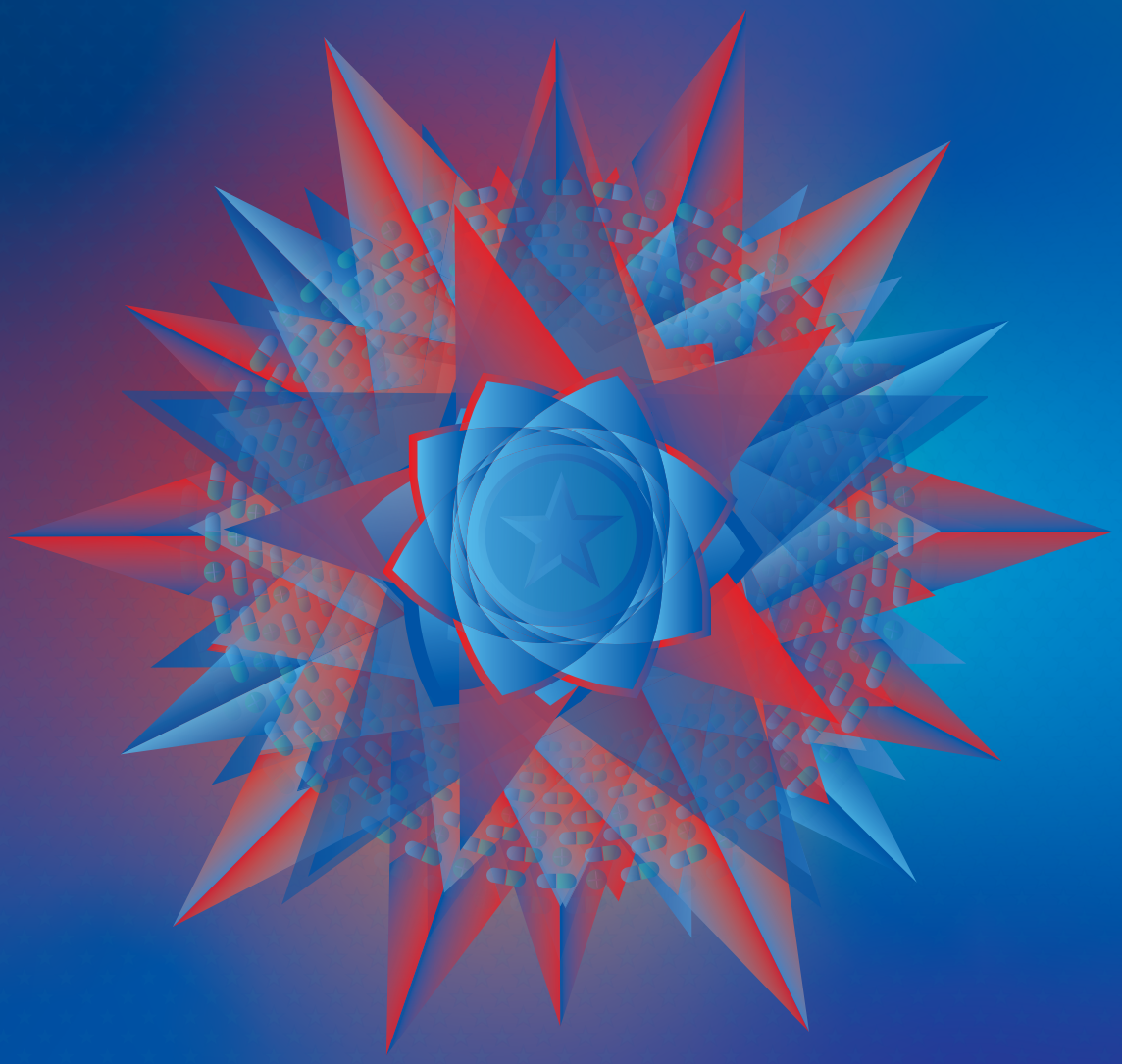
CPhI

GLOBAL BUSINESS REPORTS

INDUSTRY EXPLORATIONS



UNITED STATES BIOPHARMACEUTICALS 2020

Research and Development - Contract Services - Drug Discovery
Academic Research Regulations and Compliance - East Coast Hubs - Logistics and Distribution

Dear Reader,

Welcome to the 2020 edition of the US Biopharmaceutical Industry Report, a joint GBR-CPhI analysis. The United States Biopharmaceutical industry is widely envied around the world, and for good reason. From gene editing, to cell-based therapies, to profoundly new ways of manipulating immune cells to target cancers, today's science is being translated into practical treatments for patients at breakneck speed. Biopharma companies have achieved remarkable progress in advancing early disease detection and enabling targeted treatments with limited side effects. These innovations have catalyzed significant reductions in the number of deaths due to cancer, HIV/AIDS, and autoimmune diseases across the world. This provides reasons for optimism that America's dynamic life sciences industry will be able to collectively rise to the occasion and defeat the novel COVID-19 virus that is bedeviling society today. As we move through these uncertain times, it is crucial for investors, pharmaceutical executives, and scientific researchers involved in the US biopharmaceutical industry to remain together and informed. The way in which groups across industry, academia, government, and the broader health-care system have come together to fight this pandemic have been inspiring. Indeed, continuing to partner in this way will be critical in successfully navigating public health challenges of the future. That is the essence of why events like CPhI North America exist.

The following pages offer widespread coverage of the state of the US biopharmaceutical industry, including big pharma and its blockbuster drugs, emerging biotech and their innovative drug pipelines, and the different service providers across the value chain, from CDMO's and CRO's to AI and big data platform companies.

We sincerely hope that you have a great conference, full of business and networking opportunities. Thank you for your participation in CPhI North America, and we hope you enjoy reading our 2020 edition of the United States Biopharmaceutical Industry Report.

Alice Pascoletti
Managing Director
Global Business Reports

Anthony Pombal
Brand Director
CPhI North America

Editorial Analysis

GBR provides unique and first-hand analysis into all aspects of the US biopharmaceutical industry after months on the ground

8, 26, 43, 68, 86, 98....

Exclusive Interviews

Leading industry figures share their insights and exciting new developments with GBR

11, 15, 55, 56, 81, 87...

Industry Thoughts

Excerpts of ideas shared with GBR during interviews with over 60 of the leading players in the US biopharmaceutical industry

48, 60, 62, 88, 100...

Introducing the US Biopharmaceutical Industry

The Biopharma Investment Climate

Accelerating Pipelines: Drug Discovery and Development

Contract Manufacturing and Generics

Technology and Regulatory Services

Industry Outlook

USA BIOPHARMACEUTICALS 2020
Industry Explorations
Global Business Reports

This research has been conducted by Lucrezia Falcidia, Jason Spizer and Maria Filippova Barnachisnkaya

Edited by Mungo Smith
Graphic design by Gonzalo Da Cunha

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

United States of America

International Boundary
State Boundary
★ State Capital

0 100 200 300 Miles

INTRODUCING THE U.S. BIOPHARMACEUTICAL INDUSTRY

» As far as innovation is concerned, prices for cancer medications and some of the products for unmet medical needs are high... There is significant risk of failure so there needs to be an adequate return on investment for innovation to continue. The public forgets that the alternative to these drugs could be lengthy hospital stays, that cost the system far more money than the drugs themselves. Gene therapies, which can cost between US$1-2 million per course of treatment, can potentially cure diseases, or at least keep them at bay for 10-15 years. We need to consider how much we save as a society when hospital resources are not utilized to treat these patients. «

- James Gale,
Founding Partner and Managing Director,
Signet Healthcare Partners

Introducing the U.S. Biopharmaceutical Industry

THE MORAL IMPERATIVE TO INNOVATE

Analogous to the beginning of the previous decade, when the US faced fears over the spread of H1N1 swine flu, and was tenuously pulling itself out of a perilous financial meltdown, 2020 has brought with it a similarly calamitous series of events. This time triggered by the novel respiratory virus labeled COVID-19. The disease invaded the human population at the dawn of the new decade, and has spread rapidly and indiscriminately across borders, aided by the interconnectedness of the modern world. Daily life has been upended across the globe and the spread has deeply shaken financial markets and, most importantly, many lives have been lost.

As extreme measures are taken to lock down populations to a degree that was previously unimaginable, commerce has ground to a halt. The immediate cause of the turbulence in markets can be attributed to the actual and feared impact of the coronavirus in destroying supply and demand simultaneously. This has undermined the momentum of global economic growth to such an extent that, five weeks after reaching new all time highs in the S&P 500, the US government committed to spending trillions to keep individuals and corporations solvent. Now, as much as ever, the world is in desperate need of a solution. First to deprive the disease of its ability to spread, second to develop a therapeutic that can cure those who are infected, and finally to invent a vaccine so this disaster does not reoccur. The latter two are exactly the type of challenges upon which the American biopharmaceutical industry thrives.

The US undoubtedly is the world leader in bringing innovative therapeutics to market, and novel technologies currently being developed and commercialized are at record levels. An effective response to the coronavirus pandemic requires unprecedented collaboration across academia, the private sector, and the philanthropic community. These are all areas in which the country excels. America, and in particular its leading clusters on the east coast, has a university system that is the envy of the world, as well as tech transfer, large pharma, fast growing biotech, important corporate partnerships, a well functioning incubator system, and an abundance of talent, skills and know-how regarding discovery, clinical trials and commercialization. These qualities, along with access to liquid and efficient capital markets, power the engine of the US biopharma industry. Christiana Goh Bardon, portfolio manager at Burrage Capital, commented: "We are reminded amidst this COVID19 crisis of the tremendous importance of scientific innovation. The world is looking to our biotechnology industry to develop and provide the drugs, vaccines and diagnostics to counter this epidemic. It is only because of the years of investment and research that there is any hope to find these solutions in the short term."

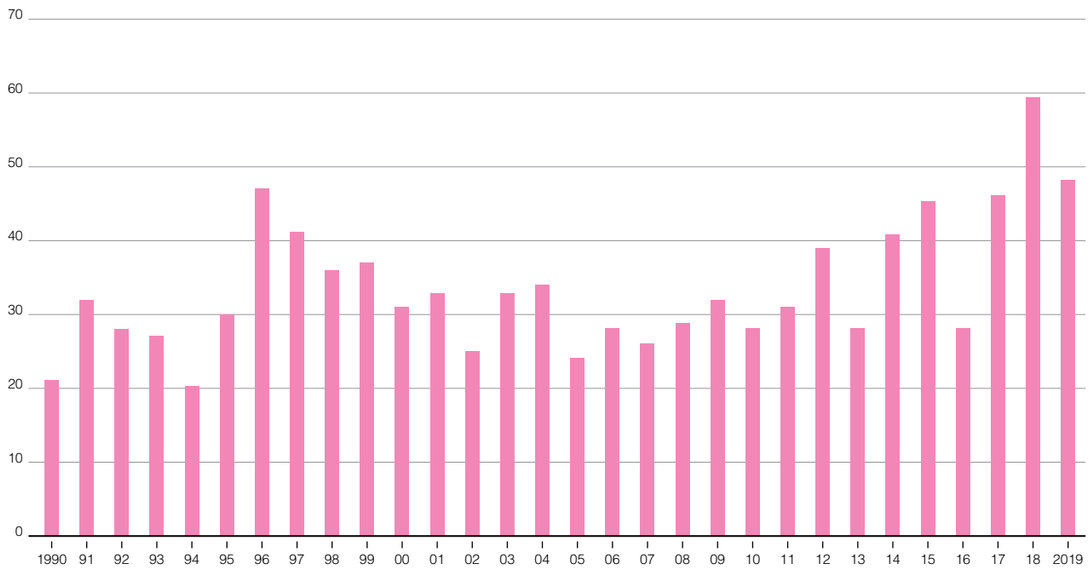
For biopharma, the past decade was a transformational one, wherein immense progress and exceptional growth were achieved. We now live in a world where a heart attack is something that you can bounce back from, where diabetes is something that patients live with every day and HIV is essentially a chronic condition. Prior to the COVID-19 pandemic, the Nasdaq Biotech index had expanded roughly 400% decade on decade. Driven by enthusiasm over the promise of cures for all sorts of diseases, investment flowed into the sector. As evidence of this ebullient era, venture capital funding into US-based biotech firms has been above a record-setting US$3.5 billion for each of the last eight quarters leading into 2020, according to Pitchbook data. It wasn't that long ago that an entire year's worth of venture funding was in the US$4 billion to US$5 billion range.

The US biopharmaceutical industry produces 57% of all the trigger new drugs in the world and, in 2019, the U.S. FDA approved 48 novel drugs, several of which represent advanced, first-in-class therapies with billion-dollar blockbuster potential. This built off of a strong 2018, that saw a record 59 novel treatments. A big spike compared to 2010, when just 21 novel drugs were approved.

These novel drugs seek to treat and cure conditions ranging from cancers to muscular dystrophy to schizophrenia. One example is Vertex Pharma-

NUMBER OF NEW THERAPEUTIC DRUGS APPROVED

Source: BCG, FDA



NASDAQ BIOTECH INDEX 10 YEAR CHART

Source: NASDAQ

We are reminded amidst this COVID19 crisis of the tremendous importance of scientific innovation. The world is looking to our biotechnology industry to develop and provide the drugs, vaccines and diagnostics to counter this epidemic. It is only because of the years of investment and research that there is any hope to find these solutions in the short term.

- Christiana Goh Bardon, Portfolio Manager, Burrage Capital

ceuticals' FDA approval for Trikafta, a cystic fibrosis (CF) treatment with the potential to help 90% of patients with the deadly genetic disorder. According to Robert Coughlin, president of MassBio and father to a CF patient: "This is another reminder of just how difficult it is to bring a drug to market, as it took 18 years and billions of dollars to finally develop a drug that worked for my son and thousands like him. It takes countless failures and major investment to bring any life-transforming drug to market, but there is another ingredient that is essential: a supportive government."

In the case of coronavirus, the US government has shown a deep commitment to incentivize and expedite the clinical, approval and manufacturing process of any therapeutic with potential to attenuate the impact of the disease.

Another factor that makes the American life sciences ecosystem robust is the steady rise of emerging biotech over the past few decades as a powerful force for innovation. As a result of this phenomenon, more drugs are being discovered by smaller firms than ever before. This is evidenced by the increasing proportion of active INDs and new drug approvals (NDAs) attributed to smaller firms. This allows CROs and CDMOs to play an increasingly important role in expediting the process of bringing molecules to commercialization. Unlike big pharma, these smaller players rely heavily on collaboration and outsourcing. However, the explosion of emerging biotech companies happened largely as a result of big pharma outsourcing its early stage discovery and development to effectively de-risk, albeit at the expense of acquiring companies at a much later stage and richer valuation. "Many, if not all, of big biotech and big pharma companies realized there is an opportunity to shrink their internal R&D footprint and many of those companies still develop and discover drugs, but they do so in confined areas where they work broadly in an external world where they can build best in class partners to build in

12>>

John Patrick Oroho

Executive Vice President and
Chief Strategy Officer
PORZIO LIFE SCIENCES, LLC

What kind of progress has Porzio made over the last year and what were some company initiatives?

Porzio Life Sciences, LLC (PorzioLS) is the industry's leading provider of compliance operations, products and services, and a wholly-owned subsidiary of the Porzio, Bromberg & Newman, P.C. law firm. 2019 was our best year to date and exceeded the prior year by 15%. We provided global transparency reporting services and systems in 46 countries around the world.

Even large organizations are looking to us for reporting and to access to our systems so they can see the data for auditing, monitoring, analytics and business intelligence. Porzio has become an outsourced transparency and aggregate spend office for many companies.

Our biggest initiative for 2020 is the launch of Porzio TPE (Third Party Engagement) software, a cradle-to-grave system, where we provide a robust workflow system to handle global HCP engagements, as well as other types of third party engagements. TPE can also provide a solution to handle a company's upstream data and workflow requirements. We have integrated our daily-updated Porzio Compliance Digest (PCD) containing global laws, regulations, and pending legislation into this system. Thus, our customers are aware of legal and compliance requirements when entering into global HCP and third party relationships.

Geographically, where is the majority of Porzio's growth coming from?

Most of our growth has been within the United States. We also have work from European companies never having done business in the US and now looking to create US commercial operations. A significant area of business growth has been from mergers, spin-offs, and private equity and venture capital investments in life sciences. We also represent R&D companies that have decided to commercialize themselves and are seeking FDA approval of their products, hiring contract manufacturers and contract distributors, as well as field-based personnel. We provide invaluable assistance in licensing, assessing and creating compliance programs, and compliance services and systems for these companies.

What is your assessment of how the regulatory landscape has evolved over the last few years?

One of the legal areas strongly impacting companies and how they market their products is the push for price transparency. There are currently 14 US states with cost disclosure laws. In four of them, companies have to justify the price of their new products. For example, they are required to share what percent of the price is attributable to research and development, licensing fees, sales forces, and marketing. In some states, you have to declare and rationalize price increases. Companies are considering how price increases might trigger reporting demands. Some companies have pledged to limit their price increases. More and more states are asking for the disclosure of typically confidential information. These laws most notably were put in force after the Martin Shkreli ("Pharma Bro") scandal.

As a result of this regulatory pressure in the US, some companies have determined parallel approvals are safest, looking for approval in Europe as well as in the US. Organizations are becoming global earlier and a big reason for that is the price pressure in US. Lower prescription prices are also becoming a strong campaign message for politicians.

What would you like to achieve for Porzio?

Porzio wants to continue to build on our services. As an organization, we began providing services by supporting companies in their state compliance needs and today, we have evolved to handling state, federal, and global compliance. We will continue to be a global compliance leader for the life sciences industry. We want to continue to be recognized as a unique organization able to provide systems, services, and regulatory and legal guidance under the Porzio family of companies. Porzio is a one-stop-shop where governance, process and systems come together to satisfy compliance obligations and provide a sound foundation for a biopharmaceutical company's operations.

How does the prevalence of biopharmaceutical companies in New Jersey compare to Boston?

There has been a bit of a renaissance here in the state of New Jersey and there is so much talent. As a result we are not seeing an out migration of companies. We are actually seeing more companies coming in than are leaving. Boston has also had strong growth and our office there is growing exponentially. ■

EXPLOSION OF MODALITIES

Source: Evercore

	Pills	Injectibles	Antibodies	Viruses	Oligos	mRNA	CRISPR	Zinc Fingers	Micro-biome	Exosomes	TPD	Digital Therapies
TODAY	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2010s	✓	✓	✓	✓	✓	✓	✓	✓				
2000s	✓	✓	✓	✓	✓							
1990s	✓	✓	✓									
1980s	✓											

<<10

areas where they otherwise have a hard time building themselves," said Michael Gladstone, a principal at Atlas Venture.

