time that would support filing was very attractive. ■

Wendye Robbins

President and CEO
BLADE THERAPEUTICS

Blade Therapeutics is advancing a risk-diversified product portfolio to address various fibrotic diseases and their underlying pathophysiology

Could you introduce us to Blade Therapeutics?
Blade Therapeutics' founding program was envisioned by our scientific founder, Hal Dietz, who is a world expert in collagen-vascular diseases. Dr. Dietz conducted some very elegant, yet simple, experiments to prove that one of the isoforms of calpain was an important regulatory enzyme in promoting fibrosis. When he tested his theory on an animal that did not have this enzyme, he was able to demonstrate that the animal was resistant to fibrosis from chemical stress.
The funding investors - MPM Capital - then decided to take the technology from Johns Hopkins University and establish Blade Therapeutics in 2015. At the same time, there was the coincidental consummation of the acquisition of InterMune and Roche, which led to a group of talented, pre-clinical chemists becoming available. The idea was to take this talented team of chemists and biologists and marry them with Dr. Dietz's technology to build a company around a very exciting new platform in fibrosis.

Could you elaborate on Blade Therapeutics' lead therapy candidate - BLD-2660?
BLD-2660 is a very novel covalent but reversable slow type binder of dimeric calpains. The candidate has been in phase 1 since July 2018 and is proving to be well tolerated. With respect to our experimental biomarker work, BLD-2660 appears to hit its target. Blade Therapeutics is preparing to start phase 1b imminently and will be completed by Q1 2019. We are also planning to file an IND in Q2 2019 with the intent to enter at least two disease populations by Q3 2019.
The hope is that this technology can be deployed in both patients with mild and severe diseases. Our initial indications could include non-alcoholic steatohepatitis (NASH) idiopathic pulmonary fibrosis (IPF), primary sclerosing cholangitis (PSC), systemic sclerosis (SSC), diabetic nephropathy (DN) and corneal fibrosis. At this stage, Blade Therapeutics is compiling a development plan and investigating all the indications to decide which will be the first for us to deploy our asset into. ■

> Like any industry, there is a mix of the old and new technologies being utilized in drug discovery and development. Within the biopharma ecosystem, there now appears to be more receptivity to newer ways of doing things. We are seeing several biopharma companies partnering with data or AI driven drug discovery companies and also embracing innovative approaches to expedite recruitment of patients for clinical trials. In the drug discovery realm, adoption of new technologies will be enhanced once there are some successes that demonstrate how these technologies can help with their pipelines.
>
> **- Gini Deshpande, Founder and CEO, NuMedii**

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therapeutic areas, something that is a necessity within neurodegenerative diseases. The space has seen a number of failures recently, including Merck's Alzheimer's drug Verubecestat and J&J's Atabecestat, as well as from Biogen, Eli Lilly, Otsuka and Boehringer Ingelheim. Last year, Pfizer halted all its Alzheimer's research and, despite the gargantuan unmet medical need, there are only five drugs approved by the FDA for the treatment of Alzheimer's. According to Clarivate Analytics, the burden of disease due to dementia is outpacing that of most other disorders. Despite large pharma and big biotechs having had setbacks in the space, this has opened up the opportunity for others. "There are many biotechs in the neurodegenerative space that are looking at aging, which is good news for the industry as there is a rise of age-related diseases across the globe," underlined Elizabeth Jeffords, chief commercial and strategy officer at Alkahest.
Not only is there an abundance of biotechs researching within the neurodegenerative space, investors and large pharma are taking interest in this, and despite Pfizer's exit, Pfizer ventures has recently invested in three neuroscience biotechs.
Biotechs focused on infectious diseases may often struggle to gain funding or achieve a significant valuation, especially compared to their oncology counterparts. This is despite the impressive work being done to address a number of significant unmet needs. For example, Amplyx Pharmaceuticals is developing first-in-class products for the treatment of life threatening infections, with a near-term focus on deadly fungal pathogens. "Existing therapies for invasive fungal infections are extremely limited, can be difficult to administer, often have toxic side effects and are ineffective against fungi that have developed resistance," highlighted Ciara Kennedy, president and CEO at Amplyx Pharmaceuticals. "We have made it our focus to advance a novel class of therapies within the fungal space, creating products which can have transformational value for patients."
Carb-X is trying to address the lack of funding within the antibacterial space. A global partnership hosted at Boston University, it has up to US$500 million to fund higher risk and potentially high-reward biotechs developing new antibiotics. Given the global rising threat of drug-resistant bacteria, accelerated antibacterial research is a necessity that the partnership is prioritizing. For the Bill & Melinda Gate Foundation (BMGF), the eradication or management of infectious diseases is one of the key focus areas. Through its US$2 billion Strategic Investment Fund (SIF), BMGF is taking the lead in addressing the under-funding associated with infectious diseases in developing countries. Given the amount of funding and research within the immuno-oncology space, as well as the fact that a key cause of death of cancer patients is a related disease (notably infection), BMGF is funding cross-collaboration research. "Since the immune system is also critical in infectious diseases, a significant amount of the learnings and tools from other therapeutic areas can be applied to the foundation's priority diseases," remarked Vidya Vasu-Devan, deputy director at BMGF SIF. "As a result, the SIF team invests in these companies to leverage the products and technologies for diseases like HIV and TB. Additionally, we always look to support companies dedicated to eliminating infectious diseases."
Meeting unmet patient needs is an imperative cornerstone to all biotechs and their research. Whilst immuno-oncology has seen a lot of attention in recent years, there has been increasing investor interest in cell and gene therapy given the rapid developments being made. This was led by Spark Therapeutics' Luxturna in 2017, the first gene therapy approval for genetic disease, and subsequently with two chimeric antigen receptor T-cell (CAR-T) therapies – Novartis' Kymriah and Gilead's Yescarta – being approved last year. There are now 300 cell and gene therapies in development with over 100 of these in clinical trials for oncology, according to PhRMA. With five approvals for 2018, 2019 is set to be an impressive year for the cell and gene therapy space. ■

Bassil Dahiyat

President and CEO
XENCOR

Powered by its XmAb antibody engineering platform, Xencor is developing a broad pipeline of drug candidates to treat autoimmune disorders, cancer, asthma and allergic diseases

Much of Xencor's pipeline is in collaboration with large pharma. What are the company's key considerations when identifying new partnerships?
Before we had our IPO in 2013 and had access to capital markets, the key consideration for partnerships was funding. Subsequent to going public, we had access to capital from the public markets, which is vastly larger and more flexible than private capital. This allowed us to make much larger investments to develop our own pipeline. Today, partnerships are driven by two key factors. The first driver would be when an asset does not fit into our core focus anymore, but the science has led us to the asset and we want to extract value from it. The second would be a program that we think can be better leveraged with external assistance. Moving forward, when looking at commercialization, we will be initially looking for partnerships but will also factor in opportunities where we can take that journey by ourselves.

Xencor has two lead molecules: obexelimab/XmAb5871, currently entering phase III for autoimmune disease, and XmAb14045, currently in an ongoing phase I study in oncology. When do you expect these molecules to be ready for commercialization?
The stage of the asset is not necessarily the most linear way to look at when the product will be launched. It depends on the therapeutic focus as well. For autoimmune diseases, the timeline is often significantly slower as safety hurdles are higher and the ability to measure the disease is harder and slower. Being optimistic, we believe that the timeline for our lead candidate could potentially be between four to five years.

Could you provide a final message to our international readership with respect to Los Angeles' biotech hub?
Los Angeles has an enormous amount of unappreciated and hidden technology value as well as human talent, both on the research and the development side. There is great opportunity for investment in the area as there is currently little competition in what is a very dynamic space. ■

Steve Worland

President and CEO
EFFECTOR THERAPEUTICS

eFFECTOR Therapeutics is a clinical-stage biopharmaceutical company focused on pioneering the discovery and development of a new class of oncology drugs known as selective translation regulators (STRs)

Could you elaborate on the recent partnership eFFECTOR has formed with Merck?
The company has entered into a clinical collaboration agreement with Merck to evaluate the combination of our Tomivosertib molecule with Merck's immunotherapy, KEYTRUDA, for the treatment of patients with metastatic triple negative breast cancer (TNBC). We believe that targeting the MNK1/2 molecule, will have significant potential to enhance the clinical activity of Merck's KEYTRUDA.
The basis of the collaboration is the strong potential that the selective translation regulator tomivosertib, in combination with checkpoint inhibitors like KEYTRUDA, could overcome some of the cellular processes that drive resistance to checkpoint inhibitors or contribute to their lack of efficacy in certain patients.

Having previously worked in all major biotech hubs in the United States, how does San Diego's biotech ecosystem compare with respect to financing and research?
San Diego continues to have a robust biotech ecosystem, both on the financing and research and development side. While we have comparatively fewer investors here than Boston or the Bay Area, San Diego has a very strong reputation for its research and early product development prowess, so we can attract VCs that are located in other geographies, thereby importing capital to the region.
From an R&D perspective, the Bay Area and Boston are extremely competitive. The advantage is that companies operating in these regions are constantly in an environment where unplanned encounters and networking can take place, as there is no lack of expertise in the regions. Here in San Diego, those organic networking opportunities are somewhat less likely. The challenge in San Francisco and Boston is that the competition for talent is ferocious. San Diego has an incredible talent pool, and many people who come here to work in our academic institutions or our biotech companies are reluctant to relocate to San Francisco or Boston. ■

Kevin Outterson

Executive Director
CARB-X

CARB-X is a global partnership hosted at Boston University, dedicated to accelerating antibacterial research to tackle the rising threat of drug-resistant bacteria

Can you elaborate on CARB-X's most recent developments?
At the beginning of 2019, CARB-X had 34 companies that had completed contracts with us, and we hope this will exceed 50 by the end of the year. Into 2020, we expect that at least 20 of those projects will represent a new class against gram-negative bacteria. Some of these are the same class; for example, we have several attempts at the LpxC target. If any one of the 20 projects are approved, it would be the most innovative thing to come out of the anti-bacterial space in more than half a century. Our goal is to see a number of these innovative products make it to FDA approval and directly improve human health.

With the world's largest pre-clinical and early development pipeline of antibiotics, why is CARB-X integral to an early-stage biotech?
Money is scarce in the anti-infective and antibiotics space, and valuations are significantly higher in other therapeutic areas, such as oncology. If an investor has a choice between a less innovative product with a higher chance of success versus a more innovative product with a higher risk of failure, we find that companies often choose the former. CARB-X has up to US$500 million to invest, and we are trying to fund products that have a higher risk and potentially a high reward by investing in developing new antibiotics, and we hope that our contribution will significantly impact the field.

We are seeing a trend towards earlier-stage investment into biotechs. Is this also reflected in the infectious disease space?
For different parts of the infectious disease space, such as Hepatitis B or Hepatitis C, this would hold true. Because of the difficulties within the business model in antibiotics in terms of how they are sold in the United States and abroad, as well as stewardship controls, we do not see sufficient private funding. ■

David Stirling

CEO
BIOTHERYX

BioTheryX seeks to deliver therapies for patients with hematological malignancies, myelogenous leukemia, cancer and immune dysfunction

Incorporated in 2007, could you provide a brief overview of BioTheryX?
BioTheryX is occupied with building a set of high value assets in protein modulation known as Protein Homeostatic Modulators (PHMs). These novel small molecule cereblon binders have clinically relevant substrate degradation profiles that offer vast therapeutic opportunities. Our long-term goal is to identify more targets so that we can change the molecule to fit the task at hand. We aim to identify effective core molecules that can be rapidly exploited using focused and prioritized chemistry approaches coupled with clinically proven translational approaches targeted for cancer and immune dysfunction. The company is developing novel therapeutic modalities to a broad array of diseases, including malignancies, neurodegenerative disorders and leukemia.

Could you outline the advantages of BioTheryX's PHM molecule?
Protein homeostasis is arguably the hottest topic in the biotech space right now. The industry's attention is being focused on the PROTAC (proteolysis-targeting chimeric molecules) approach, which is a completely unproven approach to date. The only proven approach to protein homeostasis to date, commercially and scientifically, is the IMiDs family of compounds my team and I created while at Celgene. Our strategy is thus to push our PHMs forward in their own right, due to what we view as the vast potential in that validated approach. The only two companies in the industry that have large libraries of novel small molecule cereblon binders are Celgene and BioTheryX.
In almost 90% of diseases that are well known, there are dysfunctional proteins. As patients need all the components of the immune system to have an effective immune response, we believe we can adjust dysfunctional proteins back to where they need to be. We have molecules on the shelf that we feel would work in this space, and we have to identify these molecules and move them forward in the near future. ■

Jim Dentzer

CEO
CURIS

Curis is a biotech focused on the development and commercialization of innovative therapeutics for the treatment of cancer

Following your collaborative relationship with Aurigene – which was dubbed "Curis 2.0" – what have been recent developments at Curis?
In the past four years, we have used our scientific discovery engine and leveraged the capabilities of partners like Aurigene to build a pipeline of three innovative, first-in-class drugs, all of which are potential blockbusters. This means all three drugs have the possibility of achieving revenues greater than US$1 billion.
The next step in our evolution is the shift toward clinical development of that pipeline. This year, we expect to report milestone efficacy data in all three programs.

How is Curis financing its journey to commercialization?
Curis is in the very fortunate position of having multiple financing options to choose from; we can issue equity, license geographic rights to one of our three clinical programs or we can monetize the royalties we receive from Erivedge® sales (our first FDA approved drug, which is currently marketed by Genentech and Roche).

What can we expect from Curis into 2020?
The next two years will focus on the data catalysts that we will be reporting for our three clinical programs. All three are novel, first-in-class, oral therapeutics that could potentially change the lives of patients in ways that were never possible before.
For example, Fimepinostat is our anti-MYC drug. MYC is a transcription factor gene. Essentially, it is an instruction set that helps cells multiply very quickly. It is a critical gene that is turned on during the human embryo stage, but largely turned off after birth. One exception to that is in cancer cells, which need the MYC gene turned back on to support rapid tumor growth. MYC has been studied for over 40 years by many companies and academic labs. In that time, none of those efforts has been successful in targeting and blocking it. Curis became the first to accomplish this, and in 2020, we will be reviewing clinical data for all three of our programs, including Fimepinostat. ■

Ciara Kennedy

President and CEO
AMPLYX PHARMACEUTICALS

Amplyx Pharmaceuticals is developing treatments for life-threatening infections, with a focus on deadly fungal pathogens

Could you provide a brief overview of Amplyx?
Amplyx has been in existence for approximately 10 years. For the first seven years, we were a research-focused, NIH grant-funded company, formed on a medicinal chemistry platform licensed from Stanford that focused on re-engineering effective drugs to reduce their toxicities. This work led Amplyx to the fungal space, as many drugs that are effective at killing pathogenic fungi also damage human cells, and we are now developing leading molecules for the treatment of life-threatening infections in vulnerable, immune-compromised patients.