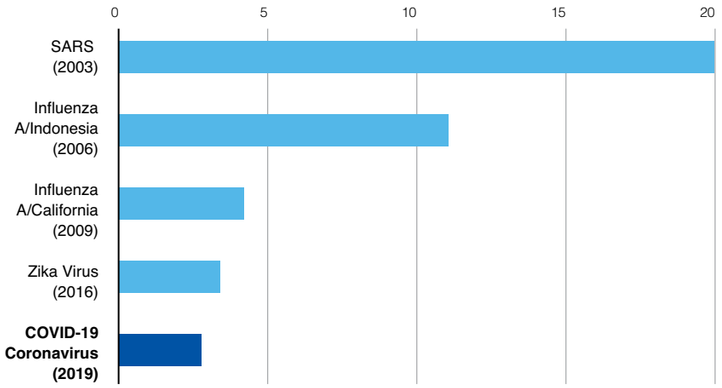
There are also numerous different modalities offered today that provide the R&D community and clinicians with a differentiated toolkit for being able to address different conditions. This gives companies the tools to tailor and refine how they think about making new medicines for specific conditions. CRISPR, messenger RNA, targeted protein degradation, microbiome and digital therapies are all tools that are now becoming more widely used.

An example is that the gene-editing power of CRISPR technology is now being increasingly directed at fighting diseases, originally genetic ones, but more recently, it has been harnessed to fight infectious diseases, including the novel coronavirus. Multiple teams inside and outside of academia are working on using CRISPR for more effective tests. Mammoth Biosciences claims it has developed a test for Covid-19 that cuts the result time from several hours to less than 30 minutes. Sherlock Biosciences has produced a protocol that could work like a pregnancy test, giving a positive signal on a test strip. Although the engineering of cells once seemed to be science fiction, the most important measure of success is how these new modalities improve the lives of patients and, in 2020, the life sciences industry is better equipped than ever.

Covid-19 has thus far proven to be an unparalleled black swan event. However, no era passes without its share of defining moments. During this generationally challenging time, companies and entire industries have shown they are up to the task of tackling the public health crisis. By harnessing all the American energy, ingenuity and expertise in the life sciences and leaning on the country's innate capacity to come together and solve big problems, the odds are good that a scientific breakthrough will occur that will resolve this crisis. This pandemic is a painful reminder that much of the work done in the life sciences industry has life and death consequences. It is critical that the industry continues on its growth path; lives will be saved as a result. ■

VACCINE DEVELOPMENT: MONTHS FROM VIRAL GENETIC-SEQUENCE SELECTION TO FIRST HUMAN STUDY

Source: FDA, clinicaltrials.gov, CMR



HISTORY OF PANDEMICS

Source: Forbes

Here are some of history's most deadly pandemics, from Antonine Plague to Novel Coronavirus (COVID–19)

Antonine Plague 165–180
DEATH TOLL > **5M**

Plague of Justinian 514–542
30–50M

Japanese Smallpox Epidemic 735–737
1M

Black Death (Bubonic Plague) 1347–1351
200M

Small Pox 1520
56M

17th Century Great Plagues 1600
3M

Throughout the 17th and 18th centuries, a series of "Great Plagues" routinely ravaged cities across Europe

18th Centyury Great Plagues 1700
600K

Cholera 6 outbreak 1817–1923
1M

The Third Plague 1855
12M

Yellow Fever Late 1800s
100–150K

Russian Flu 1889–1890
1M

1918–1919 **Spanish Flu**
40–50M

Asian Flu 1957–1958
1.1M

Hong Kong Flu 1968–1970
1M

1981–Present **HIV/AIDS**
25–35M

SARS 2002–2003
770

Swine Flu 2009–2010
200K

MERS 2012–Present
850

Ebola 2014–2016
11.3K

2019–Present **Novel Coronavirus (COVID–19)**
+300K *As of May 2020*

Jay Shukla

President and CEO
NIVAGEN PHARMACEUTICALS, INC.

Nivagen is engaged in the development, acquisition and sales of generic prescription drugs and OTC products for the North American market

What value does Nivagen bring to buyers?
The buyers in the market are consolidating, especially in the generics area. For example, Walgreens and AmerisourceBergen are buying as one group; Rite Aid, Walmart and McKesson also buy as one group, and so do CVS and Cardinal Health. This puts pressures on suppliers and lowers prices. It decreases the market size for suppliers to sell to. It also exposes business to risks when issues arise in areas such as regulation, patenting and logistics. In the pharmaceuticals space this is a particularly delicate scenario because when production halts, it is time and resource consuming to restart it.
Nivagen stresses the value of our supply track record and our role in helping buyers diversify risk. Most of our products are vertically integrated and this represents robust supply. Buyers have the following considerations: product, price, supply and quality. Price used to be the main determinant of business, but supply has superseded it, as companies have become conscious of the importance of consistency. We have an excellent track record with almost zero supply issues and an attractive portfolio of services.

What types of drugs do you provide to buyers?
We do not have a specific therapeutic area. Instead, we go after the generics with the least competition. Our strength is to identify the niche generic, execute fast and reach the market. We focus on what is less crowded and provides good return margins.
Two years ago, we changed our focus from B2 generics to developing generic injectables and ready-to-use premixes. They are not yet on the market as we are in the process of review and approval. We look at our buyers' needs. For example, being innovative in the dose form: if a pain patch is more convenient for the buyer than a gel, then we work to make that convenience a reality.

Pending patent cliffs are a big news item today. To what extent is this an opportunity for Nivagen?
In the big billion dollar plus molecule space, there are multiple filers. Most of them are vertically integrated from API to manufacturing and commercialization. For us to compete with them in the long run is difficult. We are not going after the big molecules unless there is an additional challenge we can address – something to do with formulation or manufacturing. Niches are our expertise, and we work closely with the buyers to understand how we can tailor to their needs. There is a lot of opportunity in the field of unapproved drugs. We do safety and clinical studies to make these drugs effective.

How important are partnerships to Nivagen's business?
The cornerstone of Nivagen's success is our partnerships. We co-develop products with FDA qualified manufacturing facilities. We bring value through our market intelligence capabilities, and insuring the right product selection. We also bring regulatory and product management support. Finally, and of key importance, we provide a distribution platform. There is an abundance of cost advantages and benefits from a shared construction of infrastructure. Partnerships also help in diversifying risks.

How does Nivagen's commercialization platform help foreign companies access the US market?
Nivagen helps foreign companies avoid costs associated with manpower, warehousing, distribution, customs clearance, vendor agreements and government contracts. In their route to the US market, we take care of everything. They get paid for the inventory and for royalties. To date, business has come mostly from India and Europe, but we are seeing growing interest from Chinese and Taiwanese companies. Smaller companies value partnering with us because our size allows for preferential monitoring and attention.

Over the next two to three years, what goals do you wish to achieve at Nivagen?
We want to expand and are looking to raise money through a funding round, which will allow us to scale up our team and platform, and set up a small sterile unit.
We are looking for a partner with manufacturing capabilities in the injectable space. They must be interested in a profit split. We bring them a ready-to-go product and, in turn, we expect the partner to eat up the cost of scale up. Then we split the filing fee and profits. ■

Doug Giordano

Senior VP of Business Development
PFIZER

Pfizer's CEO has outlined a plan for the company that is more nimble and poised for growth. Can you explain how business development activities can help achieve this plan?
We have a very strong pipeline right now with the potential to bring multiple breakthrough therapies to patients in the next five years, and our near- to mid-term focus for business development is to advance the pipeline to help deliver on the opportunities ahead of us.
The way we plan to deliver on those opportunities is largely the same as it's been in recent years – which is by evaluating the capabilities of our internal science and deciding whether we are able to achieve our goals with the resources we have. If not, we seek to fill the gaps through external collaborations.
Pfizer has evolved as a partner in recent years, and we recognize that breakthroughs can come from many different places. We also recognize that breakthroughs are built by pairing capabilities from different partnerships and working together toward a shared overarching vision, such as what we've done in gene therapy.

How does Pfizer's approach to business development differ from your peers?
We believe that our differentiation comes from our capabilities, such as medicinal chemistry, product development and manufacturing, to name a few. It's important for us to ensure that partners understand the true depth and breadth of our expertise, so we often bring our scientists with us to the negotiation table.
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 – including patients, innovators and investors – are positioned for success.

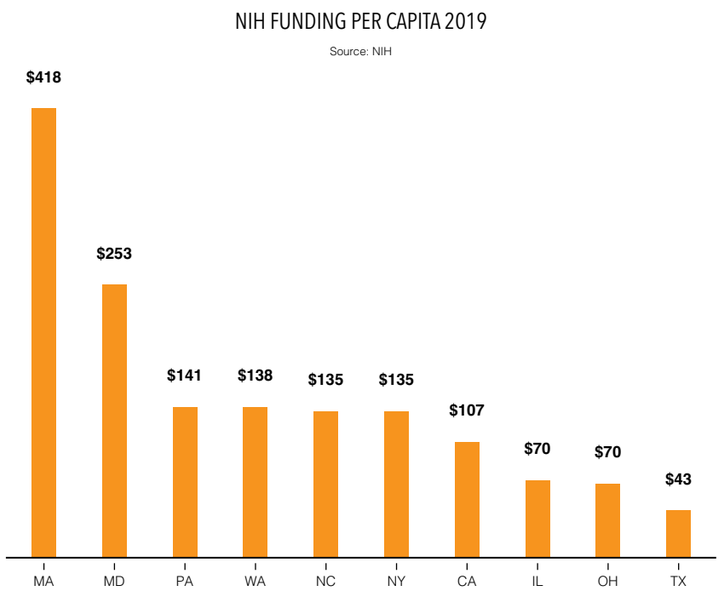
How do the joint ventures in consumer health and off-patent drugs announced last year fit into Pfizer's structure and priorities?
Pfizer had three unique businesses: an innovative business, an off-patent drugs business, and a consumer healthcare business. Each of those are now in a place where they can create the most value – Upjohn is expected to combine with Mylan to become a new pharmaceutical company, Viatris, later this year, and Pfizer Consumer Healthcare has combined with GSK's consumer healthcare business to form a new consumer healthcare joint venture and could eventually be spun off into a new company. Pfizer will become a more science-focused, high-growth company that is well-positioned to deliver breakthroughs that change people's lives.

Oncology continues to be an important area for investment and R&D. Can you shed light on Pfizer's oncology strategy, particularly in light of the recent acquisition of Array Biopharma?
Pfizer invests in areas where we see the greatest opportunity and where we believe we can deliver the best value. Our core therapeutic areas are: inflammation and immunology, internal medicine, oncology, rare disease, and vaccines.
We look to business development to enhance our expertise in certain aspects of the core therapeutic areas; for example, breast cancer and prostate cancer. We look to augment our existing pipeline through partnerships that add 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. While not as large as our Array transaction, Kineta and eFFECTOR are recent examples.
The acquisition of Array in July 2019 gave us commercial products, as well as late-stage pipeline assets that we expect to reach patients within a few years. In addition, the expertise found within Array complements the expertise within Pfizer, and we believe that by combining our efforts in this space we will be well-positioned for future growth in oncology.

What can we expect from Pfizer in terms of business development over the next 2-3 years?
In the near-term, our focus is on partnerships that will allow us to bring potential breakthroughs to fruition in the next few years. We will continue to invest in science through bolt-on acquisitions like Array and Therachon, and through research and development agreements like our recent deals with Vivet Therapeutics and Akcea Therapeutics.
True innovation and good science, even if outside our core therapeutic areas, will always be an opportunity for us. ■

Introducing The Hubs

BUILDING LASTING ECOSYSTEMS



In America there are a few states whose reputations are inextricably associated with their dominant industry. When people think of Michigan it conjures up images of cars coming off a production line in Dearborn. For Texas it is oil wells and for Hawaii, it is dazzling tourist beaches. New Jersey has a less strong, albeit equally important, connection with its pharmaceutical industry.

New Jersey is often referred to as the world's 'medicine chest' because it is home to 13 of the top 20 pharmaceutical companies globally. These include giants such as Johnson & Johnson, Merck and Bristol-Myers Squibb. In 2019, companies with a footprint in New Jersey were the source of over 50% of all novel FDA medicine approvals and Governor Scott Murphy continues to push legislation that incentivizes the biopharmaceutical industry. He reinstated and funded the New Jersey Commission on Science, Innovation and Technology (NJCSIT) and has been advocating for the passage of the Evergreen Innovation Fund, which will encourage and allow venture capital firms to partner with New Jersey businesses under a format where their investments will be matched dollar-for-dollar by the state.

The garden state has been considered the global center of gravity of the pharmaceutical industry for many decades and, although the advent of biotech has brought about new competing clusters, New Jersey's talented workforce still delivers scientific discovery in spades. The state also offers access to major airports as well as the capital markets of Manhattan; a big additional advantage for biotech companies, whose nascent science may demand massive funding on the path toward treating patients. Alongside big pharma, the state possesses a service provider network that is second to none including accountants, attorneys, clinical research organizations, contract manufacturing organizations and others that help companies bring medicines and therapies to market.

According to David Kimball, senior vice president for research and economic development at Rutgers University: "There are two fundamental advantages to being in New Jersey. One is that rent prices are cheaper and the other is the unmatched talent pool. Many of the best minds in drug development are still here from the heyday of big pharma and, as a result, New Jersey has the highest percentage of PhDs per capita of any state."

What New Jersey is to big pharma, the same can be said of Massachusetts when it comes to biotech. The Boston metropolitan area, and in particular Cambridge across the Charles river from central Boston, seems to be holding its own as the pre-eminent biotech hub in the world. The density of research institutions in Massachusetts means that it receives US$418 per head in funding from the National Institute of Health (NIH), according to figures from that organization. Boston in particular has received more NIH funding than any other US city for each of the past 24 years. In the last decade, there has been 13 million square feet of lab space filled, which has boosted the construction and real estate industries. The employment rate grew by 35% and the average yearly salary in life sciences is now US$148,000 per year, according to MassBio.

Cambridge is currently a key global hub biotechs, and I cannot think of any large pharma company that does not have an R&D footprint here. Funding and valuation in the biotech sector has been strong, encouraging large pharma companies to acquire these companies or invest in them at a very early stage to fuel their R&D activities. The energy we see in the Boston area is amazing, with the number of biotechs that are here and the incredible talent that is available.

- Vivek Sharma, Former CEO, Piramal Pharma Solutions and Decision Resources Group

Transforming cities

The history of the Boston area cluster can be traced back to the late 1970s and early 1980s, when Biogen and Genzyme, two biotech drugmakers, were founded by scientists from nearby academic institutions. Other scientists, especially from MIT and Harvard, Cambridge's two internationally renowned universities, followed suit and created innovative startups of their own. This encouraged global pharmaceutical giants, struggling with poor productivity in their existing research facilities, to set up labs in and around Cambridge, which at that time was considered to be a desolate wasteland of empty parking lots and crumbling warehouses.

Today Cambridge's Kendall Square has become the key focal point within the east coast biotech cluster, as it is home to the greatest concentration of biotechnology companies in the world. The area is home to biomedical firms large and small, but also to the investors, patent lawyers, CRO's and suppliers supporting them.

While the kinetic energy of having everyone squished together is hugely appealing to many, it also has its drawbacks. The 2019 annual report by real estate firm JLL revealed that developers cannot keep up with demand for lab space, with vacancy rates hovering at 0% in East Cambridge. Lab space is so coveted that it fetches an average monthly rent approaching US$100 per square foot. This reality is a big potential deterrent for emerging biotech companies deciding where to base their operation. It is also why the biotech boom is no longer limited to Cambridge and Boston. Areas across Massachusetts like Worcester, Waltham and Amherst are also benefiting, because they offer greater access to more affordable space and are more accessible to workers, who prefer to avoid the Boston's notorious traffic gridlock.

Furthermore, there is significant competition from other emerging clusters with a similar level of premier hospitals, universities and lower costs. Neil Belloff, chief operating officer and general

New York Life Sciences Hub

TOP LIFE SCIENCES COMPANIES

Source: EMSI

COMPANY	TYPE
Pfizer	Big Pharma
Eli Lilly	Big Pharma
Bristol-Myers Squibb	Big Pharma
Intercept Pharmaceuticals	Big Pharma
Roche	Big Pharma
Enzo Biochem	Biotech

TOP NIH-FUNDED INSTITUTIONS 2014-2018

US$1.9B
COLUMBIA UNIVERSITY HEALTH SCIENCES

US$1.5B
ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

US$1.1B
NEW YORK UNIVERSITY SCHOOL OF MEDICINE

BIOTECH AND LIFE SCIENCE IN NEW YORK STATE

Source: NewYork Bio

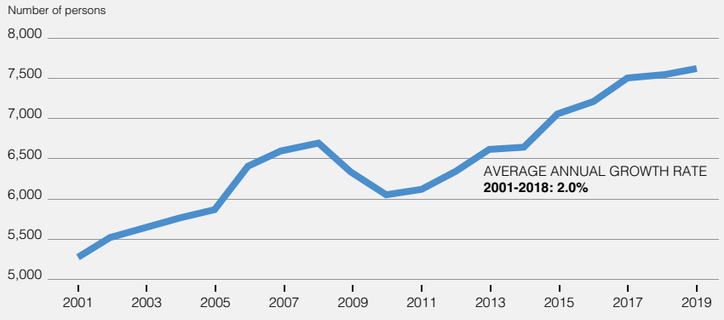
#2 RANK NATIONALLY
New York is second in the nation for bioscience jobs

US$2.6 BILLION
New York has received $2.6B in National Institutes of Health funding and 5,000+ research awards

#2 IN THE NATION
New York is second in the nation for higher education degrees in biological sciences

LIFE SCIENCES TALENT POOL: **7,648**

Source: EMSI



counsel at Eloxx, a clinical-stage biopharmaceutical company, commented: "State governments can play an important role and establish centers of excellence around their great academic institutions. Heavily taxed states like Massachusetts and New Jersey must be cognizant of the fact that states with lower tax structures are offering attractive incentives for companies and employees to relocate."

Both Philadelphia and New York City have looked to tap into the industry. These emerging clusters have a similar level of premier hospitals and universities, while also offering lower costs and some attractive incentives. More than 30 cell and gene therapy development companies and roughly 80% of all pharmaceutical and biotech companies in the U.S. have offices in Greater Philadelphia, according to data from Select Greater Philadelphia. Many of these companies have played a founding role in cell and gene therapy, and gene editing, and today, as over US$550 million has been invested in local manufacturing of these modalities. In 2019, Cranbury, New Jersey based Amicus Therapeutics, announced that it would open a global research and gene therapy center of excellence in Philadelphia's uCity Square; one of a number of announcements indicating a robust growth environment for Philly's life science industry.

New York City's life sciences market is also gaining momentum, as developers plan to bring more than 2.6 million square feet (msf) of dedicated office and lab space online over the next three years. The city has long taken a back seat to places like San Francisco and Boston in the life sciences, however, New York City offers an appealing environment, as it is already home to many of the necessary features of a mature cluster. The presence of leading technology firms, world renowned medical research centers, top-ranked academic institutions and large successful pharmaceutical and biotechnology companies positions New York City as the most sought after emerging life sciences cluster. There is also the precedent Regeneron has set by transforming itself into one of the leading biotech companies in the world, while being based in New York.

Peter Meath managing director, co-head of healthcare and life sciences at J.P. Morgan Commercial Bank spoke to the dynamism New York's life sciences industry is experiencing. "New York is one of the most fascinating case studies. Ten years ago, talking about starting an early stage biotech company in New York was almost laughable from a cost effectiveness perspective. Now it is an extremely robust area for new company development and growth, which is a testament to the work that incubators, capital providers and universities have done."

In the life sciences, location is not necessarily the most important factor, as evinced by the many virtual companies that manage to make do. However, it is clear that companies find value in clustering. In the end, having potential collaborative partners close by is important, and the possibility of serendipitous interaction with the leading minds in the sector is an opportunity that is hard to pass on. ■

New York is one of the most fascinating case studies. Ten years ago, talking about starting an early stage biotech company in New York was almost laughable from a cost effectiveness perspective. Now it is an extremely robust area for new company development and growth, which is a testament to the work that incubators, capital providers and universities have done.

- Peter Meath, Managing Director, Co-Head of Healthcare and Life Sciences, J.P. Morgan Commercial Bank

Greater Philadelphia Life Sciences Hub

Source: Cushman & Wakefield

9.7 MSF
MARKET SQUARE FOOTAGE

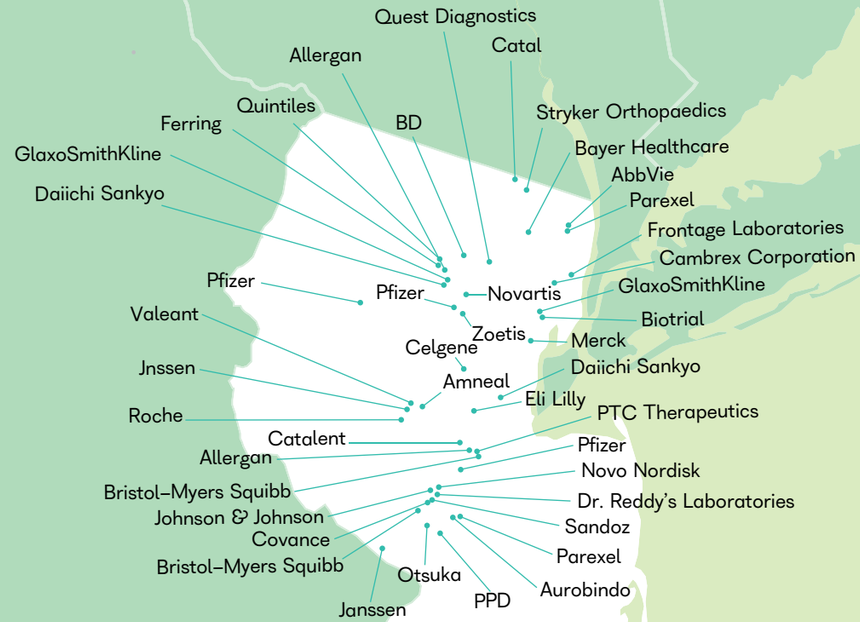
US$30.78
AVERAGE ASKING RENT (PER SF)

15K
TOTAL BIOTECH + R&D EMPLOYEES

+4%
TOTAL EMPLOYEES SINCE 2010

10.4%
VACANCY

New Jersey



PHARMACEUTICAL AND BIOTECH CLUSTERS

#2
REGION for NIH Funding

50%
of 2019 FDA approvals

27,000
LIFE SCIENCES Grads

139
FDA–REGISTERED BIOPHARMA Manufacturing facilities

Source: Choose New Jersey

Debbie Hart

Founding President & CEO
BIONJ

Why is New Jersey an advantageous place to operate a biopharmaceutical company?
New Jersey offers research, talent, funding, available space, university partnerships and industry expertise for life sciences companies. From incubators to stand alone laboratory space at research parks and hubs, New Jersey has world-class research universities, medical schools and some of the best hospitals in the country. Home to 13 of the top 20 pharmaceutical companies, there are opportunities to partner with big pharma companies, such as Johnson & Johnson, Merck and Bristol-Myers Squibb. There are no other states that have the presence of big pharma on such a large scale. This allows for great opportunities, growth and breakthrough innovations. New Jersey's location provides strategic access to the world's financial and regulatory centers, along with the most highly educated workforce in the United States. In fact, New Jersey has the highest concentration of scientists and engineers per square mile in the world. We have a service provider network that is second to none including accountants, attorneys, clinical research CROs, CMOs and others that help companies bring medicines and therapies to market. The concentration of our research hospitals, medical schools and universities, combined with the state's population density, multicultural diversity and transportation infrastructure makes New Jersey a perfect location for the life sciences industry. More than 300 CROs and 120 CMOs are located here. Finally, lab space is not only available, but at a much lower rent than in Cambridge or New York City. New Jersey has the highest concentration of specialized commercialization expertise in the world. We have seen many companies with a drug approval on the horizon coming to New Jersey to tap into New Jersey's plentiful commercialization talent. One of the areas where I am particularly excited to see growth is in the early stage innovators. In recent years, our academic institutions have increased the number of spinouts. These institutions are looking at technology transfer with a whole new eye. All of these existing strengths and new developments are coming together to bolster New Jersey's position as a life sciences hub.

What has been the most impactful incentive offered by Governor Murphy that is benefiting the state's biopharmaceutical industry?
As of January 1, 2020, the Angel Investor Tax Credit increased from 10% to 20%, plus a 5% bonus for women and minority-owned businesses as well as those located in an Opportunity Zone. The expanded Angel Investor Tax Credit is now one of the most progressive and potent tools of any state to encourage investments in early stage innovative companies. Another initiative, the NJ Ignite program, offers up to six months of free rent for companies in certain geographies. This has proven meaningful for early stage innovators. Governor Murphy also reinstated and funded the New Jersey Commission on Science, Innovation and Technology (NJCSIT). The commission just awarded its first round of SBIR (Small Business Innovation Research) and STTR (Small Business Technology Transfer) grants which will support companies at a critical time in their development. Another pending program is the Evergreen Innovation Fund, which will encourage and allow venture capital firms to partner with New Jersey businesses under a format where their investments will be matched dollar-for-dollar by the State. It also includes a component where other large companies can participate as investors and get tax credits in return. It would be the only one of its kind in the country.

Proposals coming out of DC that seem to have some traction are importation and international pricing for drugs. What is your view on these proposals?
We believe proposals, such as importation and international pricing, are the wrong approach for patients and for our health care system. Importation undermines the FDA gold-standard supply chain, will not achieve the anticipated savings and jeopardizes the health and well-being of patients. International pricing for drugs would decimate investment in the biopharmaceutical industry and reduce patient access to life saving cures.

What is your assessment on the overall health of the industry today?
In New Jersey, the life sciences industry is healthy and robust and bringing important new therapies and cures to market. In fact, in 2019, more than 50% of all novel FDA medicine approvals came from companies with a footprint in New Jersey. That innovation needs to be celebrated. In fact, at our Annual Meeting this year, we honored 31 novel drug approvals from 20 different companies. Now that's something to celebrate! ■

Robert K. Coughlin

President & CEO
MASSBIO

What does the Vertex Trikafta approval mean for patients with cystic fibrosis (CF) and what does it take to bring life-transforming drugs to market?
2019 has been the most fulfilling year for my family, in large part because Vertex's Trikafta was the first drug approved that worked for my son who has CF. Although there have been several approved CF treatments over the years, this is the first one that treats up to 90% of the CF population. This is another reminder just how difficult it is to bring a drug to market, as it took 18 years and billions of dollars to finally develop a drug that worked for my son and thousands like him. It takes countless failures and major investment to bring any life-transforming drug to market – but there is another ingredient that is essential: a supportive government. As a lawmaker, I realized that people in government have the power to either conduce or kill innovation. By intersecting policy, science and innovation, we could make Massachusetts the global leader for drug discovery and development. Creating a partnership between government, academia, and industry was the missing piece to making this a reality.

What challenges must be overcome to remain the worlds leading biotech cluster?
We have grown so much over the last decade, having added nearly 20,000 new life sciences jobs, making talent recruitment and retention a huge issue. The growth we have experienced is not sustainable, as we need to improve our infrastructure and transportation system to support current and future growth. It is no longer just about Cambridge and Boston, reas like Worcester, Waltham and Amherst are also benefiting from the boom, because there is greater access to space that is affordable and more accessible to workers.

To what extent do you fear some of the policy proposals coming out of DC may hinder innovation and remove economic incentives that encourage drug discoveries?
Policymakers do not understand the value prescription drugs bring to the healthcare system in terms of costs avoided elsewhere and to patients in terms of making them healthy and productive members of society. They also do not understand just how difficult it is to bring a new drug to market and the kinds of incentives we need to provide to investors to take the big risks required in this industry. We need to change our sick care system to a healthcare system, one that compensates companies based off of the value therapies bring to the market and to patients. For example, if you can give a patient with CF these new CFTR modulators, it keeps them out of the hospital, it keeps them from needing lung and liver transplants and it keeps them from dying.

How have the reforms made by CFIUS impacted foreign investment into biotech and are there valid national security threats associated with foreign entities taking ownership stakes in US based companies?
CFIUS shutting out money coming in from Asia was not good for our industry. I think it is even more catastrophic to our industry when bad immigration policy is brought upon us. It is extremely difficult to fill complicated positions in our industry that require a unique skillset of experience and education, and we can not always fill these positions with people from the US.

What areas of the industry are making the most notable progress in developing cures?
The industry has eradicated Hepatitis C. Our member companies are no longer just treating the symptoms of disease but are addressing the underlying cause of disease and doing so in a personalized manner. Gene therapy has also been a game changer. This technology has the ability to cure cancers, reverse blindness, cure fatal rare diseases, and more. We need to educate policymakers on the potential of these incredible innovations and ensure they do not halt innovation through harmful policies.

Where would you like to see Massachusetts biotech and biopharma industries in the future?
In the next five to 10 years, MassBio will focus on addressing challenges to keep Massachusetts the best place in the world for the life sciences and capitalizing on opportunities for growth. This includes a renewed focus on talent acquisition, especially diversity and inclusion, better demonstrating the value of our industry to patients and the healthcare system, and supporting advancements in digital health and convergence. ■

Massachusetts

50+ biotech companies,
2 million+ s.f. in lab space,
UMass–Lowell and 11 other colleges

50+ biotech companies,
WPI, UMass–Worcester,
and 16 other colleges

NORTHEAST

250+ biotech companies,
the top 4 NIH–funded hospitals
in the U.S., and 48 colleges

BOSTON
CAMBRIDGE
CORE

WORCESTER

WEST

128/SUBURBS

SOUTHCOAST

The immediate western suburbs
include 75+ biotech companies,
15 colleges,
3 million s.f. of lab space

Home of UMass–Amherst
and 21 other colleges.
Area known as
The Knowledge Corridor

Strong med device and biopharma
manufacturing capacity, with numerous
land sites in BioReady communities
and 10 colleges

#1
REGION
for NIH Funding

2010
17.8
MILLION
SQUARE FEET

over
12.4 MILLION
square feet of commercial lab space has been added to Massachusetts in the last 10 years, an increase of
70%

2019
30
MILLION
SQUARE FEET

THE BIOPHARMA INVESTMENT CLIMATE

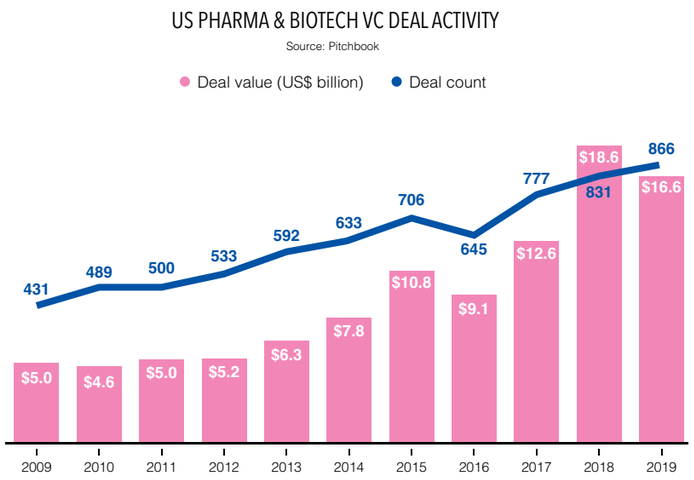
» Much of what was true before the COVID-19 outbreak in the United States is still true today. It is just going to take longer for some programs to materialize. The market value of investment capital has declined, and that will affect new capital investment. Clinical trials will take longer to enroll and some of them have been suspended. On the commercial side, the sales forces of the combined pharmaceutical-biotechnology industry are now working on a virtual basis – an unprecedented development. Things will take a while to sort out. But there is a real possibility of important efficiencies coming out of all of this. We may find out that there are new ways of doing things and that they work. «

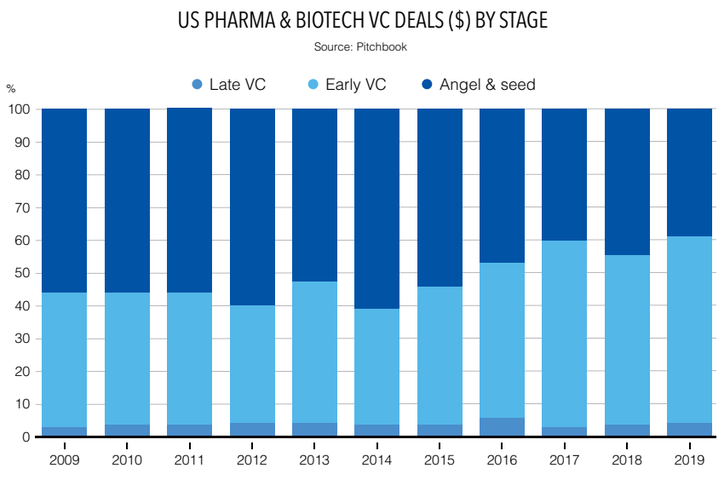
- Christopher S. Eklund,
Managing Director,
J.W. Childs Associates LP

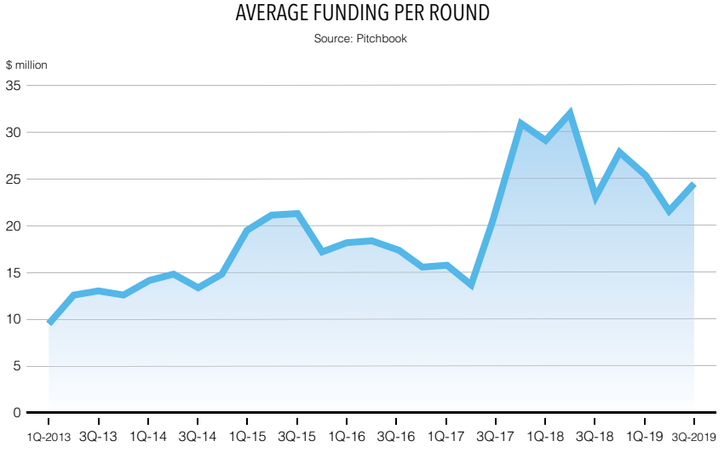
Image courtesy of PharmaLex

The Biopharma Investment Climate

FROM BULL MARKET TO UNCERTAINTY







At this years' J.P. Morgan Healthcare conference in January, the consensus view was that biopharma was going through a renaissance period, and expectations were for 2020 to be another prosperous year for the industry. Funds were readily flowing into startups pursuing novel medicines for oncology, immunology, rare diseases and next generation technologies. The sanguine outlook was justifiable given the explosive growth of capital inflows. Biotech oriented venture capital funds have doubled their assets under management over the last eight or so years, which has led to a large expansion of funding per round, and 50 plus funding rounds over US$100 million in 2019, according to Pitchbook data. This was unimaginable 10 years ago.

Fast forward three months, and companies now face questions concerning how to keep their clinical trials running, their scientists busy and their balance sheets strong, as Covid-19 threatens to upend plans and budgets.

Even under normal conditions, 80% to 90% of health-focused research never leaves the lab, according to Clarivate analytics. Many companies do not make it past the early stages of development. In many cases, they succumb to the "Valley of Death"; the period of development when companies are building their infrastructure and working on proof of concept, prior to being attractive to a broad pool of investors. Drug development is notoriously capital intensive and, with more biotechs in existence than ever before, the industry requires a steady flow of investment to keep laboratories churning out new medicines. Venture capital plays an instrumental role in this process.

Although the biopharma sector is normally somewhat insulated from the rest of the market, particularly during a health scare, it is certainly not immune to the effects of a more fearful investor psychology and a desire by many to de-risk until the pandemic blows over. Uncertainty about the timeline and nature of a recovery create divergences in opinion. For example, Robert Nelson, co-founder of Arch Venture Partners, has remained committed to investing through the pandemic. In his words: "This is a transient event, as painful and messy as it will be. A year from now, it is over. In China, people are already starting to reemerge."