Could you elaborate on the current investment climate for infectious diseases?
In 2015, the infectious disease space was making a comeback and there were a significant number of companies with healthy market cap valuations. The investment climate looks quite differently now, and there are companies that have followed all the right steps for their programs but have comparatively low market caps. Antibacterial companies are particularly suffering. Conversely, anti-viral companies are doing fine.
It must be said that the commercial landscape for antifungal products is very different to that of antibacterial products; we don't see the failed/slow uptake launches and crowed product landscape. These factors coupled with the high mortality associated with fungal infections have enabled Amplyx to raise sufficient capital to continue to develop APX001.

What is Amplyx's strategy moving forward?
We have completed our phase I study and understand the safety, tolerability and pharmacokinetics of APX001 administered by intravenous infusion. In our phase 2 study, we will investigate the ability of the product to cure patients. Following that, the next step is registration studies for Candida and rare molds. Once we have validated our targets, we will initiate our registration studies. We will then have our data package to support registration and approval of our IV and oral APX001. ■

Elizabeth Jeffords

Chief Commercial & Strategy Officer
ALKAHEST

Alkahest has a unique technology platform for elucidating changes in the plasma

Could you introduce us to your unique technology platform?
Alkahest's breakthrough research has interrogated the plasma proteome to understand which plasma proteins are most impactful to the aging process. To do this, we investigated plasma samples from a range of ages to understand if the protein signatures were in fact different. About 10% to 20% of proteins on either end of the spectrum either increase or decrease with age, with the majority of proteins preserving their function over time. The proteins which change with age, which we call chronokines, can be either beneficial or detrimental. We then target these chronokines for potential therapeutic effect.

Alkahest's partnership with Grifols has focused on the development of your proprietary plasma products (GRF 6019-6021). What have been the advantages of forming this partnership?
The partnership with Grifols involved a US$37.5 million equity investment, an upfront fee of US$12.5 million and additional funding for research and development of plasma-based products. Aside from financing, Grifols provides significant expertise to our team, having carried out substantial work distributing and ensuring safety of plasma-based products.

How does your technology differentiate you from what is currently being researched and developed in the market?
We feel we are unique in researching the plasma proteome. Our first approach is to supplement beneficial proteins that tend to decrease as we get older by utilizing our propriety plasma factions. Our second approach is to utilize protein-specific interventions that inhibit the detrimental proteins that tend to increase as we age.

What will be Alkahest's key objectives in 2019?
We will be focusing on a full clinical ramp up of our phase II trials in 2019. We have strong pre-clinical evidence, and we now need to test how the animal models translate to efficacy in humans. We are also looking at our therapeutic candidates' mechanisms of action to better understand the clinical impact of our science. ■

Raul Rodriguez

President and CEO
RIGEL

Rigel Pharmaceuticals is dedicated to discovering, developing and commercializing novel small molecule drugs for immune and hematologic disorders, cancer and rare diseases

What is Rigel's criteria with regards to partnerships?
The United States is the largest pharmaceuticals market in terms of value, followed by Europe, Japan and the rest of Asia. Rigel is working to establish partnerships outside North America to commercialize our product and, if necessary, carry out product development. The partnership agreements are based on geography, as the partner will only have rights in their respective territories. For example, Kissei Pharmaceuticals has rights in Japan, China, Taiwan and South Korea for fostamatinib, following a collaboration and license agreement entered into in November 2018. Kissei has the rights to commercialize the product and Rigel receives an upfront payment, milestones and royalties in exchange.
In Europe, we are looking for a similar agreement: a single partner that will commercialize across all the large countries in Europe, and that has a background in the specialty care area.

Given the different paths Rigel can take with immunology, what is directing the company's research?
Rigel aims to discover key immune system processes, which we know are central to some diseases. IRAK, for example, is central to many immune-signaling processes. If we are able to block IRAK, we are able to block a large segment of downstream inflammatory cytokines that are activated. As a result, there are approximately 20 diseases where IRAK is potentially involved and we are excited to explore the broad potential of R835 in autoimmune and inflammatory diseases, such as psoriasis, lupus and others. The decision on which diseases to focus on will depend on the medical need, the market opportunity, and the feasibility of the clinical trial.

What is Rigel's strategy moving forward?
Now that we have become a fully-integrated biotech company, with an FDA-approved product, we have a solid commercial foundation in place that we can leverage upon approval of follow-on indications for TAVALISSE or new therapeutics in development. ■

Michael Arenberg

CFO
DURECT

DURECT is a biopharmaceutical company developing new therapeutics based on its Epigenetic Regulator Program and proprietary drug delivery platforms

Apart from alcoholic hepatitis, what other applications is DUR-928 being trialed for?
DUR-928 offers an entire pipeline within one molecule, and we are also focusing on primary sclerosing cholangitis (PSC), which is an orphan chronic liver disease. With PSC, the bile ducts in the liver become constricted; over time this can progress to the point where a liver transplant becomes necessary. As there are currently no treatments available for PSC, the company has prioritized a phase IIa study.
In the first quarter of 2019, Durect will also start a clinical trial in psoriasis, which is an inflammatory skin disease. With this trial, we are again focusing on the anti-inflammatory and cell survival aspects of the drug. This will be a proof-of-concept study, including 20 patients who will act as their own controls.

What is Durect's strategy for commercializing DUR-928?
Durect's strategy is to develop certain indications to a point where they are viable for commercialization. The nonalcoholic steatohepatitis (NASH) indication would require a significant sales force, which we are not interested in developing at this stage. The company would, however, consider developing a smaller sales force for orphan indications such as PSC and for AH, which is not orphan, but as a hospital acute care product, could be commercialized with a relatively small and focused sales force. For those opportunities, we may decide to build a commercialization infrastructure within the United States.

Are you seeing an increasing amount of research in the epigenetic space?
There is increasing recognition that many diseases have an epigenetic component, and a significant amount of research is going into understanding how diseases can be influenced at such a high level within the cell. One of the benefits of DUR-928 is that it is endogenous, meaning that it is a naturally occurring molecule, carrying out what it was designed to do. ■

Kevin Elliot

CEO
AGILINX THERAPEUTICS
Partner
PROCELA CONSULTING

Agilinx Therapeutics, founded in 2018, plans to acquire the rights to key early stage molecules before rapidly taking them to proof of concept in humans

Could you update us on the recent developments at Procela Consulting and also introduce us to Agilinx Therapeutics?
Procela Consulting has gone from strength to strength in 2018. Last year, we were predominantly working with U.S.-based biotechs to help them access European markets and capital and to navigate the regulatory environment. This year, we have noticed an increasing number of European biotechs coming to the United States to access funding, and we are consulting on this process. However, our most interesting development has been the creation of our own biotech – Agilinx Therapeutics. Agilinx aims to develop mainly infectious disease therapies, and with a world-class team of biotech executives, we are acquiring the rights to key early stage assets from small biotechs, big pharma and academia. We will then develop these programs rapidly and efficiently to proof of concept in humans and then aim to sell to big biopharma at the optimal point of risk reward.

How are you achieving this in what is a cost-heavy process?
There is a very high failure rate in clinical trials but with smarter medicine and new ways of genomic mapping we can be much more deliberate about which compound we are bringing to clinical trial and how we select our patient group.

What will be the key therapeutic focus for the team?
The team's background is quite heavily focused in infectious diseases and the immuno-oncology space.

What will be your key objectives moving forward?
We are currently putting together a portfolio of development programs, which should include a number of molecules in infectious diseases and possibly one in immuno-oncology. The aim would be to have these molecules on board in early 2019 and to secure significant funding in the first half of 2019 to begin human trials by the end of the year. ■

Alan Rubino

CEO
EMISPHERE TECHNOLOGIES

Emisphere Technologies is a drug delivery company

Emisphere's market cap sextupled in 2018. What was the key reason behind this?
Within our 33 years of existence, Emipshere has become a leading company in converting injectable therapeutics into advanced oral formulations. We do not speculate or predict investor motivations behind market behaviours, but the most recent market reaction coincided with a series of data releases of the 10-pioneer phase III clinical trials initiated by Novo Nordisk (Novo). Novo extensively planned and communicated to the investment community when the studies would be done and they were able to execute perfectly. Emisphere's technology partnered with Novo's molecule has the potential to offer significant new solutions to millions of people with diabetes worldwide. Novo's results serves to further validate our Eligen technology.

Given the success of your Eligen proprietary drug delivery technology, what has Emisphere's strategy been?
Licensing our proprietary drug delivery technology through mutually beneficial collaborations is our core business strategy, but we mainly focus our attention on well-established companies. Our partners leverage our broad experience in researching, developing and manufacturing various carriers that utilize our unique intracellular delivery mechanism of action in order to advance their oral portfolio products. Our technology can enhance the clinical profile of both pre-market and currently marketed products, but the therapeutics that we typically target are at an advanced stage of development, de-risked, or have already received regulatory approval and are currently available on the market. The main objective when partnering is for companies to utilize our broad-based proprietary oral drug delivery platform to significantly increase the bioavailability of their product as well as to facilitate the enhanced absorption of small and large molecules without compromising their chemical form, biological integrity or pharmacological properties.

Could you provide further insights into Emisphere's Eligen technology and its key differentiator?
Our technology may increase the benefit of a therapy by improving bioavailability, absorption or by decreasing time of onset. Therapeutic molecules can be delivered orally without altering the molecule's chemical form or biological activity. Eligen is particularly focused on the oral delivery of peptides, proteins, oligonucleotides, oligosaccharides and various small molecules. The key differentiation and advantage of our Eligen carriers is the weak interaction between the active ingredient and our carrier, which significantly decreases the time to onset of action, which is almost immediate. Our technology also uses intracellular transport versus going between the tight junctions of the cells. The carrier is a chaperone that quickly takes the API through the epithelium into the stomach and then into the bloodstream, allowing for rapid absorption.

What have been the results of the market launch of Eligen B12™?
The Eligen B12 was launched on the market in 2015 as a prescription medical food indicated for the dietary management of patients who have a diagnosed vitamin B12 deficiency, associated with a disease or condition that cannot be managed by a modification of the normal diet alone. Eligen B12 uses innovative technology to enable B12 absorption directly into the bloodstream independent of intrinsic factors. Based on new CMS guideline changes, we took advantage of those changes and moved Eligen B12 to a non-Rx medical food to make it easily available to patients through amazon.com or eligenb12.com. Currently we are enjoying positive growth trends on the product aided by a small, targeted promotional effort. We have expressly pursued this effort to prove concept which has been successful in securing multiple new business development discussions with much larger commercial partners who can more fully exploit the Eligen B12 oral product.

What are Emisphere's key objectives for 2019?
Emisphere has the goal to continue expanding on our partnerships, whether it is with additional molecules with Novo Nordisk or with a number of other non-disclosed partners who are either in the feasibility or optimization stage. Hopefully a few of these promising leads will translate into full development projects which may provide Emisphere with upfront payments, development and sales milestones, plus royalties which is the core of our business model. ■

Jim Huang

Founder and CEO
ASCENDIA PHARMACEUTICALS

Can you elaborate on Ascendia's partnerships with pharma companies?

Ascendia seeks to partner with emerging pharmaceutical companies in need of our trial formulation development services, generic companies looking for innovative technology and specialty pharmaceutical companies with ideas for new product development programs. Through partnerships we can also diversify and expand our pipeline. Our goals are consistent with our partners' goals, and we aim to provide quality service, exceptional insight, timely output and fair pricing to the companies we work with. We are always looking for opportunities where we can collaborate, specifically for our proprietary development 505(b)(2) NDA programs and for co-development of challenging ANDA products.

Can you elaborate on some of Ascendia's capabilities via its technology platforms?

We develop oral, topical and injectable products, and the selection of a final dosage form is driven by the product's commercial needs, as well as the properties of the drug substance. For oral dosages, we have the capability to granulate, blend, roller compact and compress to make products with both immediate release and modified release applications. We can also develop oral drugs for controlled release products. We can provide taste-masked pediatric formulations, including suspensions and orally disintegrating tablets. Our parenteral formulations can be administered as permanent suspensions for injection, or we have the capability to lyophilize if physical stability is an issue and thus provide powders for reconstitution. Topical formulations include solutions, creams, or ointments for application to the skin or mucous membranes. ■

Dan Gold

President & CEO
MEI PHARMA

As MEI Pharma is a late-stage biopharmaceuticals company, will you also be commercializing your molecules?

ME-401 presents the first opportunity for the company to market its own drug in the U.S., either independently or in cooperation with a partner. To that end, we have initiated efforts to develop a commercialization capability so we can be ready to market ME-401, subject to successful completion of clinical studies and obtaining market approval from regulatory agencies. Outside the United States we will look for out-licensing partnerships.

Can you elaborate on the reasoning behind MEI Pharma's US$75 million private placement deal led by Vivo Capital and CAM Capital.

In 2018, we announced significant progress across our drug development pipeline, particularly with our ME-401 program in B-cell malignancies, which supported continued clinical development. As we were about to undertake the next stages of testing on our ME-401 drug candidate, we needed the capital to be able to advance the final studies and for other corporate purposes. The US$75 million private placement deal was very important to advance those programs, and we were pleased to have attracted strong support from solid investors.

What are MEI Pharma's key objectives for 2019?

One of MEI Pharma's key objectives is to get our Phase 2 clinical trial for our ME-401 study underway and completed on schedule – we have estimated that the study will take about two years to complete. We also aim to continue to invest in the company's other programs so as to bring them closer to market. ■

Jim Neal

CEO
XOMA

Could you outline XOMA's new business strategy?

XOMA is a royalty monetizer and aggregator focused on acquiring rights to potential royalties and milestones associated with partner-funded early clinical-stage pharmaceutical assets. We are able to focus exclusively on this strategy because we organically built a portfolio of 38 potential royalty-bearing licenses on drug candidates that are being developed by other companies. All the capital investment, scientific research and development of drug candidates are being done by our partners, and we expect to enjoy the benefits associated with the advancement of the programs into later-stage development and ultimately commercialization.

Could you elaborate on XOMA's most recent acquisition payment to Agenus for seven oncology antibodies being developed by Merck and Incyte?

We are building out our asset portfolio, and immuno-oncology [IO] is currently a very interesting area that generally tends to have shorter development timelines. We believe these seven IO assets have great potential. They are in mid-clinical stage development in the hands of Merck and Incyte, two extremely high-quality partners.

What is XOMA's thought process when choosing a molecule to invest in?

It starts by applying our screening methodology: mid- to early stage clinical assets in the hands of outstanding development and commercialization partners, important therapeutic categories, long period of commercial exclusivity and sizeable royalty commitments. ■

The New Age of Drug Development

Precision medicine and diagnostics

Drug discovery and development timelines are quickly evolving as more efficient methods for biomarker discovery are being used in clinical trials. Due to precision medicine approaches – where a more holistic view of each individual patient is taken – and diagnostics tools that identify sick patients more effectively, the industry is moving away from placebo-controlled trials to trials informed by real-world evidence and technology that can accurately and rapidly collect phenotypic data.