By contrast, Tony Johnson, CEO of Goldfinch Bio, anticipates the crisis will bring about some changes in how investors view allocation of capital toward less liquid, private companies: "Markets were at an all time high in the early part of the first quarter. Since then, there has been phenomenal volatility and COVID-19 is contributing significantly to that. Public companies are now much less expensive, are more liquid and you can invest at significant discounts to where prices were at the start of the year." He continued: "For private companies, it could be more challenging, because investor interests were centered around their path to becoming public in the next one to two years. It was a way of getting involved with private companies earlier, at a lower valuation, so they could generate more returns for their fund when these companies went public. The challenge now is investors may be anxious about the overall market valuation and concerned that markets may still have forward downward movement to go until they return to where they were previously. For that reason, investors may be more inclined to sit on the sidelines when it comes to investing in private companies."

Regardless of the changes in the investing environment, great investment theses, strong teams and products that are in the clinic should continue to raise money and do well. The US is blessed with an abundance of risk takers undertaking truly transformational science. Therefore, as long as the economic incentives that help generate these discoveries remain in place, the future remains promising. It is worth remembering that many of the top tech companies we have today came out of the

Third Rock was founded during an economic downturn, and we will continue to invest in medical innovation regardless of the state of the economy. We continue to launch companies that we believe have the approach and ability to advance novel approaches to the diagnosis and treatment of disease. We actively consider scientific, medical, business development and financial strategies that together may help ensure our companies have every opportunity possible to weather any headwinds that may be ahead and deliver on their missions.

- Kevin Gillis,
CFO,
Third Rock Ventures

2008-09 financial crisis. Third Rock Ventures, one of life sciences' most avant-garde firms, was a product of the bear market in which it was created. "Third Rock was founded during an economic downturn, and we will continue to invest in medical innovation regardless of the state of the economy. We continue to launch companies that we believe have the approach and ability to advance novel approaches to the diagnosis and treatment of disease. We actively consider scientific, medical, business development and financial strategies that together may help ensure our companies have every opportunity possible to weather any headwinds that may be ahead and deliver on their missions."
Given the continued political clamor around drug pricing and an increasingly unpredictable future, investors may be more hesitant to put the time, energy, and capital into new startups. Particularly at a time when they may need those resources to support existing companies through a potentially precarious upcoming 12-24 month period. The early signals, however, are that the healthcare revolution will continue and companies will remain committed to investing aggressively in entrepreneurs working to meet unmet medical needs.

Reaching Inflection Points

Clinical development programs are particularly sensitive to COVID related disruptions. With the shutdown of the healthcare system in multiple regions of the world, and hospitals in particular, the impact on clinical trial timelines has the potential to be significant. Many sites have prohibited all elective procedures, which includes non-urgent visits and treatments for most non-life-threatening diseases. Patient screening and enrollment may also be shutdown or curtailed dramatically in some geographies due to travel and logistics restrictions. Logistically complex trials, like those in cell therapy, are particularly difficult in this environment. All of these pose big challenges to small biotechs that were expecting to enroll patients over the course of 2020. In this sense, it will be a big challenge for companies to reach the critically important goal of obtaining key catalytic data that demonstrates the value of an R&D program and justifies future rounds of venture capital funding.
According to Spiro Rombotis, CEO of Cyclacel: "Managing clinical trials through this period is a major concern for every company. It could completely derail the efforts of many companies. Not everyone is exposed to the same degree. Certain densely populated cities have been most affected, so if you have been running trials in Seattle or New York City, your impact will be higher than if you were conducting trials in Salt Lake City or Memphis. It illustrates the importance of having geographical diversity to be able to accommodate a different epidemic progression, while hospitals in certain areas are taxed for resources."

A New Model for Venture Creation

One of the most important changes over the past decade has been the paradigm shift from entrepreneur-centric to VC-collaborative startup formation. Back in 2010, it was common practice for startup entrepreneurs to pitch their company to VC firms looking for Series A capital. The founders would have assembled a story, team, a strategy, and often some "friends and family" seed funding, and would then tout their proposal around the venture community to see which firms would express interest in investing. Most startups would find standalone offices or labs to rent during this process. Today this dynamic is very different. The prior "on your own" entrepreneur-centric approach is less common. Today, a venture firm, working with a talented pool of entrepreneurs-in-residence, will scan through new science or technological concepts that emerge out of academia and to push forward to form a company around these. The new startup is most often incubated or housed within the venture firm's offices in its early days while it pulls itself together, often with VCs or their teams taking on acting operating roles until a seasoned team can be recruited.
This is the model that leading VCs including Atlas, Third Rock and Flagship Pioneering have adopted and it has led to many profitable exits. In summarizing the benefits of this model Michael Gladstone of Atlas Venture said: "A crucial ingredient in the company, which is often more important than the technology or the IP, is the people and leadership of these companies. We can play matchmaker between an interesting technology and asset and a talented entrepreneur and management team. We use our incubator space to co-house entrepreneurs, so they can work with the investment team to find and identify interesting technologies and then put companies together around them." ■

Jim Neal

CEO
XOMA

How has COVID-19 impacted your operations as well as clinical trials and the development of your assets?
There were a couple of impacts – most notably, clinical trial recruitment is a big question. Some companies stopped all recruitment. Responses and the impact on their finances have been different. Thus far, oncology trials are less impacted generally, but it is a work in progress understanding the overall impact.
From a financial point of view, companies in the pharmaceutical industry are doing well, and the programs will be back on track as soon as hospital access normalizes. In fact, this crisis provides opportunity in that there is potential for more biotech companies that will see a royalty monetization transaction as a source of interesting capital if the equity markets shut down for them.
This has been positive for the execution of our strategy as a potential capital source that is valuable for the community.

What is your acquisition strategy?
The companies we look for are in early or mid-clinical stage. The questions of who will do the development and the commercialization are answered, because they are subject to a license agreement.
A transaction with XOMA allows companies to retain a higher ownership percentage of their company and we can provide them with capital that is important for them to start other programs. We typically deploy US$5 to US$15 million to companies.

Is XOMA making any investments in infectious disease assets?
We want to be agnostic to the therapeutic area focus and will look at opportunities in the infectious disease space if they present themselves. We have slight emphasis in oncology. There are many antibodies in our portfolio. The strategy is being agnostic toward therapeutic areas. If COVID-19 creates more emphasis in the area of infectious diseases and more partnerships take place with biotech and pharmaceutical companies, these are more opportunities for us to think about monetization transactions.

Could you give an insight to the steps XOMA is taking to drive value creation for shareholders?
As a biotech company, we think about the science underpinning these molecules and the impact it will have on patients. From a shareholder point of view, there are two ways one can anticipate growing returns. First, our pharmaceutical and biotech partners are investing billions of dollars into programs without us spending anything. As molecules advance in the pipeline, they become increasingly valuable. A good example is companies like Novartis that start talking about the CD40 (iscalimab) program and the impact it can have on the lives of patients, as well as on their P&L. The overall profile of our portfolio has a center of gravity around Phase 1 and Phase 2. In a couple of years, it will have a center of gravity in Phase 3, which would be a great driver to our portfolio-maturity dimension of shareholder value. The second value dimension is the acquisition of additional assets – going from 40 to the more than 65 assets we have today. This increases the revenue potential and chances of commercialization. Risk is mitigated by having a significant number of additional assets in the case one molecule fails. ■

Kevin Gillis

CEO
THIRD ROCK VENTURES

Third Rock Launched its Fund V in June. What is the strategy for the fund and what are the biggest areas of unmet medical need you look to invest in?
With Fund V, we will continue to execute on its strategy of discovering, launching and building innovative life sciences companies that have the potential to transform the lives of patients and their families. Funds raised will be used to create companies focused in many different areas of high unmet medical need including cancer, neurological disorders, rare genetic diseases, immune disorders and cardiovascular diseases.

Early stage investors have to be confident they will be rewarded years into the future, given the long timeline to commercialization. In light of the drug pricing debate and general anti-biopharma political punditry, do you see this affecting startup formation?
Third Rock was founded during an economic downturn, and we will continue to invest in medical innovation regardless of the state of the economy. We will continue to launch companies that we believe have the approach and ability to advance novel approaches to the diagnosis and treatment of disease. We actively consider scientific, medical, business development and financial strategies that together may help ensure our companies have every opportunity possible to weather any headwinds that may be ahead and deliver on their missions.

How does TRV go about stress testing ideas?
For each project, we put together multi-disciplinary teams of our people, leading scientific founders and expert advisors. We vet the opportunity and competitive landscape with industry partners, and we explore opportunities to build companies from the ground up together with large biotech and pharmaceutical companies, as well as strategic partners from the venture community. Projects are refined through nearly a dozen reviews of the vision, science, people, business and R&D plans and go through at least four go or no go decisions. ■

Michael Gladstone

Principal
ATLAS VENTURE

Atlas Venture is an early-stage venture capital firm that invests in life sciences startup companies in the U.S.

Can you provide an overview of Atlas Venture's current portfolio and the approach you take to investing?
Our company-building approach is flexible and allows us to customize the business model for the science rather than the other way around. We are investing now out of our 11th fund which is a US$350 million closed-end fund. We have a separate vehicle, a US$250 million opportunities fund which is a vehicle to invest in the Series B and later rounds of our existing portfolio companies as they grow and mature. A big part of our strategy in being an early stage investor is venture creation. We are helping to form and build many companies we invest in – at least two-thirds of our companies are ones where we work together with academic or industry experienced entrepreneurs to form and launch and often initially incubate in our office. To support that, two thirds of the floor space here in Atlas's office is incubator space for six to eight nascent companies with the expectation that in six to 12 months they outgrow that space and launch elsewhere nearby.

Is the recent success of the biotech sector more a product of the long-term bull market that we are experiencing or is it reflective of the maturing of the sector?
The last six to eight years have been great for healthcare and biotech. Underlying that are real secular changes in drug discovery and development. We are reaping the benefits of the genomics boom in the early 2000s, which yielded new drug targets, coupled with many new tools at our disposal to make drugs and to evaluate biology. Overall, the tools and information at our disposal are at a dramatically different place than they were 20 years ago, which has contributed to many transformative new drug approvals and strong capital market performance for the companies delivering those drugs.

How much of the value being driven from the industry is coming from innovative and novel drug therapies?
It is more important than ever to arrive early in a new class of drugs. It used to be that if you were the first to market in your therapeutic class, you might have that class to yourself for five to 10 years. But that period is shrinking, and now you can have several players in the same product space within a few years. Often, a disproportionate share of the market goes to the group that arrives first or second or comes in with a dramatically differentiated product. This competition and the sense of urgency it provides is a great thing for patients, and it makes it more important than ever for biotechs and pharma to address outstanding unmet needs. Showing up late with an undifferentiated product is unlikely to be commercially viable.

Regarding Covid-19, what is the timeline to bring a therapeutic to market. How does this compare to the typical timeline?
It can typically can take anywhere from two to six years to go from starting a program from being ready to enter human clinical trials. The typical timeline from clinical entry to FDA approval can be somewhere between four to 10 years. Obviously we'd like to have effective coronavirus therapies and vaccines much sooner than that, and companies and regulators are working hard to streamline this path in light of the urgent medical need.
The fastest opportunity for Covid19 is probably to repurpose existing drugs, such as antivirals or anti-inflammatories, to determine if they have clinical benefit in Covid19 infection. If you have a drug that is relatively safe in humans and you have an idea of what dose to give, repurposing it to be able to do a rapid clinical study in coronavirus is relatively quick. The road is likely longer to establish the safety and efficacy for novel therapies, such as vaccines or neutralizing antibodies, but there is already tremendous progress being made very rapidly, and multiple novel drug candidates from these classes could be in clinical trials within 2020.

What areas are primed to make the biggest breakthroughs?
There has been an explosion of new modalities, things like cell therapy, gene therapy, oligonucleotides, and targeted protein degradation. As we learn more about the genetic underpinning of diseases, these novel tools will increasingly be a powerful and direct way to directly address the central cause of many illnesses. ■

Christopher S. Eklund

Managing Director
J.W. CHILDS ASSOCIATES LP

Biotechnology is a tremendous growth market but how has COVID-19 and the market changed that?
Biotechnology is a US$550 billion global market, expected to be US$727 billion by 2025. Biotech has held up reasonably well in the downdraft and may be one area that is poised to benefit. Longer term, we are hopefully still in the early stages of this growth cycle and witnessing one of the great growth markets. Right now, across the industry, a huge amount of effort is going into developing vaccines, immunoglobulins and anti-inflammatories that target both COVID-19 and/or its key symptoms. But work also continues on therapeutics across all indications. Much of what was true 10 weeks ago, before the Coronavirus outbreak here, is still true today. The market value of investment capital has declined, and that will affect new capital investment. Clinical trials will take longer to enroll and some of them have been suspended.

Can you give us an example of an investment that has worked well for you?
The best example of this is Biohaven Pharmaceuticals, which we invested in over seven years ago. Biohaven's lead product, Nurtec, is a best-in-class therapy for acute migraine with a clean safety profile. It was approved by the FDA on Feb 27. Recently, a Phase 3 trial also showed Nurtec's efficacy as a preventative agent for migraine, making it a possible alternative to the injectable CGRP monoclonal antibodies on the market. Combining both acute and preventative treatment in a single oral dose could represent a paradigm shift in the market.

What was the appeal of investing in Omax Health and Kleo Pharmaceuticals? In the case of Omax, what potential do you see in supplementation that can enhance cognitive performance?
Omax Health is a nutritional supplement company that produces one of the highest-quality omega-3 products on the market. Omega-3 polyunsaturated fatty acids are important to virtually everyone's diet in maintaining optimal cholesterol and triglyceride levels. Since we launched that product back in 2012, we have built a portfolio of products around it, including probiotics and a line of CBD products for sleep, pain relief and joint health.
Kleo Pharmaceuticals is an oncology company that has developed an antibody recruiting molecule (ARM) that recruits a patient's own endogenous antibodies to kill cancer cells. Our KP-1237 product, a CD38-targeting ARM, recently received IND-authorization for a trial at the Dana-Farber Cancer Institute that combines KP-1237 with a patient's own natural killer (NK) cells to treat multiple myeloma in post-transplant patients. The KP-1237 ARM is designed to transport a patient's activated NK cells to the CD38-expressing tumor without killing NK cells.

What do you think of the approach of bringing research scientists in-house to incubate new companies based on early scientific discovery?
That is what happened at Kleo Pharmaceuticals. We were working with Yale Professor of Chemistry and Pharmacology, David Spiegel, who developed the concept of antibody recruiting molecules (ARMs) based on his research work in the lab. That is how the project started.

Have there been any changes in the process of capital raising in biotechnology?
Yes. Even though there is a shortage of biotech companies in some hot areas, capital-raising and M&A dynamics have changed. Buyers and investors are looking more closely at valuation and, in particular, how well a company has hit a series of inflection points and endpoints. As a biotech company, you can no longer just go out, hire a banker and launch a strategic process to raise money or sell the company. Communication with potential partners begins at any early stage, involves the science and business development teams, and continues over a period of time. In the case of an IPO, meeting inflection points is important both before and after the IPO.

Over the next two years what goals would you like to achieve at JW Childs in terms of portfolio companies? What development do you want to see?
From a direct investment standpoint, we are looking to add perhaps three or four new portfolio companies a year out of a pool of companies we look at. We look for companies that will make a difference with a breakthrough in an area of unmet need. If we like the team and we believe we can contribute meaningfully, and the valuation is reasonable, we may invest. Often, these opportunities arise from the companies we are already invested in. ■

Merger Spree

ROBUST M&A DISPLAYS VALUE DESPITE PUSHBACK

M&A activity is rampant in the biopharma industry. From Big Pharma mega-mergers to smaller acquisitions of emerging startups, the life sciences industry has seen a huge amount of deal activity in the biopharma space every year for the past decade. 2019 saw several large M&A transactions closed or announced, highlighted by the BMS-Celgene, and AbbVie-Allergan mega-deals. On the biotech side, Loxo-Lily and ArQule-Merck also made waves. According to BMO Capital Markets data, there was nearly US$260 billion in M&A deal activity for 2019. Over the past eight years, the value of biopharma M&A deals in aggregate is US$1 trillion.

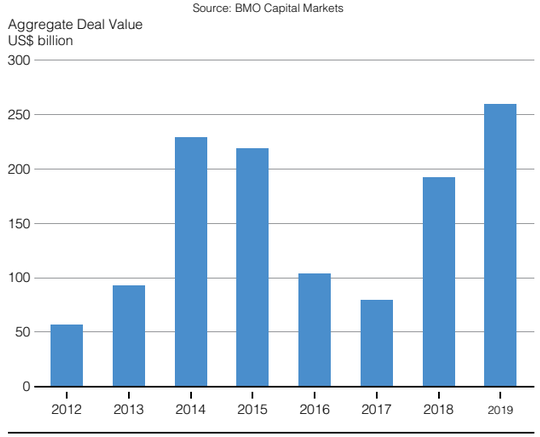
While high profile biotech acquisitions are often celebrated as wins, rarely are the bigger mergers viewed favorably. Pundits and policymakers often claim these larger M&A deals do a myriad of bad things: destroy value, distract R&D groups, consolidate market power, take out emerging competitors, and negatively impact drug pricing. The recent dissenting opinions on the BMS-Celgene merger from two Federal Trade Commission members highlighted this perspective. Both were against approving the deal, because of the possible negative competitive impact.

What these analyses failed to consider is the overall ecosystem benefits of M&A activity. It is a crucially important aspect that needs to be better appreciated by politicians and policymakers in Washington. Fundamentally, large and small M&A deals help catalyze a more efficient allocation of scarce resources across the sector, especially over the longer term.

According to Arda Ural, partner and life sciences sector strategy and transactions leader at Ernst & Young: "There is a myth that mergers don't add value. We see value being created by both mega-mergers and bolt-ons. In terms of generating shareholder value, EY research shows that mega-mergers take up to five years to be reflected in stock appreciation, whereas bolt-ons can attain that within one year. Companies that tend to do more acquisitions and divestitures have better capital efficiency and return on capital."