"It has been an evolution helped by the rapid emergence of new technologies at increasingly lower costs," remarked Rajiv Mahadevan, managing director at Precision for Medicine, when discussing how diagnostics are being incorporated into clinical trials. "The ability to identify well characterized – even rare – populations to demonstrate clinical proof of concept is paving the way for early approvals followed by expansion of indications. This approach is essentially replacing the "traditional" phase I/II/III. Contrast this with as recently as 10 years ago, where only a small handful of companies were proactively pursuing a personalized approach, or forced into it by regulators or payers. Then, the holy grail was the US$1 billion plus blockbuster, despite high failure rates. The incorporation of diagnostic tools for applications like patient stratification or efficacy monitoring has played a major role in this change in mindset."

Within the diagnostics space, Almac Diagnostics has been identifying varying types of DNA and RNA panels for solid tumors and for liquid biopsy. "We have also taken another step forward in transcriptome analysis and Whole Exome Sequencing (WES)," underlined Paul Harkin, president at Almac Diagnostic Services. "We have now brought on our RNA-sequencing services utilizing our Almac optimized Illumina TruSeq RNA Exome panel and chemistry."

Of course, with approximately 800 cancer drugs in development and 12,000 active cancer clinical trials, as well as high failure rates, diagnostics for the oncology space are gaining widespread traction. For example, Bluestar Genomics is reinventing molecular diagnostic testing using next generation and non-invasive epigenomic technologies.

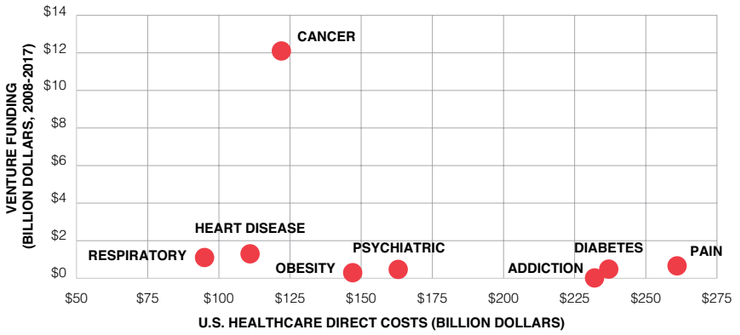
"Bluestar Genomics will expand the clinical indications of liquid biopsy vastly," said Patrick Arensdorf, CEO at Bluestar Genomics. "Moving beyond a tumor centric point of view, the expansion will be to a point where we can non-invasively look at active biology. We aim to get to the underlying biology of diseases to enable earlier diagnosis and improve clinical outcomes."

The length and costs associated with the drug development timeline have been significant hurdles to the industry. As clinical trials become more complex and costlier, precision medicine approaches and diagnostic tools will become necessary steps. Moreover, as the rhetoric around drug pricing continues in the coming years, R&D costs associated with drug discovery and development will be much discussed as the key component behind the cost structure of drugs. Diagnostic and precision medicine enable a drug development process that is as cost effective and lean as possible. ■

> "There are interesting things happening in the diagnostics space, which might be largely driven by the FDA. We might start seeing a scenario evolve where, rather than there being six or seven different assays linked to six or seven different drugs, there will be only two or three assays approved for multiple different drugs within a class."
>
> - Paul Harkin, President, Almac Diagnostic Services

U.S. Healthcare vs. U.S. Venture Funding

Source: BIO Industry Analysis



Rajiv Mahadevan

Managing Director
PRECISION FOR MEDICINE

Precision for Medicine develops specialized in-vitro diagnostic and medical device trial services to implement and support clinical research plans

Could you introduce us to Precision Medicine Group and how Applied Immunology has been integrated?
Precision Medicine Group is a service organization that works with pharma and biotech companies across R&D and commercialization. The general theme across the business is to fully enable biomarker-driven drug development, and demonstrate value to key stakeholders such as patients, providers, payers and investors. On the R&D side, the theme is to create science that will demonstrate the unique benefit of a therapeutic program. On the commercial side, the theme is to demonstrate the value of that science to the appropriate audiences, through helping payers understand how the drug should be valued and positioning the product in the marketplace in an optimal way.
Applied Immunology was built to focus on some of the important industry trends in 2011 relating to therapeutic proteins and the immunogenicity safety issue – this is the effect of an unwanted antibody response being elicited when a patient is administered a protein-based therapeutic. The industry had been grappling with this phenomenon for over 10 years. When the FDA issued guidance, I decided to develop a niche service organization alongside an eminent scientist in the field to help companies with this challenge. Applied Immunology represented a very complementary component of what Precision Medicine Group was trying to do in terms of building biomarker-based solutions for clients, along with a strategic location in the San Francisco area.

What was the key motivation behind Precision's acquisition of ApoCell?
Precision's approach to ApoCell was similar to that of Applied Immunology in terms of having a very differentiated technology that complements what Precision is currently doing in providing very specialized biomarker driven solutions to clients. ApoCell's proprietary technology – Apostream – can separate cells in any tissue type in an antibody independent way, allowing the purified cells to be subsequently assayed via any type of molecular or cell-based assay. Moreover, ApoCell has a number of other ways to characterize tissues, such as immunohistochemistry and 9-color immunofluorescence using a novel technology called Vectra Polarisd. ApoCell's offering filled a void for Precision that they previously had to subcontract to third parties.

What is driving Precisions increasing interest in gene therapy, and how are the company's services packaged to best meet market needs?
We have received a lot of traction in gene therapy, particularly AAV-based gene therapy. It is still a very young field and most of the drugs in gene therapy are in late pre-clinical and early clinical stages. We have built some interesting expertise that has really gotten the field excited, which includes the development and implementation of anti-AAV neutralizing antibody assays in a fully commercial-ready quality system for trial and companion diagnostic use. Precision Medicine Group has a number of broader services as well, and one of my roles is to identify and offer relevant service packages to these types of clients.

What is your take on incorporating diagnostics into clinical trials?
It has been an evolution, helped by the rapid emergence of new technologies at increasingly lower costs. The ability to identify well characterized – even rare – populations to demonstrate clinical proof of concept is paving the way for early approvals followed by expansion of indications. This approach is essentially replacing the "traditional" Phase 1/2/3.

The global precision medicine market is set for a CAGR of 12.48% to US$88.64 billion by 2022. How are you expecting the market to evolve in this time period?
Ultimately, the gold standard for demonstrating clinical proof of concept is a clinical trial. There are many organizations that are developing more efficient ways to run clinical trials. The industry is moving from a very old standard of placebo control to more adaptive trials with real-world evidence and a use of technology that can more accurately and rapidly collect phenotypic data. Moreover, adaptive trials with newer technologies are being more widely accepted by regulators.

How is Precision for Medicine planning to drive growth across its business areas?
Precision will continue to position itself very strategically to support innovative companies that want to find ways to shorten their drug development timelines and accelerate commercialization. We will achieve this goal by using biomarker approaches and informatics to more aggressively understand not only the clinical data but the biomarker data that enables researchers to move to another population in a dose escalation trial more efficiently. On the value side, we also need to demonstrate value to stakeholders of our clients quickly. ■

Patrick Arensdorf

CEO
BLUESTAR GENOMICS

Bluestar Genomics is creating a new standard for liquid biopsy in cancer developing diagnostic epigenomic blood tests to identify biology without biopsy

Bluestar Genomics is reinventing liquid biopsy through epigenomics. Could you introduce the company and underline your key focus areas?
Bluestar Genomics develops proprietary next-generation epigenomics and big data approaches to providing novel biomarker insights into human health and disease. We focus on translating large market needs to non-invasive tests: areas where either direct tissue biopsy has been the only method or where first-generation liquid biopsy approaches have limited performance. In cancer, our main objective is the earliest identification of the aggressive cancer biology, moving beyond current limitations to deliver this "biology without biopsy" and create new precision epigenomic medicine.
The company interprets patterns of DNA modifications and epigenetic features, such as DNA hydroxymethylation, to provide unique and dynamic biological information. With the addition of epigenomics, we escape the limitations of sequencing alone, providing new insights to unmet clinical needs in early disease and therapy response. Leveraging the ease of liquid biopsy technologies, we aim to non-invasively provide the earliest true diagnostic tests for many cancer applications using our platform technologies.

The next-generation sequencing and whole exome sequencing spaces are rapidly growing. What differentiates Bluestar Genomics' technology?
Whole exome sequencing does not consider epigenomics, and often comes with substantial cost, sample and signal limitations. Bluestar Genomics is reinventing molecular diagnostic testing using our clinical application platform, getting to novel biology. Using a non-invasive approach is one of our main differentiators. We are highly efficient, using our technology as a magnet, pulling out all the cell-free DNA fragments which relate to this active and dynamic biology, as opposed to searching only for particular rare "needles in a haystack" as in mutations. We focus our sequencing on the epigenomic markers that relate to disease biology and thus enable a higher information content. Our tests provide novel insight and quantitation of human health and disease, with our focus on precision medicine applications. ■

Paul Harkin

President
ALMAC DIAGNOSTIC SERVICES

Almac Diagnostic Services offers services for biomarker discovery, assay development, validation, clinical testing and companion diagnostic co-development

Could you introduce us to the NovaSeq as well as the increasing use of Whole Wxome Sequencing (WES)?
Most of the large pharma companies are now very interested in WES for discovery purposes, but our aim is eventually to also apply its capabilities in a clinical testing setting. The addition of Almac Diagnostic Service's new Illumina NovaSeq 6000 sequencer will benefit our clients in biomarker discovery and clinical trial projects. The NovaSeq is able to provide scalable throughput and flexibility and has powerful processing capabilities, which allows for larger sample runs, greater read depth and faster speeds, ultimately reducing sample turnaround times and increasing variant detection quality and accuracy for clients. With our investment in this new platform, we will be able to sequence the transcriptomes of approximately 384 samples, per run, in a timeframe as short as 36 hours. The NovaSeq will form an integral part of Almac's current DNA and RNA Sequencing offerings and future offerings for Whole Exome Sequencing (WES) and eventually Whole Genome Sequencing (WGS).

Given the expansion at your North Carolina facility, are you seeing a geographical shift in your client base?
We are still seeing a fairly good split between our operations in Europe and the United States. What drives the geographical location of our studies is the type of trial being conducted, whether it is United States specific or global. We are however seeing quite a number of trials that are heavily U.S.-focused, and as a result we decided to expand our facilities in North Carolina to service the market appropriately.

What key advancements can we expect to see in the use of diagnostics in clinical trials over the coming two years?
There are interesting things happening in the diagnostics space, which might be largely driven by the FDA. We might start seeing a scenario evolve where rather than there being six or seven different assays linked to six or seven different drugs, there will be only two or three assays approved for multiple different drugs within a class. ■

Contract Development and Manufacturing

"Proximity to pharma is definitely a driver for CDMO establishment, but excellent technology and service are more important factors than geography and proximity."

- Gil Roth,
Founder and President,
Pharma and Biopharma
Outsourcing Association

Image courtesy of Ajinomoto Bio-Pharma Services

Servicing Your Every Need

Opportunities grow for contract service providers

The CDMO industry has been continuing on its path of exponential growth. Fueled by the redundancies of large pharma's manufacturing lines when drugs have failed before reaching the commercial stage and the increased costs of developing and manufacturing new drugs, outsourcing manufacturing capabilities to CDMOs increasingly becomes the norm. In fact, the global contract manufacturing market is expected to grow at a CAGR of 7.2% between 2017 to 2023, according to Market Research Future, outpacing the overall growth of the pharmaceutical sector. Moreover, outsourcing penetration is set to increase from 30% in 2018 to 40% by 2020, according to Kurmann Partners, a boutique investment bank.

There is a growing trend of CDMOs and CMOs looking to offer a one-stop-shop for the development and commercialization of drugs. In recent years, the CDMO space has consolidated as a result of large pharma wanting to work with fewer suppliers. As of late-2018, the top five CDMOS – Lonza, Catalent, Patheon (acquired by Thermo Scientific in August 2017 for US$7.2 billion), Recipharm and Siegfried – accounted for 15% of overall market share. However, this is far less than the top five CROs, which control 70% of market share, according to Kurmann Partners.

Lonza – a world leading supplier to the pharma, biotech and specialty ingredient markets – completed its largest acquisition in history in 2017 when acquiring Capsugel. The acquisition has been one of the steps taken by the company to move away from a primarily API-focused service offering. "In 2016, the company took the decision to expand its services and move further down the value chain to offer drug product services for small molecules and biologics to our clients as well," highlighted Karen Fallen, SVP and business unit head for clinical development and manufacturing at Lonza. "We determined that an acquisition for solid dosage forms was the most strategic path and subsequently bought Capsugel."

Despite the size of Lonza's acquisition, most medium to large CDMOs are acquiring smaller companies to either complement their strengths with new technologies, increase market access or fill any gaps they may have within their service offering. For example, Argonaut Manufacturing Services – a contract manufacturing provider based in San Diego – recently acquired LyoGen to expand its reagent lyophilization capabilities. Cambrex has acquired Halo Pharma to add to its drug development and drug manufacturing capabilities as well as Avista Pharma Solutions. Moreover, Evonik has completed a number of acquisitions, including that of Transferra Nanosciences to add lipid nanoparticle (LNP) parenteral delivery technologies to its capabilities. "We are indeed investing in capabilities and competencies to serve some of the unmet needs of the biopharma industry," remarked Yann D'Herve, vice president for global sales and services at Evonik Health Care. "As examples, we are further developing our capabilities in continuous process cGMP manufacturing, HPAPIs and microbial fermentation including strain development… When investing in new technologies for pharmaceutical applications, there needs to be a long-term vision as the ROI is realized only when drugs are finally commercialized."

Acquisitions are not the only path CDMOs are taking to enhance their service offering as companies look to grow organically as well. Contract Pharmacal Corp. has planned a US$40 million expansion plan at its Hauppauge, New York site. Lonza has recently opened the world's largest dedicated cell and gene therapy manufacturing facility in Houston, TX, in 2018. CordenPharma has complemented its cGMP facilities in Europe and the United States with a new US$20 million commercial aseptic fill and finishing injectable plant in Caponago, Italy. Whilst some continue to grow organically, others are using this time to rebrand. The company formerly known as AGC Asahi Glass has integrated itself under the single AGC Biologics brand, following the acquisitions of CMC Biologics and Biomeva. Also following this

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> There is a demand for both one-stop services providers and niche service providers. The strategy that PCI has embarked on, in terms of providing a full-service offering, was based on feedback from our clients' demands. We have customers that will only require one particular service of our lifecycle portfolio of services, but we are definitely seeing an increase in demand for support across the product lifecycle, each phase of development and commercialization.
>
> - Justin Schroeder, Senior Executive Director Global Marketing & Design, PCI Pharma Services

Gil Roth

Founder and President
PHARMA AND BIOPHARMA OUTSOURCING ASSOCIATION

The Pharma & Biopharma Outsourcing Association (PBOA) is a non-profit trade association that represents the needs and interests of pharmaceutical and biopharmaceutical CMOs and CDMOs that operate in or sell into the United States

Could you outline the evolution of the Pharma and Biopharma Outsourcing Association (PBOA) and highlight some of the association's key milestones?
The Pharma and Biopharma Outsourcing Association (PBOA) was founded in 2014 and has grown significantly. One of our key milestones was aiding the negotiation of the generic drug user fee authorization (GDUFA) with the FDA. This was an important moment in representing CDMOs in front of the FDA and the rest of the industry. Following that negotiation and the more favourable fee schedule we built for CDMOs in the generic space, more CDMOs began to join. We understood that the more member companies we had, the bigger the impact we would have advocating for the sector's legislative and regulatory interests. Over the last few years, in concert with our work with FDA, we have added focus to Washington D.C. to work with Congress to try and help facilitate legislation to advance the interest of the CDMO sector and benefit public health.
As we have grown, PBOA has added a number of working groups and committees that specialize in particular interest areas, including quality, serialization, opioid issues and drug shortages. Personnel from our member companies participate in these groups and raise agenda items. We work on the agenda items internally within the group and then solicit further ideas from the greater membership base.

How are CDMOs geographically spread across the United States?
The main CDMO hubs are in the traditional life sciences clusters in North Carolina, New Jersey and California, but there are also key areas in Wisconsin and Bloomington, IN. Proximity to pharma is definitely a driver for CDMO establishment, but excellent technology and service are more important factors than geography and proximity. If the CDMO is renowned for a product or service, the customer is generally willing to travel. However, startups do tend to identify proximity as a key factor.

As CDMOs increasingly seek to work with biotechs at earlier stages in their development, how are their business models being impacted?
CDMOs have been diversifying and adding development services to their portfolio for a number of years, adding the "D" to "CDMO." Some companies are looking to offer a one-stop-shop solution, spanning ingredients and dosage formulation, and syncing early development and chemistry services to late-stage clinical and commercialization capabilities.
Adding more development services enables the CDMO to work with customers' molecules earlier in their lifecycle, and the "stickiness" of the sector can make a difference with customers staying with the CDMO as a molecule moves to commercial approval. That said, there is no guarantee of reaching the point of upscaling, due to the high failure rate of drugs in clinical trials, and as we saw after the last financial crash, there's always the possibility that R&D funding can dry up. So, whilst the opportunity to grow with an early-stage client is significant, the risks must be properly assessed and mitigated by taking on a variety of clients.

Are you noticing an increasing need to prioritize quality and safety at CDMO facilities?
Quality and safety are the most important aspects in both the pharma and CDMO industries, and the bar is set significantly high, as it should be. The FDA is trying to develop consistent metrics to reflect the quality state of a facility. It's a complicated issue, and we have been working with the FDA to try to ensure that the quality metrics they choose are not inherently biased against CDMOs, whose facilities tend to have a broader variety of products than in-house pharma sites.

What is PBOA's key strategy towards advocacy work in Washington D.C. moving forward?
PBOA prioritizes its advocacy role to make sure that congressional staff understands the role that CDMOs play in the healthcare system. As such, we try to ensure that well-intentioned legislative language doesn't inadvertently capture CDMOs when it is meant to refer to the license holder or marketing authorization holder: for example, when using the ambiguous term "drug manufacturer." Our advocacy work spans numerous issues, including recent opioid legislation, OTC Monograph reform and drug shortages. In the latter area, we feel that CDMOs are uniquely positioned to help alleviate certain shortages of critical medicines, or even prevent them from occurring. ■

Karen Fallen

Senior Vice President: Business Unit Head - Clinical Development & Manufacturing
LONZA

Lonza is one of the world's leading suppliers to the pharma, biotech and specialty ingredient markets

Lonza completed its largest-ever acquisition in 2017. Could you provide insight into how Capsugel has been integrated into the company?
Historically, Lonza has been primarily API focused in our service offerings. In 2016, the company took the decision to expand its services and move further down the value chain to offer drug product services for small molecules and biologics to our clients as well. We determined that an acquisition for solid dosage forms was the most strategic path and subsequently bought Capsugel. Over the course of 2017 and 2018, Capsugel was integrated into Lonza Pharma & Biotech – the traditional CDMO side of the company – as well as our Consumer Health & Nutrition business. It was a perfect acquisition for us, and we are pleased with the success of our integration efforts. We now have integrated service offerings covering the full value chain including development and manufacturing of drug substance and drug product solid dosage forms and can help customers with specific pharmaceutical and delivery challenges of their small molecules, such as bioavailability, taste masking or modified release.

With regards to Lonza's drug product capabilities in the biologics space, how have you driven growth?
For the biotherapeutics area and parenterals, we have focused on organic growth by initially securing the right capabilities and talents, basing our new offerings on strong scientific, regulatory and industrial experience. As parenteral drug products were something new for Lonza, we aimed for a step-wise approach and started by implementing drug product development services in 2016 in a new facility in Basel, Switzerland. Since then, we have successfully expanded our parenteral drug product capabilities and capacity and grown our team, and the next step for us is to offer in-house cGMP fill and finish. Through our IbexTM Solutions we will be providing customers with biopharmaceutical product support throughout the lifecycle from preclinical to commercialization from cell line construction to drug product manufacturing all in one location, including a sterile fill and finish facility that will come online in 2021.

Given that the CDMO space is becoming ever more consolidated, what is Lonza's value proposition to the industry?
As more complex molecules move towards the clinic, we are looking to offer a broader toolbox of synthetic biology solutions for development and manufacturing. With our business models, our attention is on getting our customers to their key milestones – IND and BLA – faster with reduced risk through our Ibex Design and Ibex Develop solutions. The regulatory world is changing dramatically, and we have a significant number of customers on breakthrough and fast-tracked regulatory pathways. We help our customers prepare for very fast transitions from early clinical phases through to launch.

Lonza opened the world's largest dedicated cell and gene therapy manufacturing facility in Houston, Texas, in 2018. What is the significance of this investment?
Lonza is looking at how we can industrialize the cell and gene therapy manufacturing processes and platforms. One of the key issues is a shortage in supply of viral vectors, and Houston is a direct response to this. We are developing technology and processes that enable our customers to deliver economically viable therapies for patients. For example, we are working to create greater efficiencies in areas like scaling up allogeneic cell therapies and viral vector manufacturing. However, for highly personalized medicines such as autologous cell therapies, which are specific to individual patients, the question is not how to scale up, but how to increase automation in manufacturing for individual patients.

How would you like Lonza to be perceived by the industry moving forward?
Lonza has 120 years of experience in providing services to customers, and we aim to be a second brain for them as well as an extra pair of hands. We can help them strategize the best way to get their molecule to market as efficiently and with the least risk possible. Our goal is to enable our customers to meet their greatest challenges in delivering effective and safe treatments for patients. ■

Robert A. Preti

CEO & President
HITACHI CHEMICAL ADVANCED THERAPEUTICS SOLUTIONS
General Manager
HITACHI CHEMICAL REGENERATIVE MEDICINE BUSINESS SECTOR

In May 2017, PCT was acquired by Hitachi Chemical and subsequently renamed Hitachi Chemical Advanced Therapeutics Solutions. Can you elaborate on the company's origins in the cell therapy space?
PCT was founded in 1999 as the first contract manufacturing organization in the cell therapy space. Once the industry realized that cell therapy could be effectively used for treatment, there was a rapid increase of companies in the space. As one of the first entrants in the space, we had the opportunity to work with the FDA on developing initial regulations. The development of cell therapy was slow to begin with, as it was capital intensive and there were a number of failures. However, this changed dramatically over the past decade following a number of significant breakthroughs. Within cell therapy, there is real potential to change medicine and help patients undergoing life-altering treatments. As the cell therapy space is centered on graft engineering and systemic activities, we also founded the International Society of Hematotherapy and Graft Engineering, which is now known as the International Society of Cell and Gene Therapy (ISCT).

With increasing consolidation in the CDMO space as companies build out their capabilities, what is your value proposition to the industry?
Our value proposition is very much tied into our three-tier strategy to remain at the forefront of the industry. Tier I involves harmonizing our global platforms to provide a singular-customer experience. As part of our mission, we aim to tie together all our global platforms and establish commercial capabilities in each of our locations: Japan, Europe and the United States. This provides our customers with a full range of capabilities from early stage manufacturing development to commercialization. Tier II involves leveraging our Innovation and Engineering (I&E) Center to improve quality, contain the cost of goods, provide the ability to scale and sustain manufacturing throughout the commercial life of the product. Tier III is focused on other parts of the value chain, vertical integration of the support areas for core competencies we currently have and what we need to bring in to secure our supply chain and delivery. ■

Gustavo Mahler

CEO
AGC BIOLOGICS

AGC Biologics offers scale-up and cGMP manufacture of protein-based therapeutics using mammalian and microbial production systems

AGC Biologics was created following AGC Asahi Glass' acquisition of Biomeva and CMC Biologics. Could you provide an overview of how the three organizations have been integrated?
We carried out a thorough integration period across nine different streams, including operations, quality, I.T. and supply chain. We had an ambitious capital investment approach, which included expansion at our Denmark facility, including additional bioreactor capacity to support customers that are developing orphan drugs and niche products. Moreover, we are now the largest microbial CMO in Japan. Moving forward, we also plan to expand our microbial commercial capacity in the United States.
AGC Biologics has successfully manufactured more than 200 biological projects, from pre-clinical studies through commercial approvals. With the acquisitions, we now have manufacturing facilities at a variety of scales for mammalian cell culture and microbial fermentation in Berkeley, California and Seattle, Washington as well as in Heidelberg, Germany, Copenhagen, Denmark plus Yokohama and Chiba, Japan.

How do you ensure quality standards are met across your multiple facilities?
We operate under a similar quality system and we have integrated this approach across all of our operations. However, it goes beyond that. We make sure all our team members in different offices share their best practices. We also encourage the exchange of personnel between sites so they can learn from each other and improve their own work environments.

Do you have a final message to new potential U.S. clients?
We are looking for small or mid-size customers with a mammalian or microbial product to bring to market. We are able to support our clients through the launch phase, scale up, and the delivery of the product to market in the best way possible. We are the right partner that will be able to assist them from the earliest to the final stage. ■

Yann d'Herve

Vice President Global Sales & Services
EVONIK HEALTH CARE

Evonik is one of the world leaders in specialty chemicals with increasing capabilities within the biopharmaceuticals industry

What is the significance of the biopharmaceuticals industry to Evonik and how are you expanding your capabilities in the United States?
With respect to drug delivery technologies, we have been developing in-house technologies and acquired several companies to increase the breadth and depth of our market offering. In 2016, we acquired Transferra Nanosciences (formerly Northern Lipids), a leading player in lipid nanoparticle (LNP) parenteral delivery technologies. This technology is currently used in medicines for several disease categories including oncology applications to deliver oligonucleotides, RNA and highly potent APIs (HPAPIs). We recently announced that we will be doubling our footprint in Vancouver to accommodate the increasing biotech demand for our lipid nanoparticle CDMO services. In Birmingham, Alabama, we continue to expand our controlled release injectable drug capabilities and recently made two large investments. We ramped up our capacity for the manufacturing of bioresorbable polymers that are used both in medical devices and extended release injectable drug applications. Moreover, we have increased our aseptic powder filling line capabilities in support of clients that now require larger-scale commercial production.

What are the key elements of Evonik's overall CDMO offering to the biopharmaceuticals industry?
Evonik can develop, scale-up and commercially manufacture drug substances, injectable drug products and pharmaceutical grade polymers. We are also able to formulate both controlled release oral and controlled release injectable formulations using proprietary technologies. As far as drug substance is concerned, we have specific expertise in highly potent active pharmaceutical ingredients (HPAPIs), microbial fermentation, continuous processing and polymer API manufacturing. We have recently increased our HPAPI capacity in the United States and Europe and have invested in additional fermentation capabilities at our Slovakian facility with downstream capacity for the manufacturing and purification of proteins and enzymes. We also have the ability to seamlessly transfer and scale-up lipid nanoparticle based parenteral drugs developed at our site in Vancouver to Birmingham in support of our client's up-scaling requirements.

There is an element of risk when a CDMO works with a biotech. Given that you are taking on more biotech clients, how do you manage this risk?
More than risk, I would say that there is uncertainty when working with biotechs because many of the products we help develop today will never be commercialized and because our biotech partners often rely on access to venture capital. However, we see great potential in working with our biotech partners as part of our project and customer portfolio and want to continue to support them from phase I through to drug commercialization. For a biotech company, the choice of a CDMO partner can make the difference between project failure and the further advancement of the drug through clinical stages.

How has Evonik's supply chain evolved as you expand capacity and capabilities, particularly in the biologics space?
Within Evonik Health Care, the efficient functioning of the supply chain is foundational to meeting customer expectations and to our ongoing success. Our ability to link the capabilities of our different sites through the different program steps allows us to meet the challenges presented by our clients' projects while taking complexity away from them. This ability to seamlessly integrate competencies and capabilities is a key differentiator.

What are Evonik's key objectives over the coming two years and could you outline your longer-term vision in the United States?
We will continue to build on our innovative drug delivery technologies, continuous processing know-how, leadership in polymer and lipid-based drug formulations and our microbial fermentation capabilities to help clients with their most complex challenges. As a leading CDMO, we want to help our clients extract value from their molecules and to continue to be best-in-class in our industry.
Evonik in North America has been extremely dynamic with strategic M&A. Looking at the recent acquisitions of Evonik on a global basis, many of those deals have been in North America. This underlines the importance of the region to the overall growth strategy. ■

Image courtesy of Ajinomoto Bio-Pharma Services

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> There is not necessarily an expectation on a CDMO to be disease knowledgeable. There is however benefit for a CDMO to understand the differing regulatory pathways across multiple geographies. A good example is the experience that Ajinomoto Bio-Pharma Services has had in San Diego with orphan diseases. Many of the commercial products manufactured or filled and finished in San Diego are orphan or hyper- orphan diseases, which necessitate unique regulatory strategies.
>
> **- David Enloe, President and CEO, Ajinomoto Bio-Pharma Services**

trend is Ajinomoto Bio-Pharma Services, a CDMO headquartered in San Diego, which has rebranded itself to provide its large and small molecule clients access to a broader range of services. "Today, we offer small molecule API manufacturing in Europe, later-life-cycle small molecule API manufacturing through a 50/50 joint venture with Granules India, and large molecule biologic production in San Diego, California," highlighted David Enloe, president and CEO of Ajinomoto Bio-Pharma Services. "We have also added highly potent bio-conjugation and final fill and finish services in San Diego as this space is significantly growing. Moreover, in 2019, Ajinomoto aims to combine its oligonucleotide manufacturing entity – GeneDesign - with Ajinomoto Bio-Pharma Services." 98>>

David Enloe

President and CEO
AJINOMOTO BIO-PHARMA SERVICES

> Ajinomoto Bio-Pharma Services is a globally integrated contract development and manufacturing organization with locations in San Diego, California, as well as Belgium, Japan and India, providing clinical and commercial product development, manufacturing and fill finish services

Could you provide a brief overview of the integration between Ajinomoto Althea and OmniChem to form Ajinomoto Bio-Pharma Services?