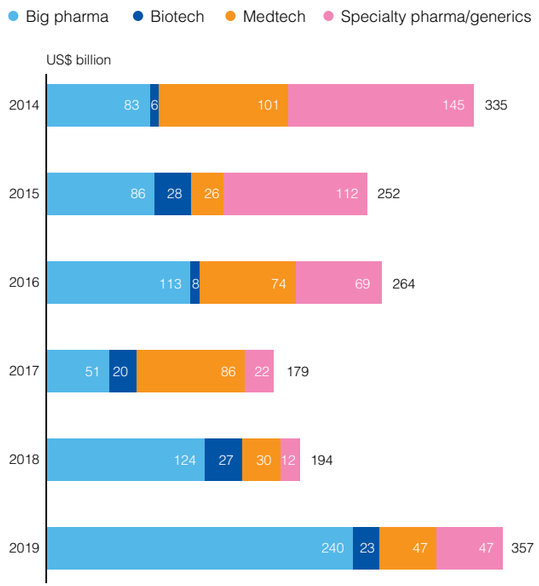
ANNUAL BIOPHARMA M&A

Source: BMO Capital Markets



GLOBAL LIFE SCIENCES M&A

Source: Bloomberg



THE TOTAL M&A VALUE OF PORTFOLIO OPTIMIZATION IN FIVE THERAPY AREAS EXCEEDS US$285 BILLION

Source: Capital IQ

	Oncology	Cardiovascular/ metabolic disease	Inmunology	Infectious disease	Central nervous system disorders
Aggregate revenues of sub-scale assets	US$14 billion	US$11 billion	US$3 billion	US$9 billion	US$23 billion
Potential deal multiple	6.0x	4.0x	5.0x	3.0x	5.0x
Potential asset value	US$84 billion	US$44 billion	US$15 billion	US$27 billion	US$115 billion
			US$285 billion		

Relative to many R&D-intensive industries, pharma is remarkably fragmented. No single player has more than a 10% market share in most broad market categories.

There is also a massive difference in the 'cost of capital' across different players in the sector. This means there is a huge variation in the ability of players to fund the long journey from idea to full market commercialization. The larger profitable biopharma companies have significant cash flows, large balance sheets, and can raise low interest rate debt at will. Contrast this to the loss-making biotech world, where access to new funding is always an issue. Even in the latter group, there are a huge variation in the cost of capital between startups, whose cost is very high, to pre-profit small and mid cap biotech companies that command better conditions. As a sector, the efficient allocation of capital and, by extension, talent and science resources is critically important, and it creates new opportunities for investors.

In short, M&A helps address some of the ecosystem's redundant and bureaucratic inefficiencies by helping the sector better allocate the scarce value-creating resources over the long term.

Another critical function of M&A is the role it plays in replenishing big pharma's pipelines. According to EY, there are looming patent expirations valued at US$180 billion over the next four years. This will ultimately lead to a permanent decline in revenue if new assets are not acquired. Big pharma therefore needs to actively pursue deals to maintain revenue lost from pending patent cliffs.

With the Covid-19 driven uncertainty in valuations in the first quarter of the year, it is still unclear how the rest of 2020 will play out on the deal front. However, regardless of these dynamics, the fundamentals of the biopharma industry are holding up and big pharma will still need to deploy cash for external innovation.

It can be argued that the fall in valuations in Q1 presents an advantageous opportunity for big pharma. However, Christiana Goh Bardon, managing director of UBS Oncology Impact Fund holds a slightly different view: "Big pharma is not so much focused on the price, but on the certainty of success of the assets that they acquire. It is not that they are willing to buy an asset today because it is cheaper than it was yesterday. What they are waiting for is the critical proof of concept, which indicates that the drug is going to be successful through the clinical and regulatory process and ultimately commercially successful. They do not really want to pay less money for an uncertain asset… The main difference in varying economic environments is that big pharma may have slightly better negotiating terms should the capital markets become more difficult. "

Regardless, in contrast to government rhetoric, the prevailing view in the industry is that M&A transactions are an essential part of a healthy ecosystem and deals will continue, albeit in a more subdued manner given the uncertainties that COVID-19 and the upcoming presidential election present. ■

Peter Meath

Managing Director and Co-Head of Healthcare and Life Sciences
J.P. MORGAN COMMERCIAL BANKING

What are your views on the state of the industry and how does J.P. Morgan help facilitate the growth of companies bringing life changing therapies to market?

Life Sciences has never been as exciting an area as it is today. Technological advancement is robust and the rate of novel technologies developed and commercialized is at record levels. That manifests itself in company formation and in capital markets, primarily through high level venture activity. The amount of money being raised by healthcare-focused funds is at all-time highs. Companies are not looking for banks simply as product providers; they value partners that can bring the full life sciences ecosystem to them and create relationships. This includes assisting them with everything from capital aspects to talent development, specific financing needs, geographic expansion plans and partnerships. J.P. Morgan has built a banking platform around the ecosystem, where we not only deliver specific products, but help companies navigate the space to help them grow and scale.

I think it is also important to note the differences in, and ultimate resiliency of, early stage venture investing in biotech through economic downturns. Biotech is a sector that has no direct exposure to issues such as consumer demand fluctuations, unemployment numbers or other macroeconomic measures.This is an industry driven by science, and the data underpinning that science. Investment considerations will be tied to the ultimate progression of that science and its measurable results in a clinical setting. Historically venture investing in the space has therefore seen little to no variance through cycles, and if this current crisis has proven anything in the space, it is that we should ultimately be investing more in certain areas for preparedness and mitigation.

What are some important considerations for emerging life sciences companies?

For biotech companies, going from an inherently science and clinical driven organization to one of manufacturing and sales is challenging and there are cultural and structural shifts that need to happen. Companies need to prepare for this earlier and complicating that fact is that the manufacturing chain is complex. Identifying the most efficient third party providers to collaborate with is very important. On the sales side, it is equally challenging. The sales function is moving away from classic direct sales to more specialized value chain models. Instead of selling to a geography, you are selling to an ecosystem that is around the disease you are trying to solve. With value based medicine and outcome based payments, the sales model is changing.

What ideas around healthcare do you believe should be more prevalent in the election discourse?

Drug pricing will continue to be an important topic of discussion in the political cycle. It is a healthy discussion to have. The movement of the market stream to more outcome-based pricing is a subject of discussion that is long overdue. There are some low hanging fruit that can be addressed such as drugs for the elderly and rare diseases, but it will be hard to build a consensus over a transformative drug pricing model. Political discourse will likely turn to the responsiveness of federal and state governments to the COVID-19 crisis, and we are too early into the situation to see how that plays out in the coming months. How the key drug and device players in the space will factor into this discussion is also uncertain, but certainly stronger private/public partnerships that lead to better innovation and ultimate preparedness will likely be a part of the dialogue.

What goals does J.P. Morgan's life science division wish to achieve over the next two years?

We are focused on building on the dedicated ecosystem we have created around the life sciences community. We want to be the holistic partner for life sciences companies to serve their needs throughout their entire life cycle, from opening a bank account, to expanding internationally and through a potential IPO and beyond. We're investing in and bringing solutions that go beyond traditional banking for our clients.

As an example of this, J.P. Morgan's acquisition of InstaMed will expand our capabilities in healthcare payments, offering healthcare providers, payers and consumers an end-to-end payments solution. We continue to evaluate opportunities to bring our clients more value as we double down on our commitment to the broader healthcare sector and serving the needs of companies in the value chain.

Our goal is for companies of every size, even very early stage companies, to view us as the first place they would go to overcome any challenges that they have in unleashing their full potential. ■

Arda Ural

Partner and Life Sciences Sector Strategy and Transactions Leader
ERNST & YOUNG LLP

The views expressed by the presenter are their own and not necessarily those of Ernst & Young LLP or other members of the global EY organization.

What themes are driving the EY Life Science practice and what are some important initiatives?

Ernst & Young LLP (EY US) is increasingly focused on life sciences and developing and deploying our services according to our clients' capital growth agenda and industry needs. In terms of advising on organic growth, EY US provides strategy and advisory services, and in terms of inorganic growth, our focus is on maximizing value creation in mergers, acquisitions and divestitures. We help our clients to generate capital in a multitude of ways, including: increasing the top line through synergies as predicated by the deal hypothesis and addressing a host of elements of cost to improve our clients' operating income. We help accomplish this across the deal cycle from identifying and valuing the target, providing financial, tax and operational due diligence, and managing the end-to-end transaction with the proven experience and deep knowledge of the sector dynamics.

What trends are driving the life science business at EY?

In life sciences, we see five major themes for 2020. First, liquidity in the market is very high. There is US$1.5 trillion of liquidity available on the private equity side and US$1.4 trillion in the biopharma balance sheets. Just to put this in context, the Fed balance sheet was US$4 trillion at the beginning of this year. Liquidity is going to be widely available for asset acquisitions, innovation and R&D initiatives. In an EY survey released in the last quarter of 2019, 68% of life science executives said they would expect an M&A transaction over the next 12 months period to deploy some of that cash.

Second, there is a need for external innovation to supplement pharma's revenue that is at risk due to looming patent expirations valued at US$180 billion over the next four years. The growth of new products launched in the previous five years is not expected to sustain the revenue decrease due to loss of exclusivity. This same phenomenon happened about 10 years ago and was referred to as the 'patent cliff', when most of the products were small molecules subject to an immediate generic exposure. This scenario will probably repeat in 2020-2024 but with biologics, and this time the loss will be more gradual, with three to four biosimilars entering the market segment. Today, big pharma has the need to supplement their top line. Data shows that biotech companies are more successful in getting Phase 2 and Phase 3 assets to approval, while established biopharma companies continue to be productive in early stages. There will be an array of acquisition opportunities and established biopharma companies need to take advantage of external innovation at an increasing rate.

Third, we are transitioning from the biologics era to an individualized therapy era, where rare diseases, cell and gene therapies and oncology are a big focus. The FDA has been productive with an average of 37 annual novel drug approvals over the last 10 years. In 2019, there were 48, 20 first in-class and 21 for rare diseases. The profile of a typical approval is shifting from broader diseases to rare disease and oncology. It is the evolving nature of the business, driven by the ability to show outcomes in rare diseases that are caused predominantly by monogenic mutations. There are approximately 7,000 rare diseases, 10% of which are being addressed. This comes at a high cost, which the payor industry remains willing to reimburse.

Fourth, M&A activity will continue with emphasis on bolt-ons rather than geographic extensions. We can never rule out mega-mergers, which will happen at a clip of one to two per year. In terms of generating shareholder value, EY research shows that mega-mergers take up to five years to be reflected in stock appreciation, whereas bolt-ons can attain that within one year.

Fifth and lastly, the industry is watching the regulatory environment very closely with impact on drug pricing and reimbursement in a US election year. The recent COVID-19 issue is also expected to create uncertainty on the supply chain, clinical trials, plant inspections and overwhelming health systems shifting focus to acute care needs.

What is your outlook on deal flow and M&A activity in 2020?

There is a myth that mergers don't add value. However, according to our recent Firepower study, we see value being created by both mega-mergers and bolt-ons. Companies that tend to do more acquisitions and divestitures have better capital efficiency and return on capital. Over the last decade the industry has seen one or two every year. While the asset value increased, the volume of transactions was down 14% year over year. Now the industry is competing for fewer assets in oncology, cell and gene therapy, rare diseases and cardiology at higher multiples. With the uncertainty in valuations in the first quarter of 2020, it is to be seen how the rest of the year will shake up. Regardless of these dynamics, it appears the fundamentals of the biopharma industry necessitate a healthy dose of external innovation. ■

James Gale

Founding Partner and Managing Director
SIGNET HEALTHCARE PARTNERS

Signet Healthcare Partners is a provider of growth capital to innovative healthcare companies around the world

What are the most influential market dynamics in defining the direction of Signet's Fund IV?
Fund IV is geared towards investing growth capital toward commercial stage businesses that produce life sciences products. We invest in service providers, such as CDMOs, or it can be companies that market the products themselves. Twenty years ago, we might have invested in a generic drug company that was producing tablets, where today we are more focused on more complex versions of generics or therapeutic products that are embodying technologies that fulfill unmet needs.

How can private equity help drive value for companies in the generics space where margins are slim?
The essence of a successful generics strategy is to lower cost of goods as much as possible, because you can't dictate price. The market price of drugs gravitates toward the lowest cost producer. There are several ways of reducing costs, which we try to help management teams address.
There are two trends that I believe will occur as a result of decreasing costs. One will be consolidation within the industry. That means taking companies that are marginally profitable and combining them to leverage the overhead across a bigger portfolio of products and sales. Secondly, finding and implementing technologies that reduce the cost of goods; this could done be through continuous manufacturing or new ways of developing API's.

What is your perception on valuations across the sectors Signet is focused on?
In both the generic pharmaceutical industry and specialty pharmaceuticals, the multiples have generally declined. Ironically, the multiples for CDMOs have gone up considerably over historical levels. They have effectively inverted, in other words. When making investments, if there are high multiples and businesses are overpriced, we have to decide whether we are able to make a return at the valuation being proposed. If not, we have to find ways to structure around these high multiples. In particular, the high multiples of CDMOs have made it more difficult for us to find investments that we like. This has the affected the pace at which we are investing. It slows it down, because it takes longer to negotiate deals, and sometimes transactions fail because we are unable to bridge the divide. Thus, we have to negotiate more deals to get to the same number of investments.

Can you comment on the financing environment for consumer healthcare today?
Interest rates are currently at historic lows. So when you think about all of the money that has been committed to private equity funds globally in the last few years, there is increasing competition for investments. Because of this large pool of money, expected rates of return have decreased. Consequently, multiples for certain businesses have increased. In today's environment, we are seeing much of the healthcare investments are being channeled towards the newer, innovative areas of treatment like gene therapy, and certain expensive cancer immunotherapies.

In terms of Signet's global investment strategy, what areas of opportunity does the company see outside of the US?
While Signet's focus is on the US market, we invest quite a bit in Europe and India as well. With regard to the finished product markets, Europe has gone through a period of retrenchment over the last 20 years and is an interesting area right now. Because of rising consumer income, certain countries in emerging markets are growing quite rapidly and are also interesting. The US, on the other hand, is becoming a more uncertain marketplace for the moment, except in new therapies or novel medications, and so needs to be evaluated selectively.
As far as CDMOs are concerned, the US is still the center of innovation and drug research. As a result, US domestic CDMOs are of great interest. There are also a number of good companies in Europe and India in the CDMO space. Signet is active in trying to invest in these companies. However, while there still is an interesting market for European innovation, the US still tends to dominate as to the scale of innovative activity. ■

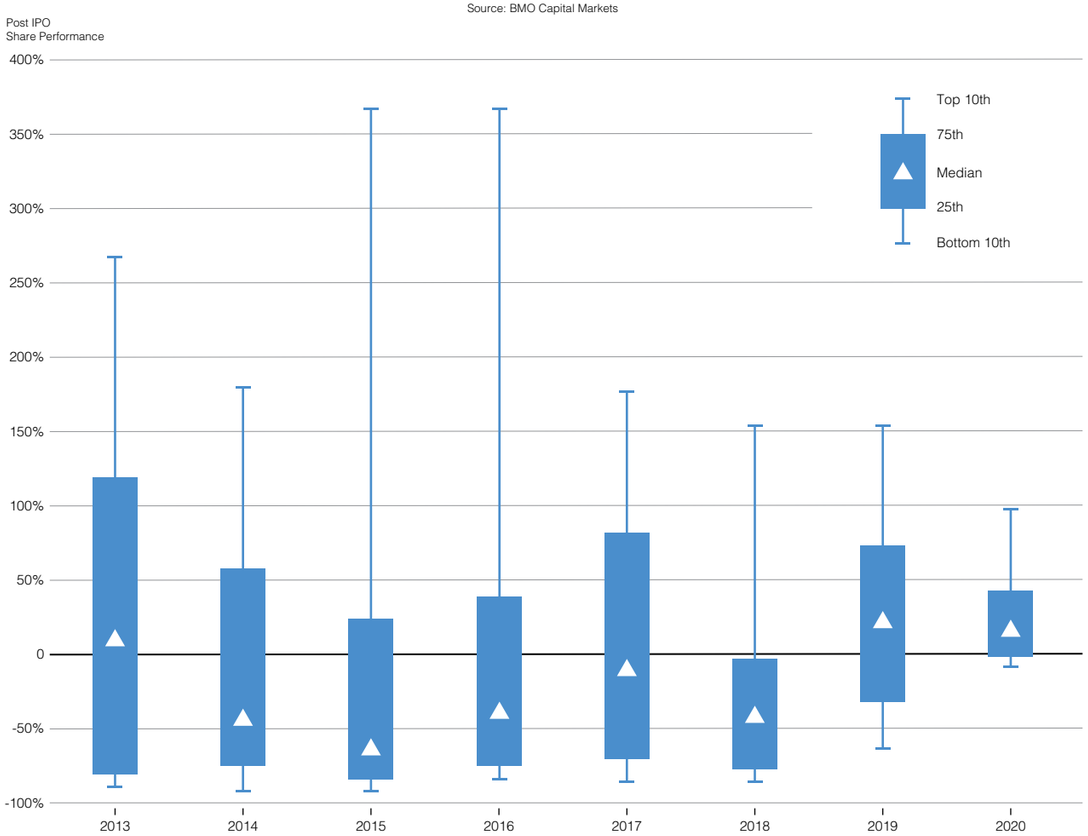
To List or Not to List

BIOTECH SEEKS TO CONTINUE IPO HOT STREAK

During the nineties and early 2000s, it was common to have multiple quarters without a biotech company going public. That has not been the case over the course of the last ten years, as no quarter has come and gone without a biotech IPO. During the past two years in particular, the public markets have provided biotech with important liquidity to push forward drug development programs. Heading into 2020, the XBI, an exchange traded fund that closely replicates the performance of the biotechnology segment of the U.S. market, was near all time highs. The investment firm Jefferies reported in January that 51 biotech companies raised a total of US$5.6 billion in 2019, a tick down from the 67 that generated US$6.7 billion a year prior, but nonetheless another historically strong year. Their shares gained an average of 49%in 2019, and Jefferies analysts said that they expected a 'healthy IPO appetite for at least the first half of the year,' before the approach of the November election.
To start 2020, four companies: Beam Therapeutics, Black Diamond Therapeutics, Revolution Medicines and Schrödinger,all originally filed to raise US$100 million from their initial public offerings. But as their offering dates neared, all four amended their IPO estimates to about US$180 million. When the bell rang, the results exceeded even those increased expectations. Each had raised more than US$200 million. The firms are all developing hot technologies or tackling popular drug targets. Beam is developing CRISPR base-editing therapies for rare genetic diseases. Black Diamond, Revolution, and Schrödinger are pursuing small-molecule drugs for cancer.