Our rebranding to Ajinomoto Bio-Pharma Services reflects our unified company's commitment to providing our large and small molecule clients access to a broader range of service offerings. We are now in a position where we have aligned our efforts to be able to provide our clients with a wide range of CDMO (Contract Development and Manufacturing Organization) services, including small molecule manufacturing in Belgium (formerly OmniChem) and large molecule manufacturing, as well as aseptic fill finish services, in the United States (formerly Althea).

Today, we offer small molecule API manufacturing in Europe, later-life-cycle small molecule API manufacturing through a 50/50 joint venture with Granules India and large molecule biologic production in San Diego, California. We have also added highly potent bio-conjugation and fill and finish services in San Diego because this space is significantly growing. Moreover, in 2019, Ajinomoto aims to combine its oligonucleotide manufacturing entity – GeneDesign - with Ajinomoto Bio-Pharma Services.

Given Ajinomoto Bio-Pharma Services' broad geographic reach, how is the company able to maintain a high standard of quality?

As we have integrated the company, we have adopted one quality system and one user experience across the board. We can deploy our combined expertise towards a program much more efficiently and with much more institutional memory and knowledge than before. As we have a broad geographic reach, we can also provide support from the United States or Europe to our colleagues in India and Japan. Moreover, we have appointed a global head of quality, who is responsible for maintaining our quality standards worldwide.

Importantly, we have succeeded as a CDMO in drawing a direct connection between our employees' work and the patients whose lives we are impacting. In doing so, our ongoing commitment to quality permeates throughout our entire organization.

What is Ajinomoto Bio-Pharma Services' value proposition to smaller biotech companies?

We position ourselves as being just down the hallway from the biotech companies that have a more virtual organization when it comes to manufacturing. We have outstanding quality and regulatory experience within the fill and finish and biologics manufacturing space, which is highly valued by smaller biotech companies.

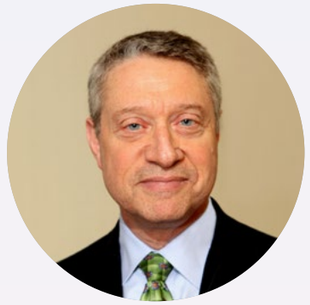
One unique aspect of the company, within the highly potent space, is that Ajinomoto Bio-Pharma Services is, to my knowledge, the only commercial scale manufacturer that provides antibody drug conjugate (ADC) process development, analytical, drug substance and drug product manufacturing all under one roof in the United States. Our new 57,000 sq. ft state-of-the-art facility, which opened its doors in January 2019, can utilize our AJICAP bio-conjugation proprietary technology for ADC manufacturing, which allows developers of therapeutic ADCs to better control both the location of payload conjugation to an antibody along with fine tuning the quantity of the payload attached. This is a unique offering to our customers when it comes to specificity around the binding properties of ADCs. Our history of supporting smaller biotech companies' development of orphan and other niche indication therapies has prepared us to partner with clients' ADC and highly potent products in this quickly growing space.

What is a key challenge Ajinomoto Bio-Pharma Services faces with respect to scaling up?

The scaling up challenge is about repeatability and robustness of the process. We often need to quickly figure out how to manufacture a product safely and securely so that the drug can be fast tracked for approval.

What will be Ajinomoto Bio-Pharma Services' key objectives moving forward?

Ajinomoto Bio-Pharma Services in San Diego has been experiencing a 20% plus annual growth rate for the past five years. We have multiple programs that we are supporting through the final stages of their production and pre-registration process. We are a world class organization that can support customers big and small, and our goal is to continue building relationships, especially with large pharma customers. We also aim to continue to integrate our global service offerings and leverage the best practices of each of our sites in Europe, Japan and India. ■



Steven Klosk

President and CEO
CAMBREX

Cambrex is a CDMO specializing in small molecule APIs, advanced intermediates and custom development and manufacturing

Cambrex recently acquired Halo Pharma (Halo) in September 2018 and Avista Pharma Solutions in January 2019. What was the strategy behind these acquisitions?

With the acquisitions, Cambrex has created the opportunity to broaden the company's service offering in its continued mission to become the leading small molecule company. The acquisitions significantly increase the customer base and funnel of projects, allowing Cambrex to offer an integrated service offering for small molecules from pre-clinical development through to commercial launch.

The small molecule pharmaceutical market continues to grow at the fastest rate seen in more than a decade, with a robust funding environment for early-stage clinical programs as well as an increasing trend for pharmaceutical customers to outsource more of their small molecule requirements.

Halo Pharma has added drug development and drug product manufacturing capabilities, while Avista Pharma Solutions brought early stage development and discovery, standalone analytical services, solid state sciences and microbiology testing to our portfolio of services, and we have structured the business into four main business units accordingly: drug substance, drug product, early stage development and testing and generic APIs.

As the CDMO space becomes increasingly consolidated, what is your value proposition to the industry?

The company's global manufacturing offering now stretches from milligram scale through to multi-ton supply, as well as integrated services that can support a project from discovery – through preclinical development and clinical trials and on to commercial launch. This offering supports customers involved in all types of pharmaceutical products, ranging from niche or orphan drugs, to global blockbusters, in both patent-protected branded and generic medicines.

What will be Cambrex's key objectives for 2019?

The company is focused on delivering the integration of the recently acquired drug product and early stage development and testing businesses with the existing drug substance manufacturing capability, which has added over 800 employees and six new facilities to the Cambrex business. ■

> Lonza's growth in 2018 came from both sides of our business – small and large molecules. We are seeing an increased demand within the pre-clinical and clinical areas particularly, with a healthy pipeline of new molecules in early phases. This gives us a good view on the future market and helps to seed the commercial offering. We are still seeing a very strong demand from our large pharma customers and increasingly from small biotech who often have quite specific needs from a CDMO – this is an area of growth for Lonza.
>
> - Karen Fallen, Senior Vice President: Business Unit Head, Clinical Development & Manufacturing, Lonza

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Undeniably, CDMOs are moving towards offerings inclusive of large molecule capabilities, in line with the growing pipelines of biotechs across the United States. Moreover, CDMOs are increasingly offering more of a holistic service to biotechs and integrating themselves at earlier stages of their development timelines. "Smaller, resource-constrained biotech firms often can favorably leverage the experience of a large partner like Evonik to positively influence the outcome of their programs," highlighted D'Herve.

With hundreds of biotechs increasingly outsourcing their development and manufacturing in the key hubs of San Diego, San Francisco and Cambridge-Boston,

Image courtesy of Evonik Health Care

Top 5 CDMOs have

15%

of total global market share

Top 5 CROs have

70%

of total global market share

Source: Kurmann Partners

contract service companies are looking at how best to serve them. More and more, contract service companies are offering quasi-consulting services and guidance in areas such as regulation and commercialization. Often, biotechs have very small teams of scientists and there is a knowledge gap when it comes to upscaling and market entry strategies.

Although contract service providers have long veered towards diversifying their service offering, CDMOs, and especially CROs, need to make sure they are not spreading themselves too thinly. AGC Biologics has found a niche in orphan drugs and biologics with small patient populations. CordenPharma, whose portfolio

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Stephen Wang & Ryan Yoder

SW: Chairman & CEO
RY: VP Business Development
KINGCHEM LIFE SCIENCE

DO

SB

Kingchem provides contract development and manufacturing services to the pharmaceutical and chemical industries

Kingchem has evolved from distributing chemicals to manufacturing pharmaceuticals. Could you provide an overview of Kingchem Life Science and your global operations?

SW: Kingchem began 25 years ago as a distributor of products from China to the United States and Europe. For the first 10 years, we focused on third-party representation and bringing products into the U.S. and European markets. We realized that we could provide more value to our customers by combining our own R&D and manufacturing with our business model of third-party representation. While we continue certain traditional third-party agency business with our long-term business partners, our own R&D and manufacturing now dominates the majority of our business.

RY: In 2002, we acquired a plant in Fuxin, China, that today manufactures chemicals for several industries. Over the past 10 years, we have invested over US$40 million in this plant to grow its capacity and continuously improve the operating standards, with another US$15 million occurring over 2019-2021. Our chemical supply for pharmaceuticals has grown significantly as we have continued to improve our quality systems. Subsequently, we have become a major player for registered starting materials (RSMs).

Kingchem recently acquired a GMP facility in St. Francis, Wisconsin. How does this acquisition fit into the company's overall strategy?

RY: We currently have over 60 employees working in R&D across Dalian and Fuxin in China, but this acquisition expands our R&D capabilities into the United States. Moreover, the acquisition gives us GMP-manufacturing capabilities based in the United States, which has been welcomed by many of our customers. This enables us to provide a full spectrum of products and services for our clients. Where China is producing RSMs, our facility in Wisconsin is focusing more downstream on GMP intermediates and APIs.

What is your value proposition for biotechs and large pharma companies, especially in light of recent trade tensions between China and United States?

RY: Our tag line "Western Management, Eastern Value" speaks well to our customers. We are a U.S. company that owns assets in China, which constitutes a different business model and value than companies that are Chinese with a presence in the United States. We are not alone in facing the impacts of the tariffs and trade relations between the United States and China, and our customers understand this because their entire supply chain may be affected. We hope to increase confidence within the United States through our recent founding of Kingchem Laboratories in Wisconsin, which provides domestic manufacturing assets to compliment those in China.

What is Kingchem's growth strategy moving forward and what is your longer-term vision?

RY: Our strategy is to continue growing our plant in China and to upgrade our Wisconsin plant; we recently invested over US$500 thousand on the analytical equipment and software in Wisconsin, with another US$4.5 million in other facility investments to occur there by the close of 2021. In addition, we are hiring new staff as we upgrade both of our plants in China and the United States. We strive to continuously raise the bar with respect to sustainability to ensure that we are prepared for the future. For example, a lot of companies are concerned about sharing IP with a company that is doing business in China, but Kingchem has a rigorous IP protection program in place, and we feel very confident that our customers can trust us. Kingchem is excited to be able to leverage our strengths in China as a key producer of RSMs where we have built a strong customer base over the past 25 years, as well as downstream products through our new facility in the United States.

SW: As a company, our growth is a non-stop process and we need to continuously improve our position and build a better foundation for future growth. We will continue to add more staff in R&D, quality control and marketing, as well as to add hard assets to our manufacturing capacity. Moreover, we will further strengthen our R&D and manufacturing position to enable us to better serve the life sciences industry. We will continue to develop our technology to better serve our clients across multiple sectors. ■

Paul Hennessey

Senior VP Sales
CONTRACT PHARMACAL CORP. (CPC)

Contract Pharmacal Corp. manufactures and packages pharmaceuticals, over-the-counter drugs and dietary supplements for pharmaceutical companies, retailers and wholesalers worldwide

Established in 1971, Contract Pharmacal Corp. (CPC) has been in operation for 38 years. How has the company and your service offering evolved during this time?

The fact that we are a one-stop-shop has set us apart in the market and helped to grow our business significantly. Companies can come to us with anything from an idea to an early stage molecule, and we can take them from a very early stage, all the way through development and eventually commercialization, including aspects such as testing and packaging. We are involved in the method development work, and analytically we have a tremendously talented team that can develop methods on both the pharma and supplement side of the business.

Over the years, CPC has continued to add significant capacity in blending, tablet compression, encapsulation, coating and powder filling. We have added capabilities such as milling, granulation and drug coating on seeds. We continually help our partners innovate to stay a step ahead of their competition. With respect to packaging, we do a significant amount of bottling, blistering and powder filling. For one particular customer, we added eight packaging lines to do single dose sachets and stick packs, making CPC the largest OTC drug producer of single dose powders in the United States. We are also in the process of expanding our facilities, where we will more than double our capacity to 40 billion doses per year by the end of 2021.

Given the planned US$40 million expansion at CPC's Hauppauge, NY site, what is your strategy for gaining greater market share?

There is so much potential in the industry, even in solid dose, which remains the most popular dosage form by far and will continue to be as it is an inexpensive way to deliver drug products to the market. Personalized medicine will become more commonplace over the next couple of decades, and we will see how solid dose can play a role in the personalized medicine area.

Are you investing into innovative drug delivery technologies?

CPC has been very thoughtful when acquiring innovative technology equipment, and we want to ensure that we are doing so with an eye towards efficiency. What is instrumental in controlling healthcare cost is optimal efficiency at the highest quality. We invest in technologies to optimize our operations and increase the efficiencies within our business, such as increasing batch sizes. We have just installed our second 400ft3 blender, which allows us to manufacture batch sizes of 8000 kg, allowing us to spread the one-time costs of batch manufacturing over a greater number of doses. Our aim is to relentlessly drive out waste and non-value added activities to control costs, providing our partners with an improved cost structure to gain market share. Our partners' success in turn helps CPC achieve its growth objectives.

Has CPC seen the serialization regulations mandated by the United States Drug Supply Chain Security Act (DSCSA) as a hindrance or an opportunity?

On the surface, the new serialization regulations might appear as a hindrance, but it is actually an opportunity. We have been considering how we can deploy that same technology on the consumer side – referring to over-the-counter products – of our business to help drive innovation. By printing a QR code on our nutritional products, for example, this could drive a consumer to a web page that provides detailed information about where their product has come from and what specific raw materials were used. We are trying to take something that is a requirement on the prescription side of the business and find a way to turn it into a competitive advantage on the OTC products.

What are CPC's key objectives moving forward and what would be your final message to the industry?

Having industry-leading quality, service and products is a benchmark for companies like CPC that want to lead in the life sciences space. We have our operational mindset geared towards quality in every interaction that we have and to pervade everything we do. We will continually look at ways to improve and optimize our business to help our clients deliver the lowest cost, highest quality products to the market to ensure their success. ■

Marc Kikuchi

Chief Executive Officer and Head, North America Generics
DR REDDY'S LABORATORIES

Dr. Reddy's was established in 1984 in India and is a US$2.3 billion company present in nearly 40 countries, with the United States accounting for about 40% of sales

With substantial growth in the past year, could you underline the recent developments at Dr. Reddy's in the United States?
The company undertook a significant exercise to develop its strategic roadmap to drive sustainable growth for the company over next three to five years. Because of this strategic realignment, we have chosen six spaces that will drive significant growth for the company going forward. These are: the United States, India, Russia, China, API and Global Hospitals. Each of these chosen spaces have their strategic moves laid out to drive sustainable growth. We also have new professional management in place with almost 80% of management council members having joined in last two years. With this new team, we are poised to revive the growth for the company and deliver on shareholder return.

With a portfolio covering generics, APIs, Biologics and differentiated formulations, what has been your strategy for growth in the developed markets?
Among developed markets, the United States is our key focus market, followed by the EU and Canada. In the U.S. market, we are looking to increase significantly our portfolio offering, to be driven by a number of launches. These launches span various dosage forms, and many of them are likely to be complex, limited competition opportunities. We look forward to bring significant value to the U.S. healthcare system and patients by providing affordable options for many of the branded drugs.

Dr. Reddy's has a broad therapeutic focus, including oncology, gastroenterology and dermatology. Is there a particular therapeutic area that is gaining traction for you?
Our portfolio choices for the U.S market are not restricted to any specific therapeutic area. The current in-market portfolio and the pipeline includes dosage forms spanning oral solid dosages (OSDs), injectables, topicals, transdermals, softgels, etc. Among these dosage forms, we currently have much stronger presence in OSDs and complex injectables, many of which happen to be in the oncology space. We recently launched a first generic of an opioid-use-disorder drug in a sublingual film. ■

Contract Manufacturing Market CAGR

7.2%

growth between 2017 to 2023

Source: Market Research Future

If a potent compound can be visibly seen in the workplace environment, then it is too much, both from an occupational and quality/ product safety standpoint. As potent compounds are potentially toxic even if the compound cannot be seen, then it needs to be quantitatively assessed. Quantitative assessment needs to continue taking precedence as potent compounds become stronger and more potent. This is a message that all companies should take notice of.

- Allan Ader, Co-Managing Director, SafeBridge Consultants

Michael Quirmbach

Chief Business Officer
CORDENPHARMA

CordenPharma is a CDMO supporting pharmaceutical and biotechnology companies, with cGMP facilities across Europe and the United States

Could you update us on the recent developments at CordenPharma?
As of November 2018, we have completed our US$20 million investment in CordenPharma Caponago (IT). The construction resulted in a new commercial aseptic fill and finish injectable plant, consisting of two highly flexible filling lines enabling the manufacture of a broad range of vials, Pre-Filled Syringes (PFS) and cartridges using state-of-the-art nest and tub technology. One of the new lines is already operational, with a successful PAI FDA inspection for two products, which will increase the manufacturing capacity to 20 million units per year and add expanded lyophilization capacity.
Furthermore, we are in the process of completing the final instalment of a new manufacturing line in CordenPharma Plankstadt (DE), which had begun at the end of 2017 with a target completion date during Q1 of 2019. The facility is dedicated to producing Veterinary Drug Products for 500kg-scale batch sizes to supply a complex innovative product for application in the veterinary health market. The expansion of the production capabilities at CordenPharma Plankstadt are the result of a new, long-term custom manufacturing agreement for an animal health application, which the company recently signed.

What is your value proposition for small biotech companies and your strategy to gain more market share in this space?
The value we bring to these companies is our proven experience in manufacturing and regulatory knowledge ranging from initial support for clinical phases all the way to commercialization of their products. In addition, our offering spans the cGMP spectrum, from the production of their APIs to their Drug Products, packaging and shipping across a broad range of global commercial markets. We offer a fully integrated opportunity organized under five distinctive technology platforms and nine manufacturing facilities, whilst also allowing them to choose from our range of services more selectively.

What are some of the challenges that a CDMO faces in terms of maintaining a facility to the highest standards?
A key challenge for a CDMO, especially for those working with highly potent and oncology compounds, is having adequate containment infrastructure, systems, processes and state of the art safety, health and environment methodology in place to make sure there is no cross contamination and adequate protection between products and operators. Overall, this is a very complex subject for any pharmaceutical company or CDMO. While maintaining all these pre-requisites in place is costly, it is a small price to pay to alleviate greater unforeseen costs down the road. Microgram quantities of oncology compounds are enough to cause contamination issues and potentially severe adverse reactions to patients.

Are you seeing a continued trend of outsourcing from biotechs and large pharma?
We are continuing to see many companies outsourcing their manufacturing assets and offloading their facilities. A lot of the large pharmas are divesting facilities to focus more on their core expertise in marketing and initial R&D. This is a trend we are also seeing across Asia, including in China. A lot of Chinese companies have reached out to us in an effort to release their products in the United States. They are currently lacking the experience or expertise to manufacture, so are inclined to outsource their services to U.S. and Europe-based CDMOs.

What are the key milestones for CordenPharma moving forward?
CordenPharma's key milestones are continued growth of our technology platforms to reinforce our position as an industry leader in these segments. We still have significant capacity available to accommodate further growth, especially in our two U.S. facilities where we are currently involved with a few late phase III assets. If these go to commercialization, we feel confident our sales could double in the United States in the coming years.

Could you provide a final message to our international readership?

While the pharm industry goes through significant changes and is confronted by cost pressure from governmental institution, the demand for the research of new medications tackling unmet medical needs (both in developed & emerging countries) remains high. CDMOs play an important part in today's pharma value chain - from outsourcing of single services to full supply chains - with the latter being the future of the industry. ■

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is split between biotech and pharma, has strengths in a number of therapeutic areas but particularly in oncology. "We have extensive manufacturing capacities combined with strong capabilities in highly potent and oncology manufacturing, both for Drug Substance and Drug Product, within four cGMP facilities – two in Boulder, Colorado for Drug Substance and two in Europe (Germany and Italy) focusing on Drug Product manufacturing for oral solid dosage and injectable sterile fill and finish respectively," remarked Michael Quirmbach, chief business officer at CordenPharma.

Although opportunities continue to present themselves for contract service providers, molecules are becoming more complex as well. They are increasingly having to deal with high-potency active pharmaceutical ingredients (HPAPIs) at their facilities, which is leading to greater numbers of risk assessments being carried out by their clients. SafeBridge Consultants – provider of the Potent Compound Safety Triangle™ of services in industrial hygiene, toxicology and industrial hygiene laboratory services – has evolved over time to become a product safety company due to the increasing need for toxicological risk assessments of contaminants. "We conduct assessments of capabilities of CMOs and pharma companies including due diligence assessments as part of M&A activities for companies to help them decipher between the 'contenders' and the 'pretenders,' and our services have increased in relevance as compounds have become more potent," highlighted Allan Ader, co-managing director at SafeBridge Consultants. "Additionally,

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> A key challenge for a CDMO, especially for those working with highly potent & oncology compounds, is having adequate containment infrastructure, systems, processes and state of the art safety, health & environment methodology in place to make sure there is no cross contamination and adequate protection between products and operators.
>
> - Michael Quirmbach, Chief Business Officer, CordenPharma

Allan Ader

Co-Managing Director
SAFEBRIDGE CONSULTANTS

SafeBridge is a provider of the safety services in toxicology and industrial hygiene laboratory services to the pharmaceutical, specialty chemical and food industries

Could you outline SafeBridge Consultants' evolution since its conception as well as the recent integration of Toxicology and Regulatory Services (TRS)?

SafeBridge Consultants was formed in 1997 having spun out of Roche and Syntex. We provided the technical support for the Times Beach, Missouri clean-up project – the largest dioxin remediation in the United States at the time. During our time with Syntex and Roche, we gained a lot of experience in potent compounds and gained direct experience in the pharma industry, and we used this experience and our relationships to build our client base. There are three key aspects to our business: toxicology, industrial hygiene and laboratory analysis, which we named the Potent Compound Safety Triangle™ . Our toxicologists establish acceptable limits for occupational exposure both in the air and on surfaces; the industrial hygienists evaluate exposure through qualitative and quantitative assessments; and our laboratory specializes in the measurement of very small quantities of chemicals on filters. Over time, we have expanded our service offering and geographic scope, with offices opening in New York in 2004 and the United Kingdom in 2005.

We conduct assessments of capabilities of CMOs and pharma companies, including due diligence assessments as part of M&A activities for companies to help them decipher between the 'contenders' and the 'pretenders,' and our services have increased in relevance as compounds have become more potent. Additionally, we have become a vital resource to quality programs in pharma and biotech to assess the potential for cross-contamination and we have become the experts in product safety and cross-contamination by developing Permitted Daily Exposure (PDE) values for determining cleaning limits. Over time, we have evolved from being an occupational health and safety consultancy firm to also becoming a product safety company, due to the increasing need for toxicological risk assessments of contaminants, impurities and to protect against potential cross-contamination from one drug product to the next.

Toxicology and Regulatory Services (TRS) was purchased by our parent company – Trinity Consultants, and is a subsidiary of SafeBridge – to expand our risk assessment capabilities. It primarily focuses on food and beverages, cosmetics and flavor and fragrances, and has a quality assurance area that is able to evaluate toxicological studies and make sure they are being run according to current regulatory protocols and with proper quality assurance checks.

What key trends are you noticing from your client base at the moment and how is this influencing your service offering?

Product quality – all our clients are working diligently to meet the cross-contamination guidelines and genotoxic impurities regulatory guidelines – is the hot topic at the moment, because without quality you will not have safe and efficacious drug products.

Additionally, there are more APIs out there that are considered potent. One trend that has not been good is that companies are assessing their capabilities qualitatively instead of quantitatively. The more potent the drug, the more quantitative the assessments need to be.

How are you strategizing SafeBridge's growth moving forward?

We have identified the need and have started to conduct more due diligence assessments as part of pharma and biotech M&A activities. We also have a number of projects where we are being asked by the drug innovator to assess the business risk of making the drug at a CMO. Companies typically only send in their quality and operations staff when assessing a CMO, but not their EH&S staff. This is beginning to change and so due diligence is a big area of growth for us.

Could you provide a final message to our international readership?

If a potent compound can be visibly seen in the workplace environment, then it is too much, both from an occupational and quality/product safety standpoint. As potent compounds are potentially toxic even if the compound cannot be seen, then it needs to be quantitatively assessed. Quantitative assessment needs to continue taking precedence as potent compounds become stronger and more potent. This is a message that all companies should heed. A systematic and scientific approach is to develop robust OELs, ASLs and PDEs; develop sensitive and validated analytical methods; and go out and measure potential worker exposure and validate cleaning for minimizing product cross-contamination to meet these established values. ■

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we have become a vital resource to quality programs in pharma and biotech to assess the potential for cross-contamination, and we have become the experts in product safety and cross-contamination by developing Permitted Daily Exposure (PDE) values for determining cleaning limits."

As small biotechs, which do not have the capacity to upscale, and large pharma companies, which have been refocusing their activities around their core expertise, continue to outsource their development and manufacturing, greater demands and expectations will be put on contract service providers. Despite this, the opportunities being afforded to them are enticing, especially given that more international biotechs are looking to CDMOs as a gateway to commercialize their products in the U.S. market. ■

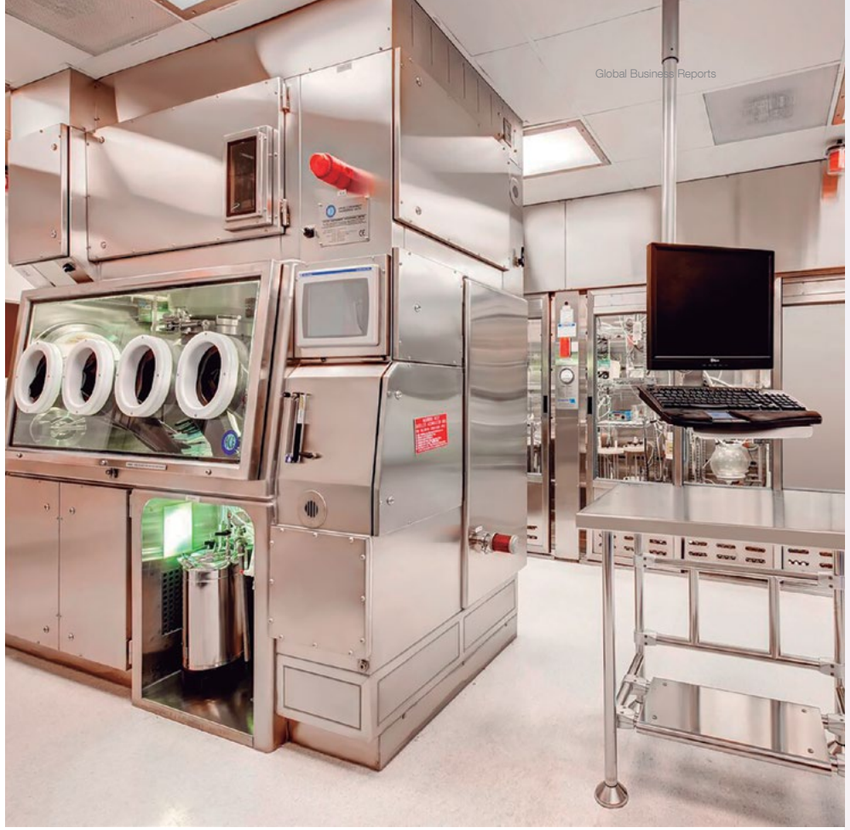


Image courtesy of CordenPharma

Kamlesh Oza

Senior Vice President
Global Sales ACG Capsules
ACG

Headquartered in Mumbai, India, ACG is the world's second-largest manufacturer of empty hard-shell capsules

The pipeline of biotechs and large pharma is increasingly moving towards biologics. How are you strategizing to meet future demand?

ACG does have a strategy to predict market demand. We know which products are in the market and which of those will follow the oral route. As a company that has a focus on innovation and differentiating ourselves in the market, we are looking at doing things differently moving forward with innovation to support the biologic oral administration opportunity.

With new serialization regulations mandated by the United States Drug Supply Chain Security Act (DSCSA) coming into effect, how has ACG been preparing for the change?

ACG is in the fortunate position that we can adapt to almost all of the various serialization options that are available, and offer these options to our customers. We offer end-to-end track and trace solutions for serialization. We work closely with pharmaceutical companies across the globe as a track and trace implementation partner. Our application integration capabilities, combined with our strong service support, enable us to cater to every serialization requirement in a very regulated industry.

What are ACG's key objectives for the capsules division in the United States moving forward?

ACG is the only company in the world offering an end-to-end solution to the pharmaceutical industry. Our aim is to bring the synergy that we have to the entire pharmaceutical value chain allowing them to benefit from the solutions that we can offer. All four companies work together to continually support our customers and find solutions when challenges arise. Although the company is headquartered in India, we have expanded our facilities to Croatia and have recently inaugurated a facility in Brazil. The establishment of facilities in the United States and other geographies with a concentration of pharmaceutical and Nutritional manufacturing capabilities. Most importantly ACG is and will always be easy to do business with. ■

Nataliya Katsnelson

Director – Business Development
GLOBAL CLINICAL TRIALS

What is GCT's value proposition for small U.S.-based biotechs?

GCT's value proposition is our competitive pricing, quality assurance and fast patient recruitment.

Moreover, research sites in Eastern Europe are based in large hospitals and regional centers, thus eliminating the risk of a potential shutdown. We also have very high level of patient compliance in Eastern Europe. In Eastern Europe, patients are more open to participate in clinical trials.