BIOTECH POST-IPO STOCK PERFORMANCE BY ANNUAL COHORT

Source: BMO Capital Markets



Of course, a big part of this IPO success has been the nature of the broader funding environment. The amount of private capital going into these companies has increased over the last few years, almost doubling at both the median and the average, the IPO offerings themselves are also up 20 to 30% over that same period. And these two things, combined with a more accommodating environment, have led to post IPO valuations that have never been so high in the history of the industry. Median post IPO valuations in 2019 were north of US$400 million, based on Evercore ISI figures. Five years ago, only the most premium companies were able to achieve that.

In light of the COVID-19 virus, it is fair to question if these rich valuations are sustainable. However, in looking at biotech's performance during the financial crisis of 2008-09, it appears to be less sensitive to macro economic swings than other sectors. During the 2008-09 recession, the NASDAQ biotechnology index (NBI) outperformed the S&P 500, gaining 1% versus the 23.0% downward correction in the S&P. Likewise, during the 2001 recession, NBI was down 0.1%, while the S&P had fallen 8.9%.

Q1 2020 has posed similar challenges to public markets. However, biotech remains resilient. "Biotech will create many new drugs that will transform the outcome of patients. The underlying fundamentals of innovation, regulatory environment and demographics continue to be strong. Innovation is at an all-time high and we are just entering the new era of novel therapeutics such as gene and cell therapy. A collaborative regulatory environment means that our companies are working efficiently with the FDA and EMEA to navigate their drugs through a complex clinical trial and approve process. An aging demographic means that, as the population ages world-wide, there are growing medical needs and hence a marketplace for these therapeutics. Short term disruptions aside, the long term health of the industry is strong. Biotech is, if anything, more attractive now than it has ever been, because we are back to two-year lows," said Christiana Goh Bardon managing director of UBS Oncology Impact Fund.

While we are all trying to solve COVID-19, all other diseases will not go away and there is still a huge need for innovative, transformative platforms and therapies. That is why it is likely biotech will continue to press forward with IPOs even through this very difficult and uncertain time. ■

Christiana Goh Bardon

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

Across the different funds, what is the portfolio construction, and what areas do you find most appealing in terms of capital allocation?

We continue to believe oncology is one of the most exciting areas of drug development. The level of innovation in oncology is at an all-time high. We are developing treatments that transform the outcome of patients, and sometimes even cure a patient of their cancer.

Targeted therapeutics continues to be a hot area of drug development in cancer. It is an area where we can develop personalized therapies for patients by using drugs that address their specific mutations of the patients tumor. From that perspective, I think the personalized medicine approach can improve efficacy rates, streamline clinical trials, and also minimize exposure of the drug by only treating patients who are known to be potential responders. It is one of the most exciting and fruitful areas of oncology drug development.

How does the long timeline for drug development affect your time horizon when it comes to investing?

One of the other reasons we like oncology is because you can achieve your proof of concept relatively early. In oncology, you can assess whether a drug works early in the phase 1 trial. You can do so by administering the drug to patients known to have a specifically targeted mutation. If your drug hits that mutation, within ten patients of study, you can determine if your drug is working. From that perspective, you can generate an early proof of concept.

The market has been wildly volatile over the last two weeks. Are there any steps you are taking to de-risk, or are you still standing by your outlook going into the year?

We have undergone a tremendous correction over Q1 with coronavirus and we feel biotech valuations to be attractive. Our long-term perspective on this industry has not changed however. We think that the industry will invent many drugs that will transform patients lives.

Given the sudden stop in economic activity, do you see markets creating discounts which will expedite potential M&A in the sector?

We have had a very healthy biotech investing environment since 2011. Our companies have seen record amounts of financing. If we enter a period of economic slowdown of the capital markets, our companies are well-financed to continue to move forward with clinical trial work for the next few years. In general big pharma is not so much focused on the price, but on the certainty of success of the assets that they acquire. It is not that they are willing to buy an asset today, because it is cheaper than it was yesterday. What they are waiting for is the critical proof of concept, which indicates that the drug is going to be successful through the clinical and regulatory process and ultimately commercially successful.

Are there any pockets of value that are being created as a result of the market pullback?

We see several exciting opportunities and interesting valuations because of the pullback. I foresee a strong snapback after the world has recovered from coronavirus. I do not think coronavirus has fundamentally impaired our company's ability to discover drugs, take them through clinical trials and the regulatory process. Biotech is, if anything, more attractive now than it has ever been, because we are back to two-year lows.

What would be your policy prescription for fostering an innovative environment moving forward?

The most important thing is strong support for fundamental science in this country. It is imperative, not only for the health of the country, but also for the health of the economic sector. Biotechnology is one of the fastest-growing sectors in the world and a sector where the US completely dominates. I continue to applaud the FDA and their outstanding work. They have continued to be efficient and collaborative with our industry.

Over the next two years, what is your vision?

I think that biotech is on a long term bull run. Biotech will create many new drugs that will transform the outcome of patients. The underlying fundamentals of innovation, regulatory environment and demographics continue to be strong. Innovation is at an all-time high and we are just entering the new era of novel therapeutics such as gene and cell therapy. ■

ACCELERATING PIPELINES: DRUG DISCOVERY AND DEVELOPMENT

» The most important thing is strong support for fundamental science in this country. We continue to need healthy financial support for the NIH and scientific and clinical research. It is imperative not only for the health of the country, but also for the health of the economy. I would remind an incoming president that biotechnology is one of the fastest-growing sectors in the world and a sector where the US completely dominates. There is no other country in the world that can compete with our research and drug development capabilities. We are creating the most exciting drugs worldwide. I continue to applaud the FDA and their outstanding work. They have continued to be efficient and collaborative with our industry. «

- Christiana Goh Bardon,
Managing Director,
UBS Oncology Impact Fund Managed by MPM Capital,
Portfolio Manager,
Burrage Capital

Image courtesy of Goldfinch Bio

TOP 10 US BIOPHARMACEUTICAL COMPANIES BASED ON REVENUE

Source: GBR

2

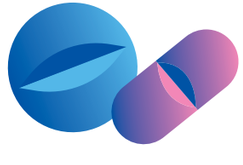
Roche

Full-year revenues 2019: **$50 billion**
Full-year revenues 2018: **$45.31 billion**
% revenue growth year-on-year: **11%**
FY 2019 EPS: **$20.77**
%EPS growth year-on-year: **13%**

5

GlaxoSmithKline

Full-year revenues 2019: **$43.54 billion**
Full-year revenues 2018: **$39.65 billion**
% revenue growth year-on-year: **8%**
FY 2019 EPS: $1.46
%EPS growth year-on-year: **4%**



8

Sanofi

Full-year revenues 2019: **$27.77 billion**
Full-year revenues 2018: **$26.64 billion**
% revenue growth year-on-year: **4.1%**
FY 2019 EPS: **$2.51**
%EPS growth year-on-year: **-67%**

Pfizer

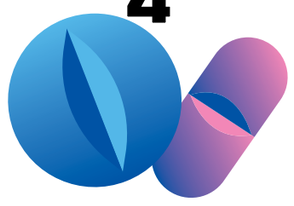
Full-year revenues 2019: **$51.75 billion**
Full-year revenues 2018: **$53.65 billion**
% revenue growth year-on-year: **-4%**
FY 2019 EPS: **$2.95**
%EPS growth year-on-year: **1%**

1

Merck & Co

Full-year revenues 2019: **$46.84 billion**
Full-year revenues 2018: **$42.29 billion**
% revenue growth year-on-year: **11%**
FY 2019 EPS: **$3.81**
%EPS growth year-on-year: **64%**

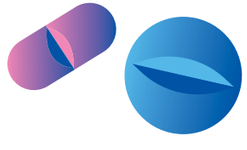
4

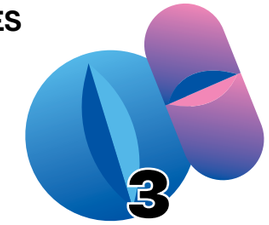


Bristol-Myers Squibb

Full-year revenues 2019: **$26.15 billion**
Full-year revenues 2018: **$22.56 billion**
% revenue growth year-on-year: **16%**
FY 2019 EPS: **$4.69**
%EPS growth year-on-year: **18%**

9

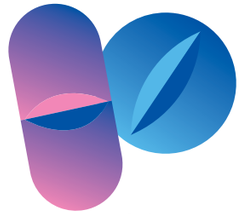




3

Novartis

Full-year revenues 2019: **$47.45 billion**
Full-year revenues 2018: **$44.75 billion**
% revenue growth year-on-year: **9%**
FY 2019 EPS: **$5.28**
%EPS growth year-on-year: **12%**



6

Johnson & Johnson

Full-year revenues 2019: **$42.19 billion**
Full-year revenues 2018: **$40.73 billion**
% revenue growth year-on-year: **3.6%**
FY 2019 EPS: **$5.63**
%EPS growth year-on-year: **Unchanged**

7

Abbvie

Full-year revenues 2019: **$33.27 billion**
Full-year revenues 2018: **$32.75 billion**
% revenue growth year-on-year: **1.6%**
FY 2019 EPS: **$5.28**
%EPS growth year-on-year: **44.3%**

10

AstraZeneca

Full-year revenues 2019: **$23.57 billion**
Full-year revenues 2018: **$20.49 billion**
% revenue growth year-on-year: **15%**
FY 2019 EPS: **$3.50**
%EPS growth year-on-year: **1%**

Drug Development and Discovery

BIG PHARMA FAVORS COLLABORATION

The challenges facing the pharmaceutical industry a decade ago helped put in motion a fundamental transformation in the structure of the biopharmaceutical industry. It was getting more expensive to develop new drugs, competition from generics was increasing, and investors had come to expect high returns on capital. Furthermore, complaints from consumers and payors (including the federal government) about excessive drug prices were becoming more strident, and the number of new drugs reaching the market each year was below expectations. There was no single solution to all of these problems, but one major change would address most of them: Improve the effectiveness of drug discovery and development.
Around the same time, small emerging biotech companies faced a difficult IPO environment and were in need of partnerships to continue progressing their development programs. Accord-

45>>

Daniel J. O'Connor

President & CEO
ONCOSEC MEDICAL INCORPORATED

How is OncoSec's TAVO™ helping the patient population that is seeing no positive result from using Keytruda and Opdivo?

Checkpoint therapies, like KEYTRUDA® (pembrolizumab) and OPDIVO® (nivolumab), have been highly successful for some patients, but not the majority. In fact, about 70% of patients who receive checkpoint therapy do not see their tumors go away. Those tumors lack essential immune elements that enable checkpoint therapies to be effective. They are metaphorically referred to as 'cold' tumors – while 'hot' tumors are likely to receive a benefit from anti-PD-1 checkpoint therapies.

OncoSec's lead product candidate, TAVO™ (tavokinogene telseplasmid), is administered using our proprietary electroporation gene delivery system (EP) and designed to help turn 'cold' tumors 'hot'. TAVO has demonstrated anti-tumor activity with whole body (abscopal) effect in metastatic melanoma and four other cancer types both as a monotherapy and in combination with anti-PD-1 checkpoint inhibitors.

TAVO is DNA-based interleukin-12 (IL-12), a hormone-like messenger, which facilitates communication between cells of the immune system to signal immune activation and inflammation. TAVO is administered directly into the tumor using EP, which employs a series of momentary energy pulses. Those pulses increase the permeability of the cell membrane and facilitate uptake of IL-12 coded DNA into cells. This non-invasive, non-physical method is easy to perform and avoids systemic toxicity issues historically associated with the use of intravenous cancer immunotherapies.

OncoSec is currently running two KEYNOTE clinical programs in partnership with Merck – a pivotal study in late-stage checkpoint resistant metastatic melanoma (KEYNOTE-695) and a phase 2 study in metastatic triple negative breast cancer (KEYNOTE-890).

The pivotal KEYNOTE-695 study is a multicenter, open-label, single-arm, non-comparative trial evaluating TAVO plus EP and KEYTRUDA combination therapy in approximately 100 patients with unresectable or metastatic melanoma who are progressing or have progressed on KEYTRUDA or OPDIVO. To date, the response rates from this study have far exceeded the single digit response rates expected with KEYTRUDA monotherapy in this late-stage checkpoint refractory 'salvage' setting. The KEYNOTE-695 study has been granted Fast Track and Orphan Drug designations by the FDA. OncoSec expects to complete enrollment in KEYNOTE-695in 2020 and submit a biologics license application (BLA) filing as soon as possible thereafter.

The KEYNOTE-890 study is a phase 2, multicenter, open-label, single-arm, non-comparative study evaluating TAVO plus EP and KEYTRUDA combination therapy in approximately 25 patients with inoperable locally advanced or metastatic triple negative breast cancer (mTNBC). In December 2019, OncoSec presented interim data of 28.5% objective response rate (ORR) at the San Antonio Breast Cancer Symposium (SABCS). This study is now fully enrolled, and OncoSec expects to expand its TNBC clinical program with Merck in 2020.

What are some of the key partnerships that OncoSec has and how will they help spur growth?

OncoSec has established several world class strategic partnerships that we are leveraging to enhance our pipeline opportunities. Our relationship with Merck and the two ongoing KEYNOTE clinical programs is a prime example of that.

Beyond Merck, we recently entered into a strategic partnership with China Grand Pharmaceutical and Healthcare Holdings (CGP), and its U.S. affiliate, Sirtex Medical US Holdings (Sirtex).

How do you view the effectiveness of business incentive programs in New Jersey?

I have been a very vocal supporter of the New Jersey Technology Business Tax (NOL) program. It allows for your operating losses and your research and development tax credits to be sold to a profitable company. That means we can receive revenue without selling stock or licensing our technology. OncoSec received approximately US$885,000 in non-dilutive capital through the NOL program for the 2019 year.

What objectives is OncoSec seeking to accomplish over the next year?

2020 is a break-out year for OncoSec. With the US$30 million investment from CGP and Sirtex, we now have the resources we need to drive both our TAVO KEYNOTE clinical programs to the finish line. We expect to complete enrollment in the pivotal KEYNOTE-695 study this year and will then submit our BLA filing for FDA review. The KEYNOTE-890 study in metastatic triple negative breast cancer (TNBC) is already fully enrolled and we're looking forward to expanding our relationship with Merck in TNBC this year. We're also continuing to advance our novel visceral lesion applicator (VLA) program designed to reach and target deep internal tumors with our EP technology. This is truly a groundbreaking program that has the potential to revolutionize cancer immunotherapy. ■

»

Pfizer has evolved as a partner in recent years, and we recognize that breakthroughs can come from many different places. We also recognize that breakthroughs are built by pairing capabilities from different partnerships and working together towards a shared overarching vision, such as what we have done in gene therapy. We have learned from the past that synergistic relationships are often the most powerful, as some products on the market today would not have been the breakthroughs that they are without the collaborative nature of the partnerships from where they emerged.

- Doug Giordano,
Senior VP of Business Development,
Pfizer

«

<<43

ing to Robert Coughlin, president and CEO of MassBio: "We needed to work with big pharma companies to convince them that the day and age of having campuses that do high throughput screenings were not going to create enough blockbuster drugs fast enough to overcome the patent cliff that they were facing. We had a few hundred 'baby biotech companies' that were not going to be able to have an IPO. How do you invent a drug if you are a biotech company, when the old model was to come out of a world-class academic center, license to entrepreneurs, raise VC money and then go public? We had to think of a new model and we came up with the concept of external innovation, whereby big pharma would slow down on campus development and start doing licensing deals, acquisitions and outsource their innovation to smaller early stage companies"

Today, this symbiosis is an accepted part of the drug development process and both big pharma and emerging biotech companies actively pursue partnerships and collaboration. This is particularly true for high risk, novel targets. Big pharma tends to prefer targets that are better

validated, which typically means lower required investment and shorter development timelines. Where big pharma tends to shine is in terms of identifying compounds and screening. Since there is still an enormous amount of value creation that comes later in the pipeline as a candidate approaches commercialization, pharma companies tend not to spend so much time on discovery and earlier-stage research.

Instead they turn to companies pursuing great science and partner and collaborate in the hope that the science will develop into new medicines that bring about lifestyle improvements for patients.

Johnson & Johnson, for example, created an innovation arm to specifically accelerate early-stage innovation worldwide, and through this channel provide scientists and entrepreneurs with access to internal experts who can facilitate collaborations across the pharmaceutical sector. Similarly, Pfizer has its Center For Therapeutic Collaboration, which was founded on the notion that scientific and global health challenges are too complex for any one player in the healthcare ecosystem to solve alone.

"Pfizer has evolved as a partner in recent years, and we recognize that breakthroughs can come from many different places. We also recognize that breakthroughs are built by pairing capabilities from different partnerships and working together towards a shared overarching vision, such as what we have done in gene therapy. We have learned from the past that synergistic relationships are often the most powerful, as some products on the market today would not have been the breakthroughs that they are without the collaborative nature of the partnerships from where they emerged," said Doug Giordano, senior VP of business development at Pfizer.

To point to an example of the new collaborative model, Goldfinch Bio, is working with Gilead to expand its kidney genome atlas, which identifies and validates targets for diabetic kidney disease. The deal will allow Goldfinch to expand its database by an order of tenfold, to tens of thousands of patients. "This will allow us to have statistical power and to become the world leaders in the kidney area, leveraging human genetics to meet novel drug targets," said Tony Johnson, Goldfinch Bio's CEO.

The deal has US$2 billion potential for Goldfinch, and for Gilead, it positions them to use Goldfinch as the kidney arm of their business.

A final factor driving collaboration is that, although the majority of biomedical innovation is developed by emerging biopharma companies today, many have never marketed a therapy before. Over time, these companies either successfully bring their products to market or, in most cases, their assets or whole company are acquired by big pharma. This is an area of the business that greatly favors revenue generating big pharma, because they have the budget and expertise in commercialization and marketing. Figures from Fierce Pharma show the marketing spend on AbbVie's anti-TNF monoclonal antibody, Humira, was US$577.3 million in 2019 alone. This figure is well ahead of its competitors, but Pfizer spent US$202.9 million marketing its JAK inhibitor Xeljanz for rheumatoid arthritis. This is not something smaller companies have the wherewithal to do.

Overall, collaboration between big pharma and emerging biotech has been a force for good for all players involved, but most of all for sick patients who now have access to life changing drugs as a result of an expansion in therapeutic focus and risk taking that otherwise would not have occurred under the previous model. ■

Tony Johnson

CEO
GOLDFINCH BIO

How does Goldfinch Bio translate the recent breakthroughs in genetics and biology into new therapies?

The premise for Goldfinch Bio is that we can leverage new advances in our understanding of kidney disease genetics and pathophysiological mechanisms to identify novel treatments for patients with diseases of the kidney. We have established the kidney genome atlas and the human biology platform as an important source of novel therapeutic targets.

The kidney genome atlas built by Goldfinch Bio (KGA 1.0) is focused on patients with proteinuria and a large subset of these patients have a disease called focal segmental glomerulosclerosis (FSGS). This is an orphan indication for which there is no approved therapy to date. Our KGA 1.0 has just under 23,000 participants and is proprietary to Goldfinch Bio. We have undertaken whole genome sequencing and coupled these data with clinical data from electronic medical records in the entire cohort. In addition, expression data have been generated from kidney tissue biopsies in a subset of patients. Together, these data enable the identification of novel human genetic driven targets.

The human biology platform is applied to achieve human validation of these potential genetic targets. In our laboratories we have established human stem cell-derived kidney podocytes, a cell type which protects against proteinuria, and human stem cell-derived kidney organoids. We grow kidney organoids in the lab in vitro and transplant them under the kidney capsule of rodents in vivo. The advantage is that they become vascularized together with the rodent kidney. This allows us to do PK-PD experiments i.e. dose the animals and measure the effects of the drug on the transplanted human stem cell-derived kidney. GFB-887, our development lead transient receptor potential canonical 5 (TRPC5) inhibitor for FSGS and diabetic nephropathy was protective against damage caused by upregulation of the TRPC5-Rac1 pathway in the transplanted human stem cell-derived podocyte and kidney. Our approach is unique because we measure treatment effects in a physiological setting. Finding targets from our genome atlas, validating them with this approach prior to establishing a drug discovery program is a cost-efficient way to confirm that our drug discoveries are relevant to kidney patients.

Can you contrast the traditional treatment of dialysis with the potential paradigm shift Goldfinch Bio is offering?

Since kidney transplants are not readily available, most patients are dependent on dialysis. The latter ties the patient to a machine for several hours a day, usually three days a week which can significantly impede a normal working life. In contrast, at Goldfinch Bio we are developing a disease modifying therapy for patients whose FSGS or diabetic nephropathy is driven by the TRPC5-RAC1 pathway and for which our TRPC5 inhibitor, GFB-887 should be highly efficacious. This therapy aims to delay or prevent kidney failure and improve the quality of life for these patients. This personalized approach will enable patient selection earlier in the disease process based on a simple urine test. If effective, reducing dependence on kidney dialysis could have a substantial impact on resource allocation for patients who progressed to end stage kidney failure.

In 2019 you announced partnership with Gilead Sciences and Takeda. What is the importance of these collaborations and potential they hold for bringing novel treatments?

Both are very important. The Gilead deal has allowed us to expand the kidney genome atlas from KGA 1.0 (FSGS) to KGA 2.0. The latter is focused on diabetic nephropathy with 12 million patients in the US alone and 150 million patients worldwide. We are expanding the kidney genome atlas to 40 thousand diabetics with nephropathy and 40 thousand diabetics without it. This will facilitate sufficient statistical power to identify novel human genetic-driven drug targets. For Goldfinch Bio, the Gilead partnership provided capital to progress the pipeline and facilitated establishing ourselves as leaders in the kidney therapeutic area, leveraging human genomics and clinical data to identify novel drug targets. If just five targets from this partnership are marketed, there is close to a US$2 billion potential for Goldfinch Bio. Our novel technology allows Gilead to discover, develop and commercialize therapeutics for diseases of the kidney. ■

Advancing Oncology

INNOVATIVE THERAPIES MAKE BIG STRIDES

Few things in life are more frightening than finding out a loved one or close friend has been diagnosed with cancer. Fortunately, thanks to medical and therapeutic advances, the probability of a cancer diagnosis becoming a death sentence is far less likely than it once was. Each year, the American Cancer Society estimates the number of new cancer cases and deaths that will occur in the United States. For nearly 30 years, the trend towards fewer cancer deaths has been moving in a positive direction, with less cases of mortality year after year. In their latest report, Cancer statistics 2020, data demonstrates that since peaking in 1991, the death rate associated with cancer declined by 29%, which translates to 2.9 million fewer cancer deaths.

Contributing to the decline have been innovations including targeted therapies and immunotherapies that have played a key role, alongside efforts to reduce behaviors associated with cancer risk such as smoking, as well as various medical innovations, such as early screenings. The 2010s started with clinical trial results centered on the use of checkpoint inhibitors; drugs that unleash a powerful immune system attack on cancer cells. The results helped usher in a new era for cancer immunotherapy. Innovations in this area are transformational, as the therapies purpose, in metaphorical terms, is to disable the brakes that cancer cells use to fend off an attack on them by the immune system T cells. It gives hope that even stage IV metastatic cancers can be halted and managed more like a chronic disease.

Although checkpoint therapies like KEYTRUDA and OPDIVO have been highly successful for some patients, the majority experiences no positive response. In fact, about 70% of patients who receive checkpoint therapy do not see their tumors go away. This should not detract from the marvel of these drugs. Many scientists believe checkpoints do not need to be replaced, but rather augmented with new drugs that can further cajole the immune system into fighting cancer. This has led to an unprecedented amount of clinical research combining checkpoints with other medicines to try to find a magic bullet to treat cancer.

50>>

Our R&D approach is a functional genomics approach. We treat tumor cells with the miRNAs on an individual basis to see whether they go into apoptosis or that you can inhibit proliferation. This is already the first indication of the potential function of the particular miRNA. This approach is unique compared to the approach of other miRNA companies in the field as what they started off with was descriptive differential expression profiling. In a disease situation miRNAs can be up or down regulated. If you analyze the RNA from disease samples versus normal samples on a microchip with miRNAs, you can check for up and down regulation. What you do not have with differential expression is the spatial temporal information and you do not know if the up or down regulation of the miRNA is a result or a cause of a defect. If you have a non-bias functional genomics approach, you immediately have information on the potential function of the miRNA.

- Roel Schaapveld, CEO, InteRNA Technologies

Anthony Capobianco

Founder and President
STEMSYNERGY THERAPEUTICS

System Synergy Therapeutics, Inc. (SSTI) is a biotechnology company focused on discovering drugs that target biomolecules and cellular processes fundamental to cancer

How has the progression been from virtual company you founded to where you are today?

It has been a great journey. We decided to start by repurposing a drug that had already been in a clinic. We then transitioned to figure out how to make our own drugs. From 2008 to today, we have built a robust pipeline and made our first deal with our first compound – a partnering deal with Exelixis. We developed a Wnt pathway inhibitor from scratch and since the development of the molecule, we have been working to bring it up through the ranks. We received the bulk of our funding from the SBIR program. As we are building our company through the pipeline and submitting grants, they are getting vetted by scientists and the NCI is providing the funding for it, which is important because it allows us to target non traditional pathways. Over the years, we have developed a compound called SST215; we published a paper showing that it had better efficacy and less toxicity than the best attempt to date for a Wnt inhibitor.

What medical need are you addressing with your Notch and Wnt pathway?

Oncology is the biggest target for us. We do not focus specifically on any cancer type, because the targets we are going after are fundamental for the cancer stem cell populations. What you can find is that Notch and Wnt are re-activated in most cancers. When we get something to clinical stage, we want to evaluate that inhibitor in any cancer that will benefit from it.

In terms of advancing the development to the clinical stage, what is your method?

For each one of our assets, our business model is that we do the discovery, we optimize the scaffold, secure the IP around that scaffold, and pick the clinical candidate that we are most comfortable with. We want to bring each one of those candidates as close to IND as we can, as we start to look for partners. We do not want to be a clinical phase company at this stage of the game. We are happy to have partnerships at the IND level and let the clinical stage companies then drive it through the clinic. We think this is the best way to target pathways that might not be on the radar of big pharma and we can de-risk them by scientific review in the SBIR program.

What is SSTI's financing strategy moving forward?

The fundamental part of our strategy has been making sure that we are funding these projects through the SBIR program. If we bring on an investor that wants to buy into our strategy, we need US$10 million from an active partner to help grow out our programs for everyone's benefit. It keeps our equity solid and does not dilute it out. We are four scientists realizing our dream, taking our basic science knowledge and translating it directly into drugs that help heal people.

What are your thoughts on how to boost entrepreneurial ecosystems around universities to create more spinoff companies?

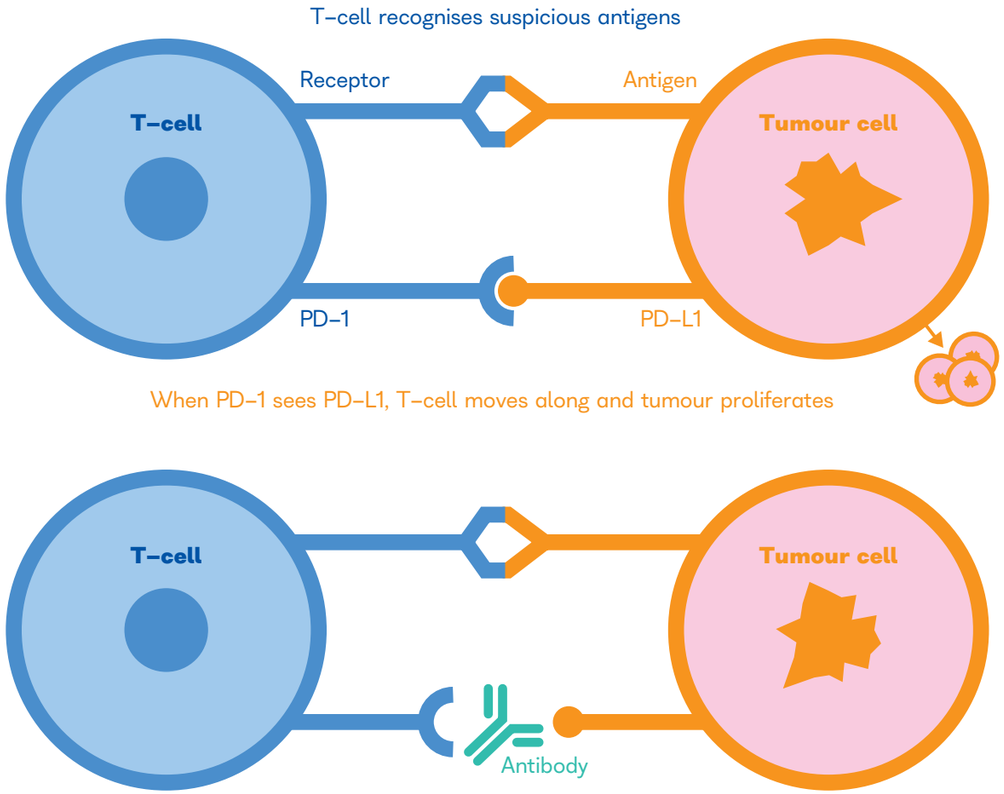
You can fund an academic lab, but there is a gap in getting from the lab to something that industry is truly interested in. Getting the funding necessary to achieve this needs to go beyond the academic grant system. What the universities fail to do is identify how to get investment philanthropy into those young companies. If you couple that with a cancer center, you should be able to do the biochemistry of your pathway, and drug screen all the way to clinical trial, because you pump it back into universities. If it is done right and has phase one trial documents and the entire infrastructure for IND, it would allow for efficient progression. The problem is finding that US$2-3 million per project that you need in excess of an SBIR grant.

What goals does SSTI with to achieve over the next 18 months?

I would like to have two compounds in IND. Financing is our biggest hurdle, and we are working to exploit all possible mechanisms out there. We want to get our pipeline drug candidates in front of those who want to buy in, either pharma partnerships of venture capital financing. We are ready to make a difference. ■

IMMUNOTHERAPY DISPLAYS ITS PROMISE

Source: The Pharmaceutical Journal



<<48

One example is Oncosec's TAVO that is being paired with Merk's Keytruda in clinical trials. According to CEO Daniel O'Connor: "Tumors that lack essential immune elements that enable checkpoint therapies to be effective are referred to as 'cold' tumors, while 'hot' tumors are likely to receive a benefit from anti-PD-1 checkpoint therapies… OncoSec's lead product candidate, TAVO, is administered using an electroporation gene delivery system (EP) and designed to help turn 'cold' tumors 'hot'. TAVO has demonstrated anti-tumor activity with whole body (abscopal) effect in metastatic melanoma and four other cancer types both as a monotherapy and in combination with anti-PD-1 checkpoint inhibitors."

Another company working on the development of a drug to be used in combination is Cyclacel. It is interested in harnessing the potential of a class of drugs called cyclin dependent kinase (CDK) inhibitors,to overcome cancer resistance. "The problem with cancer resistance is not chemotherapy, it is the genetic resistance of cancer, as the daughter cells become smarter, learn how to escape drug effects, and become insensitive to the drug, leading to mortality. The idea was to use the body's own defenses and amplify them," said Spiro Rombotis, CEO of Cyclacel. "We are all chasing this goal of how we can suppress one or more of these proteins that have a relatively short life – we call these transcripts. The idea is to intervene and block the transcription of a cancer cell to teach the daughter cells to escape the effect of the drug. If we can do that successfully, we can take a drug like CYC065 and combine it with a drug that has stopped responding, and the drug will work again. Our goal is to lower the bar by making the cancer cells sensitive."

An alternative to immunotherapy and chemotherapy is targeted therapeutics. The sequencing of human cancer genomes over the past decade has played a big role in bringing targeted therapeutics to where it is today, because it demystified the genetics of cancer. We now have a blueprint of cancer genes in every type of cancer and information about the frequency and type of muta-

Spiro Rombotis

CEO
CYCLACEL PHARMACEUTICALS

What was the scientific discovery that drove the creation of Cyclacel?

Sir David Lane PhD founded the company in 1996, which stemmed from his discovery of the p53 gene, which is dysregulated in most people with cancer. In 2001, the Nobel Prize for Medicine was awarded for the discovery of cyclin dependent kinases (CDK), enzyme drug targets functioning downstream of p53. We became interested in harnessing the potential of this new class of drugs, called CDK inhibitors, to overcome cancer resistance.

This problem is different to the cancer resistance observed with chemotherapy, as it is caused by genetics gone haywire. Genetic resistance occurs as cancer cells and their daughter cells become smarter, learn how to escape drug effects, and become unresponsive to therapy, leading to treatment failure and mortality. Prof. Lane's idea was to take advantage of the body's own defenses and, in particular, a process of disposing useless cells called apoptosis. This molecular machinery is defective in people with cancer, which enables tumors to escape and multiply out of control. The goal of treatment with CDK inhibitors is to reverse this blockade and enable apoptosis in cancer cells.

We hypothesized that if we could lower the levels of these anti-apoptotic proteins, such as MCL1 or cyclin E, with small molecule pharmaceuticals, we could reengage apoptosis. Perhaps we could then restore sensitivity to cancer drugs that stopped working because of the emergence of resistance. Therefore, we work to develop drugs that can stop cancer cells from becoming smart.

Can you comment on the drugs you have in your pipeline, CYC065 and CYC140?

Fadraciclib (or CYC065), is a CDK inhibitor targeting two enzymes; CDK2 and CDK9. It is a leader in a class of drugs seeking to lower MCL1 protein levels. CYC140, which was also discovered in our laboratories, is a Polo-Like Kinase inhibitor targeting the PLK1 enzyme. PLK1 plays a crucial role in mitosis or cell division, the last stage of the cell cycle. During mitosis the parent cell nucleus splits into two nuclei. The parent cellular material stretches along a longitudinal axis, called the spindle, with the two nuclei on either end or pole. Following spindle formation the two daughter cells pull apart and reorganize as two separate cells with their own nuclei at their core. CYC140 acts by an anti-mitotic mechanism in cancer cells by interfering with their division, causing multipolar spindles or incomplete mitosis resulting in the destruction of cancer cells.

Cyclacel has had clinical success in treating both solid and liquid cancers, like leukemia. Can you tell us about the results in both areas?

We have strong preclinical and now early clinical evidence that fadraciclib works in both liquid and solid tumors, which is a rare occurrence. Fadraciclib has shown confirmed partial response and prolonged stable disease, as a single agent, in heavily pretreated patients with advanced cancers referred for treatment with first-in-human, investigational drugs. These observations occurred mostly in patients with increased levels of MCL1 and/or cyclin E supporting the drug's mechanism of action.

In liquid cancers clinical data are coming mainly from two types of leukemia – chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML). In both of these leukemias we are treating patients with a combination of fadraciclib and the approved drug, venetoclax, a BCL2 inhibitor.

In AML, MCL1 plays a major role in blocking apoptosis. The contribution of BCL2 is not well studied. However venetoclax in combination with a generic drug called azacitidine has been approved by FDA for front line therapy of elderly AML patients. Thus far we have seen antileukemic activity with the combination of fadraciclib and venetoclax, in terms of reductions of leukemia cells in the peripheral blood of patients who have relapsed or are refractory to front-line treatment.

We are in an early stage with our trials; late phase 1 with around 50 patients enrolled so far. We are preparing for phase 2 development having seen activity in solid and liquid cancers.

For the time being we are primarily concerned with the impact of COVID-19 through the second half of 2020, the broad availability of testing for the whole population and whether we see an ebb and surge pattern in the next two years until vaccines become available. ■

<<50

tions that occur. This has revealed new genes and pathways important for cancer development and, in some cases, has already led to new approved cancer therapies. In addition, genetically sequencing tumor tissue samples guides the therapeutic agents selected for a subset of cancer patients. This tailored approach, termed precision or personalized medicine, selects patients most likely to respond and spares those that are unlikely to respond from untoward side effects. Recent discoveries that it is possible to sequence DNA in the blood to detect cancers provide hope that this approach can be used to identify cancers earlier and follow the response to therapy. Through the study of rare cancers, mutations have been identified in genes that regulate the epigenome, the cell's machinery for activating and deactivating genes. These studies have revealed that these same pathways are dysregulated in many common cancers and play key roles in cancer pathogenesis and resistance to therapy.

Many investors in the cancer space find this line of therapies appealing both for the potential social value it can bring in alleviating suffering, but also for its ability to generate future profits. According to Christiana Goh Bardon of Burrage Capital: "It is an area where we can develop personalized therapies for patients by using drugs that address the specific mutations of the patients tumor. From that perspective, I think the personalized medicine approach can improve efficacy rates, streamline clinical trials, and also minimize exposure of the drug by only treating patients who are known to be potential responders. It is one of the most exciting and fruitful areas of oncology drug development."