How have you seen the biotech ecosystem change in New Jersey over the past five years?

There has been a drastic increase in the number of biotechs in Princeton. It is interesting to see how small biotechs access funding for their trials and then go on to be successful components of the New Jersey biotech landscape. The biotech industry in New Jersey is constantly changing with many companies coming from other states, including Philadelphia, Delaware and even California.

Could you provide a final message from GCT to the U.S. biotech community?

As a company, GCT looks forward to establishing new and reliable partnerships with companies in the biotech industry. Our role is to provide a bridge between patients and biotechs globally in order to find innovative, life-saving treatment options and provide access to patients all over the world. ■

Marcus Hompesch

CEO and Chairman of the Board
PROSCIENTO

Will ProSciento remain focused on metabolic diseases?

In our experience, there is a healthy market for a focused model around a therapeutic area, which is science-driven and deep in expertise and experience on a given indication.

Where are ProSciento's clients mainly located and is there an emphasis on proximity to your labs?

We have a strong North American and European footprint, and a rapidly growing footprint in Asia.

How is ProSciento able to translate its quality of services to sites across the globe?

ProSciento is a quality-driven organization. We have demonstrated a data acquisition rate significantly above 95%, which is almost unprecedented in the industry. We have been able to keep complex studies with demanding methodologies at an extremely high quality and rapid timeline, which is owed to our focus on one therapeutic area.

At sites, among other aspects, quality is generated by subject matter expertise around clinical and medical monitoring. As we have a focused approach on metabolic diseases, we can send clinical monitors to the sites that know what to look for with regards to the quality of data capturing and imaging.

What are ProSciento's key objectives moving forward?

CROs have the responsibility to bring a focused commitment and deep science to their clients, and this is precisely what we aim to do. ■

Hugh Davis

Chief Business Officer
FRONTAGE LABORATORIES

Frontage operates a 'two countries, one system approach', due to its operations in the United States and China. How have your operations in China evolved in recent years?

As one of the only bioanalytical and clinical sites that had the same quality standards in China as the rest of the world and was in compliance with CFDA standards, Chinese domestic companies knew they could trust us as a high-quality provider. We have a quality-approved system that we not only use in the United States, but also have replicated in China.

With regards to the Chinese market, there is a substantial number of new portfolios, assets and platforms being established each year, which are focused on innovation. As part of a five-year strategic plan, China identified biotechs as a key driver for their economy and thus invested a significant amount of funds and effort into growing the sector. Today, the biotech industry is significantly developed, and many companies have well-trained, English speaking teams who are constantly working on innovative technologies within the life sciences space.

As Frontage prepares to list on the SEHK in 2019, what will be your key objectives moving forward?

One of the key goals moving forward will be to grow our biologics business to equal our small molecule business in revenue. Generics are still part of our business plan, but a significant amount of this business will be around innovation. The imminent IPO will give Frontage the opportunity to attract outside funds that will allow us to grow the business. ■

Service Providers of Tomorrow

"Across the entire industry, we do not see the level of serialization readiness that is required, and it will be interesting to see what the FDA and EU will do in terms of enforcing the deadlines for companies that are not ready."

- Justin Schroeder,
Senior Executive Director - Global Marketing & Design,
PCI Pharma Services

Image courtesy of PCI Pharma Services

Packaging to a Deadline

Serialization regulations puts packaging into the limelight

The pharmaceutical industry has long been happily reliant on a steadfast and somewhat muted packaging sector. However, over the past decade, the pharmaceutical packaging industry has significantly increased in importance. Contract packaging organizations (CPOs) have emerged, and the industry is set to reach the US$100 billion market value mark by 2022, according to Allied Market Research. Whilst the digitization of the supply chain and more innovative products are playing into this, the overarching reason is the serialization requirements coming into effect. "We have seen a significant amount of development with regards to serialization and nearly all of our customers are live," highlighted Shabbir Dahod, president and CEO at Tracelink. "The number of serial numbers being commissioned each month has dramatically increased from 60 million numbers in March 2018 to 300 million numbers in March 2019. Overall, 1.5 billion serial numbers have already been commissioned and over 30 billion serial numbers have already been reserved."

Breaking Down the Regulations

The U.S. Drug Supply Chain Security Act (DSCSA) was enacted in Congress on November 27th 2013 with the aim of making drug products safer by creating a framework for enabling pharmaceutical product traceability. The DSCSA required each individual product to have a unique product identifier. However, by June 2017, the original enforcement date, when the FDA published a draft guidance on product identifiers and verification in connection with the DSCSA it noted that pharmaceutical manufacturers still had not installed the technologies required.

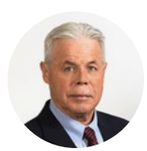
The new date of November 26, 2018 has come and gone, and still many questions remain around when it can be expected to be ready. The mandate for serialization regulations is to protect the supply chain from counterfeit products, but the compliance surrounding the implementation and installation of serialization capabilities is lagging behind, as demonstrated by the FDA's delayed enforcement dates. "There is currently no supportive infrastructure at all," remarked Julien Faury, vice president for operations at Adents. "The solution providers and big wholesalers are pushing their own individual visions for 2023, which is the year by which full unit-level traceability, including aggregation, will be mandatory and the FDA is launching some pilot programs just now. The change with serialization is going to take some time to unfold and the industry still needs to build an infrastructure that will be able to handle the change."

Image courtesy of Adents

Indeed, stakeholders need to come together to be ready for the upcoming deadlines, which culminate on November 27, 2023 where a full enhanced drug distribution security system comes into effect and unit-level traceability is mandated. The United States is not alone in implementing such requirements, with the EU's Falsified Medicines Directive stating, as of February 2019, that product identifier, serial number, lot or batch number and expiry date have to be printed in human-readable format and encoded in a 2D data matrix on the secondary packaging of saleable units of prescription medicines to be FMD compliant.

The implementation of serialization needs a thought-out strategy given the interdisciplinary nature of the requirements. This may begin with the upgrading of packaging lines with additional equipment and modification of the risk evaluation. Opportunistic and forward-looking packaging companies may have been prepared a few years back to take on board changing serialization requirements, but it has now become an essential consideration for all. "PCI has been involved in commercial serialization for the United States, Europe and emerging markets for approximately seven years," underlined Justin Schroeder, senior executive director for global marketing and design at PCI Pharma Services. "We have put tremendous energy and resource into preparing our clients for these deadlines. Across the entire industry, we do not see the level of serialization readiness that is required, and it will be interesting to see what the FDA and EU will do in terms of enforcing the deadlines for companies that are not ready."

> We see the serialization process as an opportunity, as we have had some clients who either consolidated some business with us or transferred their business to us as their CMOs were not yet ready, or were not willing to invest in serialization capabilities.
>
> - Joe Luke, Vice President - Sales & Marketing, Reed-Lane



Moving forward, stakeholders involved in packaging have a real opportunity to add significant value to their offering. When looking at readiness of the industry to embrace the serialization requirements, CPOs, CMOs, consultants and others can take advantage of the 7% CAGR forecast by Technavio for the global pharmaceutical packaging market over the coming five years. ■

Justin Schroeder

Senior Executive Director – Global Marketing & Design
PCI PHARMA SERVICES

PCI Pharma Services provides integrated pharmaceutical development services to the global healthcare market

Could you update us on PCI's developments over the past year?
In the past 12 months, we have acquired three companies to expand our capabilities. Our acquisition of Millmount Healthcare, a commercial packaging company based in Dublin, was an opportunity to gain more market access and a global market presence for commercial packaging, as well as clinical trial packaging. The acquisition also allowed us to retain a strong position within the EU as Brexit talks continue to leave uncertainty within the region. In February 2018, PCI acquired Pharmaceutical Packaging Professionals (PPP) located in Melbourne, Australia. PPP is a leading provider of clinical trial manufacturing, packaging, labeling, storage and distribution services. Their early-stage drug manufacturing capabilities include oral dosages and sterile and non-sterile drug manufacturing of investigative medicines. PPP benefits from a significant amount of government incentives geared towards executing early-stage/Phase 1 studies in Australia.
PCI has long desired to be geographically present on the West Coast of the United States, and Sherpa Clinical Packaging proved to be a very attractive opportunity. Sherpa is a provider of clinical trial supply services and with efforts including supporting small and emerging clients. Our relationship with Sherpa strengthens the company's position as a leader in outsourced clinical support services and offers our clients a rapid pathway to execute their early stage studies.

Could you elaborate on how PCI sets its acquisition targets?
In addition to keeping a close pulse on industry trends, PCI heavily relies on feedback from our customers and where they require our services geographically. It is an increasingly global market. We traditionally had facilities in Europe and the United States, from which we serviced the rest of the world. The company now also has a presence in Australia and we would like to expand our presence within the Asia Pacific region.
PCI is targeting international partners with the aim of nurturing a PCI global network. The company has a significant number of international clients using PCI as a pathway to commercialize products or execute trials in the United States, but we also have U.S. and European clients who are looking to expand into emerging markets. Likewise, we see international clients looking to access the North American and European markets, particularly for biosimilar commercialization.

What key trends are you seeing in serialization and anti-counterfeiting?
PCI has been 100% focused on serialization readiness and we have recently announced the installation of our latest comprehensive serialization system, located at our manufacturing center of excellence in Tredegar, United Kingdom.
PCI has been involved in commercial serialization for the United States, Europe and emerging markets for approximately seven years. We have put tremendous energy and resource into preparing our clients for these deadlines. Across the entire industry, we do not see the level of serialization readiness that is required, and it will be interesting to see what the FDA and EU will do in terms of enforcing the deadlines for companies that are not ready. We have been very consultative to our clients in helping them prepare to meet serialization requirements, as well as helping them develop their global anti-counterfeiting strategies. We hope the serialization initiative is just the first step in supporting delivery of safe medicines around the world.

The FDA has seen a record year in terms of approved generic drugs. Has this had an impact on PCI's business and operations?
PCI has seen more impact from specialty drugs and orphan indications than the increase in generic approvals. Generally, more generic and bio-similar products are entering the market, and we believe that this increase will impact the market in terms of the profile of branded drugs and the competitive environment within the market. The biosimilar medicines now being approved have the opportunity to change significantly the scope of the market for biotech products and injectable delivery, particularly as these generic equivalents are being developed with advanced deliveries such as prefilled safety syringes and increasingly auto-injectors. PCI has invested considerably in this area to support the shift. ■

Julien Faury

VP Operations
ADENTS

Adents provides end-to-end traceability solutions to secure local and global supply chains and provides an integrated serialization solution covering all track and trace needs

How well prepared is the biopharma infrastructure for serialization?
There is currently no supportive infrastructure at all. The solution providers and big wholesalers are pushing their own individual visions for 2023, which is the year by which full unit-level traceability, including aggregation, will be mandatory, and the FDA is launching some pilot programs just now. The change with serialization is going to take some time to unfold, and the industry still needs to build an infrastructure that will be able to handle the change

How is Adents able to leverage its experience in serialization from other industries into the more complex biopharmaceutical supply chain?
We are able to support on the road to drug serialization compliance by providing solutions that streamline their compliance operations. By the end of the decade, 80% of global drug supply will be serialized, and with deadlines fast approaching, we can provide a serialization solution that is quick and easy to deploy at our clients' sites. The blockchain-based technology solutions we provide integrate seamlessly with existing line equipment and enterprise information systems.
Serialization requirements for pharmaceutical products can differ vastly from one country to another. This increases the need for a solution that is fully configurable, highly flexible and adaptable to the industry's ever-changing legal landscape. A pharmaceutical company usually handles hundreds of thousands of prescriptions every year, and with serialization regulations, millions of serial numbers need to be generated, data needs to be collected and managed, events need to reported and huge amounts of information need to be securely stored. Adents aims to provide a future proof solution for our clients within the pharma space. The solution is focused on providing a trusted cloud native architecture with the highest standard of security plus exceptional connectivity with third parties, as well as the flexibility to ensure permanent compliance. Once the compliance objective is fulfilled, pharmaceutical companies and CMOs should be able to benefit from the massive amounts of data generated during the serialization and track & trace process. ■

Shabbir Dahod

President and CEO
TRACELINK

TraceLink is the world's largest integrated digital supply network connecting the life sciences supply chain

How have TraceLink's operations evolved since the introduction of the Drug Supply Chain Security Act (DSCSA) in 2013?
TraceLink has grown significantly over the years, and we have expanded our team from 35 employees in 2014 to over 500 in early 2019. The company has also expanded globally from having one office in Boston to having five global offices.

How is TraceLink readying its client base for all the serialization requirements?
The number of serial numbers being commissioned each month has dramatically increased from 60 million numbers in March 2018 to 300 million numbers in March 2019. Overall, nearly 1.5 billion serial numbers have already been commissioned, and more than 30 billion serial numbers have already been reserved. TraceLink handles close to a million files a week, which are processed through our system.
In order for all companies to go live, we have a network of over 274,000 entities, which connect all of the contract manufacturers, pharmaceutical companies, 3PLs, wholesalers, repackagers, hospitals and pharmacies. In Europe, TraceLink launched Smart Rx Manager, an online solution for pharmacies to meet regulatory compliance deadlines.

TraceLink recently announced a US$93 million investment round to accelerate the expansion of your information-sharing network platform. What is your value proposition to the market?
TraceLink's core value proposition is that we have a network platform, which means that companies can integrate once and interoperate with everyone, allowing access to hundreds of thousands of trading partners with a single connection. This platform offers significant time and costs savings compared to point-to-point connections while also ensuring quality. The cloud-based, multi-tenant platform was purpose-built to provide massive scalability and high quality for our customers. There are of course personalization aspects, which come into play through configuration based upon very specific system needs. We have capabilities within the product to let customers define their own workflows and integrations. ■

Jonathan Retano

Founder and CEO
PHARMAFUSION

Pharmafusion provides data warehouse and business analytics solutions for the pharmaceutical industry

Pharmafusion's mission is to simplify analytics for the biopharmaceutical value chain. What was the insight that led to the conception of Pharmafusion?
Pharmafusion was conceived through an understanding of the needs of pharmaceutical industry leaders and my knowledge of data management and analytics. We envisioned Pharmafusion as a platform that could provide a fully packaged experience to the user to address the frequent pain-points of pharmaceutical commercial operations. Subsequently, we developed a turnkey platform that has all the datasets for pharmaceutical analytics one requires, all on one platform.

Could you elaborate on your award-winning Pharmafusion platforms?
We have a number of different solutions at Pharmafusion that we use to help facilitate a streamlined analytics process for our customers. SpydeRx, for example, is used to monitor competitor activity in all drug classes through a daily notification of price changes, new entrants and FDA filings. Pharmafusion 360 is our award-winning, enterprise-wide data warehouse and business analytics platform that was designed for commercial pharmaceutical operations. Our philosophy was to easily pivot the platform so it can be used in-house. For a small company that does not have the adequate infrastructure, it can be placed on the cloud. For larger companies, it is a subscription-based service. A unique feature of the platform is our analytics concierge. This allows for a 'wingman' approach to help our clients if they are in need of assistance when analyzing their data.

Given the general conservatism towards the uptake of technology in the pharmaceutical industry, how have you seen this change over the past two years?
In our everyday lives, the uptake of technology is very fast. Although the pharma industry has been relatively slow in its uptake, this began to change in 2017. It has definitely turned in the past year, and we are now seeing a far greater confidence in what data analytics and technology can do for a company's operations. ■

Pharma 4.0

The revolution sweeping the biopharmaceuticals value chain

Industry 4.0, or the fourth Industrial Revolution, is bringing with it a new way of thinking through the advancement of technologies. AI technologies, big data, data analytics and robotics have all begun to have an impact on the biopharmaceuticals value chain from drug delivery and development to manufacturing, logistics and compliance. In drug delivery and development, data analytics applied to incredibly large data sets from clinical trials is identifying trends and patterns to better inform the processes. "Recently the field has seen remarkable success with immunotherapies, especially in the area of oncology," underlined David Craford, president and CEO at Cytobank,

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With all the broad conversations around changing life science supply chain trends, particularly with the influence of technology, we are trying to understand how these developments impact our clients' risk profiles.

- Douglas Carey, Managing Director, U.S. Life Sciences Practice Leader, Marsh

Mark Jara

Principal
RXS

RxS provides end-to-end solutions for multi-channel sample management by simplifying sample management and sales force automation into one master system

What was the demand for a multi-channel sample management platform when RxS was established?
When the FDA implemented the Prescription Drug Marketing Act (PDMA), companies were scrambling to find solutions. At that time, working at a distribution company, I took the position to build out the first infrastructure to track sample distribution for their clients. As technology continued to evolve, we kept on building out this system, from a holistic perspective for all representative-based sampling. The system grew significantly and various clients started to find value and show a demand for this type of platform within divergent lines. This led to the establishment of RxS.

How has RxS' client base evolved and what has been the adoption rate of the company's multi-channel platform?
When RxS was established, we started with small to mid-size pharma companies, but large pharma clients have driven our exponential growth over the last three years. Initially, the sweet spot in our client base was within the small to mid-size pharma segment because we are very consultative and can add significant value. Small pharma tends to have gaps in people, technology expertise and compliance expertise, and RxS offers solutions that overcome these gaps. However, more recently large pharma has seen this value and have become more interested in our solutions because the associated risk of adopting new technology has lessened. Our exponential growth is correlated with the market's willingness to embrace technology.

What is RxS' key objective for 2019?
Our expansion approach is two-pronged. First, we will extend support of our U.S. operations with ancillary support including technical and program development. Second, we will support regionalized multichannel initiatives specific to the company and brand. Sampling can differ significantly across continents, but we believe that we can already expand our international footprint with regards to our services and platforms. Poland is our first step into the EU, and we are also looking at opportunities in Canada. ■

Manu Goel

SVP and Client Partner
GENPACT

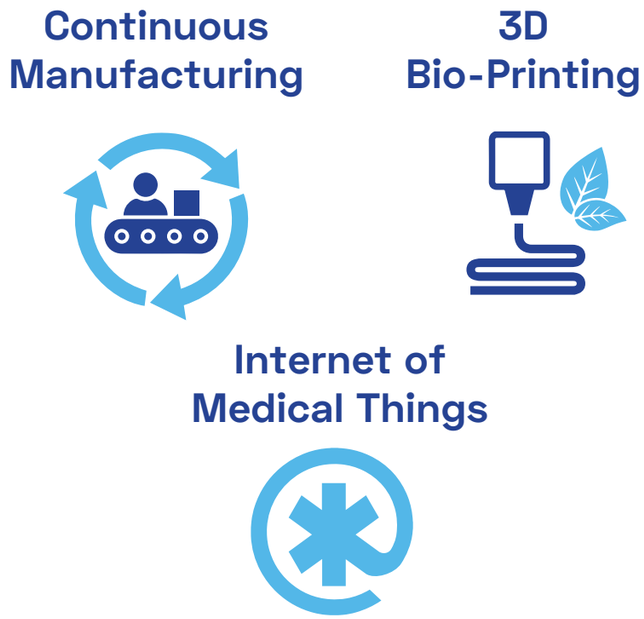
Genpact is a global professional services firm delivering digital transformation

How rapid has the uptake of Genpact's AI-based solutions been by big biotech and large pharma companies?
Genpact has signed contracts with the top 15 pharma companies. We have found that there is a fear of the unknown with regards to AI, and thus educating companies on how AI can be deployed and provide complete visibility and auditability is a key component. The system that we have developed gives results that are accurate and have high confidence levels, and, if the client wanted to, they could manually audit each and every element of the solution.

Could you elaborate on the advancements of Genpact's Cora platform?
We have spent a few years developing our Cora platform, which enables different capabilities such as automation, analytics and AI. This platform learns over time and blends seamlessly with our operation's insights and domain expertise. Our aim is to digitally disrupt business models and transform customer experience through an interoperable AI-based platform of capabilities. Our value proposition to our clients is that we can digitally transform customer experience through automation, analytics and AI to gain predictive insights, agile operations and a strong competitive advantage.

What is Genpact's strategy moving forward?
Genpact's aim is to continue expanding within R&D for life sciences companies. Our focus will remain on regulatory affairs and patient safety for the next few years. We have developed the capabilities and have proven that our solution works, and now we are entering a stage where we need to scale up and deliver on the promises we have made to the industry.
We also have the vision to expand our footprint into the supply chain management space. We have recently acquired Barkawi Management Consultants to help expand our global supply chain management transformation expertise. The acquisition has added consulting and digital technology capabilities for supply chain management and aftermarket services, which will enable us to help drive our clients' growth. ■

Pharma 4.0 Emerging Technologies



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which developed a SaaS platform for machine learning-based analysis of high-complexity life sciences data. "This has driven pharma to generate and analyze higher complexity data to understand the immune system and the host-immune response as they attempt to maximize the value of the information they can get from every clinical trial patient sample. Especially in early phase trials, pharma will run very high complexity technologies on their samples."
Indeed, the analysis of data is revolutionizing the approach to clinical trials, but its impact is wide reaching across the value chain. RxS has formed end-to-end solutions for multi-channel sample management by simplifying sample management and sales force automation into one master system. "As we are in a very divergent market with diverse demands, RxS decided to integrate different solutions into one system," highlighted Mark Jara, principal at RxS. "We understand the complexities that drive the market and, having been on both sides of the industry – pharmaceutical and service –, we decided to build our infrastructure to support these complex environments."
Moreover, Pharmafusion has an award-winning, enterprise-wide data warehouse and business analytics platform for commercial operations. Away from analytics, advanced technologies are transforming the manufacturing process of drugs. The pharma industry has batch manufactured for well over 50 years, but continuous manufacturing is slowly being practiced with the first drug product – Vertex's Orkambi – made by the process in 2015. This is being replicated in the manufacturing of APIs. The clear advantage in the increase in capacity and capability as well as improved safety as reactions are carried out at a far smaller scale. Evonik, who has been using the practice in the manufacturing of specialty chemicals, has now developed continuous process cGMP manufacturing capabilities for pharmaceutical products as well.
However, the areas of the value chain seeing the greatest impact from Pharma 4.0 are logistics and the supply chain, in part due to the implementation of the Drug Supply Chain Security Act (DSCSA). For example, Adents has been using blockchain-based technology for its serialization solutions. Smart network technologies and personalized medicine are also driving an evolution in the supply chain. As supply chains become ever more complex, advanced technologies will continue to enable a faster and smarter system. "Many technological advancements impact how organizations do business," underlined Chris Cassidy, president of global healthcare logistics strategy at UPS. "Some include big data, artificial intelligence, robotics and blockchain. UPS recently created an Advanced Technology Group to focus on enhancing our smart network technologies, and part of that is looking at how to build out a healthcare network-within-a-network. We will go forward fast using smart technologies to move healthcare and life sciences packages with the right levels of visibility, speed and control."
The uptake of new technologies can be slow, with many companies unwilling to have first implementer status. However, now a few years on from the dawn of Industry 4.0, the benefits of these new technologies can be seen and are increasingly becoming the norm. Pharma 4.0 is truly upon us and is set to revolutionize the biopharmaceutical industry. ■

> Blockchain technologies are uniquely positioned to help create trust, transparency and accountability between many parties in the supply chain. The industry is very open minded and willing to adapt to the changing technological environment. They have seen the benefits of Industry 4.0 technologies and are willing to move into a new technological era.
>
> - Julien Faury, VP Operations, Adents

Chris Cassidy

President,
Global Healthcare Logistics Strategy
UPS

UPS is a global logistics service company

What are the key imperatives for UPS's long-term healthcare focus?
Healthcare is facing increasing end-to-end regulatory compliance requirements, cost pressures and demand for downstream patient-centric services. As such, the role of healthcare logistics is becoming increasingly critical and strategic to organizations. Industry mega trends include the rise in a middle class demanding home health, personalized medicines and growing aging populations managing chronic diseases. UPS's vision is to inspire trust and to empower innovation to improve patient care across the healthcare and life sciences ecosystem.

Particularly as new therapies increase in complexity, how is UPS meeting increased biopharma and specimen logistics demands?
Product integrity is key to healthcare logistics. Controlling the temperature and security of biologic drugs and diagnostic specimens across any supply chain is unique and challenging. Add to this equation the fact that the growth rate of biologics continues to rise. This market was expected to reach US$15 billion in 2018, according to one source, representing a 12.7% year-over-year growth. UPS continues to have world-class expertise in both global transportation and specialized healthcare areas such as cold chain packaging optimization. As firms seek asset-light models for entering new markets, we have 8 million square feet of cGMP- or cGDP-compliant healthcare distribution space. For freight and parcels requiring strict temperature environments and those requiring around-the-clock monitoring, we have UPS Temperature True™ and UPS Proactive Response™ services that put extra focus on service and recovery for high-value and high-consequence life science shipments. Furthermore, Marken, UPS's clinical trial subsidiary, continues to demonstrate our commitment to the life sciences industry. Marken is the leader in direct-to and-direct-from-patient services, so combining its capabilities with UPS's healthcare services shows our strength in global clinical trials logistics. We will continue to create customer value for specimen logistics by leveraging Marken's high-touch care against a hybrid transportation solution that benefits from UPS's expansive network.

Alongside trends toward precision medicine, there is renewed focus on patient's individual needs. How does UPS cater to these trends through its home care and direct-to-patient offerings, and what are the implications of these services?
The traditional patterns of standardized care centered on hospitals and practitioner clinics are being complimented with a new philosophy of care delivered directly to the patient, tailored to individual patient needs. This evolution of sophisticated therapies and diagnostic models - think telehealth and personalized medicine - shows just how far healthcare has shifted to proactive wellness. This makes supply chain speed, agility, safety and compliance even more imperative.
"Over-the-threshold" home health delivery services are complex. When you add in temperature-sensitive therapies, a traveling care provider and a patient that may be infirm, or active and working, you introduce logistics complexities that go beyond standard care and standard e-commerce. UPS has in place systems that enable home health such as UPS My Choice®, which allows consignees to take control of shipments, have advanced visibility, electronically sign or reroute critical shipments. The UPS Access Point™ network allows deliveries to be routed to convenient pickup locations near a patient's home.

As an increasing number of pharma and biopharma companies look to outsource supply chain operations to 3PLs, how can UPS use blockchain and other technologies to stay competitive?
UPS recently created an Advanced Technology Group to focus on enhancing our smart network technologies, and part of that is looking at how to build out a healthcare network-within-a-network. As we start to see the full emergence of track and trace and product serialization for greater security and traceability, innovations will go a long way to create efficiencies, enhance agility and help safeguard critical shipments. UPS recently joined the Blockchain in Transport Alliance with the goal of developing blockchain standards and education across the supply chain industry. ■

Looking Ahead to 2020

"We are likely to face some tough legislation and proposals from the administration as policy makers respond to the outcry against drug pricing due to the perception that the drug developers are to blame."

- James Greenwood,
President & CEO,
Biotechnology Innovation Organization

Image courtesy of Frontage Laboratories

The Next Step

Shaping the future of the U.S. biopharmaceuticals industry

2019 is set to be a year of uncertainty for the United States, whether it is through a potential downturn in the economy, the lasting impact of the 2018 to 2019 government shutdown, increased trade tariffs with China or a change in the makeup of NAFTA. Nevertheless, while most industries will expect a slowdown, the biopharmaceuticals industry should remain resilient, driven by its unconditional desire to keep innovating. By embracing precision, biotechs are reducing drug discovery and development timelines by improving success rates and thereby reducing overall costs. Increased innovation in the generics space due to a need for differentiation is benefitting patients. New drug discovery technologies could translate into a valued opportunity for CDMOs and disruptive technologies, such as big data, artificial intelligence and blockchain will eventually revolutionize the biopharma value chain.

Although geopolitical factors will have an impact on many players, the industry has proven itself to be adaptable, and its overall growth is unlikely to be offset. However, the upcoming presidential cycle and the rhetoric around drug pricing has the possibility to unbalance the sector and to disrupt the incredible technological advancements and medical breakthroughs being made by U.S biopharmaceutical companies at this moment. The entire industry needs to come together to educate politicians, and most importantly the population, of the value it currently brings. This will take ever greater precedence as it becomes a key fixture in the campaigns for the 59th quadrennial U.S. presidential election. If drug pricing and the factors at play are understood, a balance can be struck whereby innovation is incentivized and supported for the good of the population. ■

“With the convergence of technology, healthcare delivery is getting smarter. The traditional patterns of standardized care centered on hospitals and practitioner clinics are being complimented with a new philosophy of care delivered directly to the patient, tailored to individual patient needs. This evolution of sophisticated therapies and diagnostic models – think telehealth and personalized medicine – shows just how far healthcare has shifted to proactive wellness. This makes supply chain speed, agility, safety and compliance even more imperative.”

- Chris Cassidy,
President,
Global Healthcare Logistics Strategy,
UPS

“U.S.-based manufacturers will likely be more focused on complex, difficult to manufacture injectable products. There is still a lot of room for innovation in generics, and I think this is where U.S.-based manufacturers will focus their attention.”

- Chris Rector,
Vice President – Sourcing and Supplier Relations,
ClarusONE Sourcing Services

“We are evolving how translation is done at universities. The future of translation is going to be with startups, which will be aided by a more robust entrepreneurial ecosystem.”

- Richard Sudek,
Chief Innovation Officer and Executive Director,
UC Irvine Applied Innovation

“The industry is moving from a very old standard of placebo control to more adaptive trials with real-world evidence and a use of technology that can more accurately and rapidly collect phenotypic data. Moreover, adaptive trials with newer technologies are being more widely accepted by regulators.”

- Rajiv Mahadevan,
Managing Director,
Precision for Medicine

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