Adding to the robust development of cancer therapeutics are early stage, pre-IND companies like Stem Synergy Therapeutics, whose initial academic research found that WNT and Notch signaling promise to have a major clinical impact on treatment of colorectal, breast, esophageal, lung, sarcoma, and other cancers. Since 2018, the company has worked in partnership with Exelixis to develop better inhibitors for the WNT pathway. According to the company's founder and president, Tony Capobianco: "One of the exciting pieces of preclinical data we like is when we can show that our WNT inhibitor has better efficacy with less toxicity than competing inhibitors. We also developed a Notch one selective inhibitor that has fantastic efficacy without the on target toxicity, whereas all the other inhibitors being developed are pan-Notch inhibitors that have much higher toxicity, and that is part of our approach—to maximize efficacy and minimize toxicity."

In summary, cancer remains pervasive, but there is hope that it can one day be a chronic, manageable disease. In order to achieve this goal, there is a need to continue to collaborate with stakeholders across the health care system and maintain an ecosystem that supports and encourages the development of innovative new therapies. ■

Randy Milby

CEO
HILLSTREAM BIOPHARMA

Can you please provide an overview of Hillstream Biopharma?

Hillstream is a privately owned, oncology-focused company. Our first asset is Salinomycin (HSB-1216), which is derisked but not yet approved. Salinomycin was originally tested in Germany for ovarian and breast cancer and had great results, but its toxicity profile was not completely understood and optimized for randomized controlled trials. Hillstream has proprietary technology to widen the compound's therapeutic window by increasing the dose without side effects and collateral damage to healthy cells. We have compelling animal data suggesting that it is safe to administer at a higher dose. Our initial indication is small-cell lung cancer, and we intend to have our pre-IND meeting with the FDA at the end of 2020 and have the IND by mid-2021. The market opportunity for this asset is between US$1billion to US$2 billion. Hillstream's second asset is DNA delivery, TNF Alpha, which is a potent cytokine, and it has not been approved in the United States but is in the market in Europe. A small company took it to phase 3 in the U.S., but their trial failed due to high toxicity levels and the company ultimately ran out of funding. Since the company had significant positive Phase 2 data in soft tissue sarcoma, Hillstream is taking this TNF alpha and putting it inside our QUATRAMER™ drug delivery technology to improve the pharmacokinetics and prevent collateral side effect damage.

How is Hillstream harnessing the immune system to improve cancer drug delivery?

Hillstream's QUATRAMER™ technology encapsulates the drug or cytokine. The critical factor here is that the drug or active is encapsulated. The size of the nanoparticle is 80 to 100 nanometres. The nanoparticle gets taken up by the leaky vasculature of the tumor and is then taken up by the lysosomes. The change in the PH of the blood versus the acidity within the lysosome releases the payload inside the tumor. We believe we can place other biologics inside the nanoparticles as well. Since the actives are encapsulated inside the nanoparticle when it is in the peripheral bloodstream, you do not see off-target toxicity or collateral damage. ■

Roel Schaapveld

CEO
INTERNA TECHNOLOGIES

Can you take us through the basics of the research that led to the creation of InteRNA?

InteRNA was incorporated as a spinoff from the Hubrecht Institute, Utrecht, the Netherlands. The academic founders of the company used deep sequencing in combination with proprietary bioinformatics to identify novel microRNAs (miRNAs) in deep sequencing data sets. At the time of their research, there were already miRNAs discovered, mainly by Thomas Tuschl when he was at Max Planck Institute for Biophysical Chemistry and at the Rockefeller University. His IP went to Alnylam, which today is the biggest siRNA company in the world. We found new miRNAs that Thomas Tuschl had not found, and we were able to file a patent application on these discoveries. There was interest from industry for these miRNAs, not only for therapeutic application, but also for diagnostics application.

We took a selection of our novel miRNAs, as well as a selection of already known miRNAs from the public database, and we cloned them on an individual basis in lentivector (lentiviral vector). Once we had the viral particles produced, we ran various kinds of high throughput functional genomic screens in cell based assays.

Our R&D approach is a functional genomics approach. We treat tumor cells with the miRNAs on an individual basis to see whether they go, for example, into apoptosis or that you can inhibit proliferation. This is already the first indication of the potential function of the particular miRNA. This approach is unique compared to the approach of other miRNA companies, as what they started off with was descriptive differential expression profiling. In a disease situation miRNAs can be up or down regulated. If you analyze the RNA from disease samples versus normal samples on a microchip with miRNAs, you can check for up and down regulation. What you do not have with this differential expression approach is the spatial and temporal information, and you do not know if the up or down regulation of the miRNA is a result or a cause of a defect. If you have a non-bias functional genomics approach, you immediately have information on the potential function of the miRNA.

Can you elaborate on the development of InteRNA's INT-1B3 drug development candidate?

Our screenings gave us multiple miRNA drug candidates. We then implemented transcriptomic analysis, mainly based on RNA sequencing with bioinformatics, to identify which messenger RNAs (mRNAs) are regulated by the individual miRNAs. This information gave us insights in the biology of all our candidates. We prioritized INT-1B3, a lipid nanoparticle (LNP) formulated synthetic mimic of a tumor suppressor miRNA, as we found that it has a dual mode of action. Firstly, it targets tumor cells directly, pushing them into apoptosis and inhibiting their proliferation and migration. Regulation of specific mRNAs leads to activation of the PTEN tumor suppressor pathway in parallel to inhibition of the oncogenic Ras/MAPK and PI3K/Akt signaling pathways. In parallel, we discovered that INT-1B3 regulates the tumor microenvironment and ultimately elicits a long term T-cell mediated immune response. INT-1B3 regulates the enzymes CD39 and CD73 thereby reducing adenosine levels and downregulating the adenosine-A2A receptor pathway involved in the escape from immune surveillance. Further it makes immune cold tumors hot through recruitment of CD8+ $T^{effector}$ cells and downregulation of immunosuppressive LAG-3/FoxP3 $T^{regulatory}$ cells. Based on this biology, we find INT-1B3 a very attractive drug candidate in the immuno-oncology field.

We aim to initially develop INT-1B3 for treatment of patients with hepatocellular carcinoma (HCC) and triple-negative breast cancer (TNBC). Yet the compound also qualifies for other cancer indications like melanoma, lung cancer (NSCLC) and pancreatic cancer as we found in our preclinical studies.

What is InteRNA's strategy for pushing forward the development of the company's drug candidates?

We are looking for partnerships for our CNS programs and, in first instance, not for our lead candidate INT-1B3. We have an anti-miR that can knock down an overexpressed miRNA in temporal lobe epilepsy patients, and are currently in discussions with CNS focused pharma for early stage collaboration on this candidate. For our lead candidate INT-1B3, we would like to reach proof of concept in a Phase 1b/2a trial to create several strategic options with regard to potential Phase 2b trials and/or exit scenarios. ■

Expanding Therapeutic Focus

EASING THE BURDEN ON PATIENTS

Patient advocacy groups play a critical role in drug development. They drive innovation, fundraise and financially support companies to do the necessary research and development. Often, it is the patients who drive the narrative in Washington, state capitals and in the overall pharmaceutical industry. The patient advocacy groups have databases to help identify patients, which can be extremely helpful for clinical trial enrollment. In CF, for example, the availability of new genetic therapies has meant that CF patients are routinely sequenced and their genotypes are known, which has been extremely helpful in recruiting patients for clinical trials.

- Neil Belloff,
COO, General Counsel and Corporate Secretary,
Eloxx Pharmaceuticals

One of the trends in US biopharma is that the growing scope of companies developing therapeutics that target unmet medical needs. Even in areas in which substantial progress has been made, like cystic fibrosis (CF), there remains a need to develop effective and affordable drugs for diseases that are related. Likewise, there remain segments of a disease population with rare gene mutations that prevent the most common treatments from working effectively.

The former is the case for those who suffer from exocrine pancreatic insufficiency (EPI), which can be closely related to CF. People with CF have breathing problems because mucus clogs their lungs and makes them vulnerable to infections. Thick mucus also clogs the pancreas and hinders the release of digestive enzymes. About 90% of people with CF also end up developing exocrine 57>>

James Sapirstein

President and CEO
AZURRX BIOPHARMA

What was the appeal and opportunity you saw that made you want to join the AzurRx team?
I was semi-retired and working on different projects with several companies and I had a chance to look at AzurRx's data in cystic fibrosis (CF) for the treatment of exocrine pancreatic insufficiency (EPI) and a couple of things appealed to me. First, the data from the company's two Phase 2 studies was compelling. Second, I saw that there is significant potential for a non-porcine synthetic product in this setting. Finally, I saw that the company was extremely undervalued and believed that, with proper execution, the only direction for valuation was up. I have a history of turning companies around, and really enjoy doing it. I saw the opportunity to do it again with AzurRx.
MS1819, the company's lead product candidate, definitely has the potential to be a life changing therapy.

Can you characterize the size of the market AzurRx is targeting?
Our lead indication is targeting a condition known as EPI which affects about 35,000 CF patients and about 100,000 chronic pancreatitis patients in the U.S. In patients with EPI, the pancreas is damaged and does not produce the digestive enzymes, particularly lipase, needed to break up food in the GI tract so that it can be absorbed. Patients with EPI struggle with a nutritional deficit – they cannot gain or keep weight, which is critical for CF patients. The current standard of care is to replace these enzymes with porcine derived enzymes – a therapy known as PERT (pancreatic enzyme replacement therapy). With PERT therapy, CF patients with EPI have to take 25-40 pills daily throughout their entire lives. In addition to the high pill burden, PERT therapy has risks.
Our lead product, MS1819, is a yeast derived, synthetic, regenerative oral medication that has the potential to be a substitute for the porcine-derived product. MS1819 has an encouraging safety profile and does not confer the risk of fibrosing colonopathy. Also, we believe it can dramatically reduce the daily pill burden -- down to 8-16 pills per day.
MS1819, targets both the CF and chronic pancreatitis (CP) communities. The CF market is basically comprised of branded generics, with the main product being Creon from AbbVie, which has around US$1 billion in sales.
The barrier to entry is high and no one has been able to displace Creon and Zenpep. Given our unique profile, we believe that we will be able to add new patients to the mix and create a marketplace for our product. With at least a US$1.2 billion market for just Creon and Zenpep in the U.S., even if we were to capture just a small percentage of it, we see this as a very attractive market.
CP offers a huge opportunity, especially in Europe and Asia.

What studies does AzurRx need to perform to gain approval from FDA to market the drug?
We are preparing to initiate a Phase IIb program for MS1819 in CF in the second quarter, with data expected by the first quarter of 2021. We then anticipate meeting with the FDA to discuss a Phase 3 trial design. We are preparing to be Phase 3 ready by mid-2021 and, assuming that we only need to do a single study, we hope to launch commercially in CF in late 2022 or early 2023. For CP, we are planning another study to be run in parallel with our CF study and are planning to have a second indication for MS1819 for the treatment of CP in 2024.

Can you discuss the company's financial position and the resources available to execute on your plan?
AzurRx has used two financial instruments. First, we established a US$15 million equity line with Lincoln Park Capital, to remove a financing overhang that was weighing on our share price. Second, we raised US$6.9 million in a private placement that, together with the equity purchase agreement, gives us capital until 2021. Additionally, we have an active business development program aimed at generating potential partnerships that could provide us access to non-dilutive sources of capital. Our efforts are targeting pharmaceutical development companies that are interested in the gastroenterology space and looking to fill their pipelines with a differentiated agent offering attractive margin potential. Because our development program is relatively efficient and inexpensive, it would not be a big reach for a pharmaceutical company to come in and co-develop or partner with us.

What steps is AzurRx taking to show value to the market?
My goal as CEO is to execute on our clinical, regulatory and business development initiatives as seamlessly and in as timely a fashion as possible. We have a lean organization that is operating with a very clear mission. We expect to complete our combination study and provide top line results by year end. Our Phase IIb study in CF will begin enrolling patients next quarter, and we anticipate releasing topline results in early 2021. We have designed both studies to showcase the safety and efficacy of MS1819 and believe that their results will be significant events to unlock value. Because the combination study is open label, it is possible that we may provide interim updates as the trial progresses. Assuming successful outcomes, we look forward to moving MS1819 into at least one pivotal trial in 2021. As I indicated, we have an active business development program and are constantly evaluating potential partnering opportunities. Naturally, should we decide to pull the trigger on a collaboration, we would only do so if we believed that it would provide value to both patients and our stakeholders. ■

Robert Foster

CEO
HEPION PHARMACEUTICALS

Hepion evolved from Contravir in 2019. What was the thought process behind the change?
The name change reflects a transformation in the strategic direction of the company. In 2016, the main focus of the company was anti-virals, namely the treatment of hepatitis B and a treatment for shingles. I was asked to take over as a CEO of Contravir in October of 2018 and made a review of our products and take a strategic view of where the market was going and where the opportunities were to maximize shareholder value. I decided to halt the development of our late stage developments and emphasize the early stage program, which is centered on the CRV431 molecule. The data was telling us that we had a molecule that had very strong anti-fibrotic properties and I wanted to see if the molecule could be developed further, initially in the indication of liver disease and specifically in non-alcoholic steatohepatitis – also called NASH.

Can you give us an update on the development process of CRV431?
CRV431 now has two IND (Investigational New Drug) applications that have been accepted by the FDA. The first IND was for hepatitis B virus (HBV) and the second was for NASH – the latter is the indication we are pursuing now. We have completed the pre-clinical program. The package is complete and we have conducted a phase 1 single ascending dose study in human volunteers and are now conducting a multiple ascending study in healthy volunteers. We are getting ready to enter into a proof of concept phase 2 in NASH in 2020. We have made a lot of progress in the clinic and in non-clinical studies. CRV431 is an anti-fibrotic drug and we are focused on its application for NASH. If the anti fibrotic mechanism continues to be strong, which I believe it will, it may be used in other anti-fibrotic indications. To that extent, about 45% of all the death that occurred in the developed world has some type of fibrosis component.

Can you comment on the obesity epidemic and how it is driving the need for medical solutions to fatty liver disease?
Obesity is a global problem and fatty liver disease can affect as many as one in four of the population. Of those, some will go on to develop NASH, which is a more aggressive form of non-alcoholic fatty liver disease. NASH may affect up to about 12% of the US population. It is vitally important that we develop solutions to treat the global population for this epidemic of fatty liver disease and NASH. If we do not find good treatments for liver disease, the outcome will be severe with increased morbidity and mortality from cardiovascular disease and liver related events such as liver transplantation and liver cancer.

With the clinical studies for CRV advancing steadily, what are the company's plans and milestones for 2020 and beyond?
One of our key events slated for the first half of 2020 is the completion of our multiple ascending dose study of CRV431. We will also initiate a phase 2 proof of concept, a short study that is only 28 days long. We will be looking for safety, tolerability as well as biomarkers for NASH and fibrosis. We will be monitoring specific markers to determine to what extent we may anticipate how these will behave in a longer NASH study. This study will prepare us not only for our longer phase 2 program, but also for our phase 3 program.

What is your final message to the pharmaceutical and investment community about why they should be interested in Hepion?
People should pay attention to Hepion because this is a company that is truly undervalued. My previous company, Aurinia Pharmaceuticals, was under-valued for a long time. More recently, however, investors paid attention to our previous drug, voclosporin, for the treatment of lupus nephritis and have now driven the company's market cap to over US$2 billion. When I look at Hepion, which is approximately only US$20 million market cap, I believe that CRV431 is at least as good as voclosporin and addresses a market that is much larger than lupus nephritis. I believe the upside is very substantial in terms of both CRV431's potential in NASH fibrosis and market value. ■

<<54

EPI, according to Cleveland Clinic data. Patients with EPI struggle with a nutritional deficit and cannot gain or keep weight, which is critical for CF patients. The current standard of care is a therapy known as PERT (pancreatic enzyme replacement therapy). With PERT therapy, CF patients with EPI have to take 25-40 pills daily throughout their entire lives. In addition to the high pill burden, PERT therapy has risks of a condition called fibrosing colonopathy at higher doses.
In response, AzurRx is developing a product (MS1819), that is a yeast derived synthetic, regenerative oral medication that has the potential to be a substitute for the porcine-derived product. The company believes MS1819 has an encouraging safety profile and does not confer the risk of fibrosing colonopathy. They also see potential to dramatically reduce the daily pill burden down to 8-16 pills per day.
There is also significant market opportunity. According to James Sapirstein, AzurRx president and CEO: "The barrier to entry is high and no one has been able to displace Creon and Zenpep. Given our unique profile, we believe that we will be able to add new patients to the mix and create a marketplace for our product. With at least a US$1.2 billion market for just Creon and Zenpep in the U.S., even if we are to capture just a small percentage of it, we see EPI as a very attractive market. "
Another segment of the market with unmet medical needs are rare and ultra-rare diseases. Premature stop codon diseases fall under this category. The population of CF patients with these diseases is 10-15%, and for this subset,there is currently no approved therapy. Eloxx Pharmaceuticals is developing novel ribonucleic acid (RNA)-modulating drug candidates, each designed to be a eukaryotic ribosomal selective glycoside (ERSG) formulated to treat these rare and ultra-rare premature stop codon disorders.
One of the biggest reasons for the increased attention and capital pursuing rare diseases has been the influential role of patient advocacy groups. According to Neil Belloff, COO, general counsel and corporate secretary, Eloxx Pharmaceuticals: "Patient advocacy groups play a critical role in drug development. They drive innovation, fundraise and financially support companies to do the necessary research and development. Often, it is the patients who drive the narrative in Washington, state capitals and in the overall pharmaceutical industry. The patient advocacy groups have databases to help identify patients, which can be extremely helpful for clinical trial enrollment. In CF, for example, the availability of new genetic therapies has meant that CF patients are routinely sequenced and their genotypes are known, which has been extremely helpful in recruiting patients for clinical trials."
In summary, the progress made across the industry is not only advancing in some of the most well known disease categories, but also in areas that have long been neglected. It is a strength of the US healthcare system that there are private companies that willingly embrace enormous financial risk to bring drugs to market for small segments of the population. This has hugely beneficial implications for patients and gives renewed hope to those who once thought they would never be cured. ■

Neil S. Belloff

Chief Operating Officer, General Counsel and Corporate Secretary
ELOXX PHARMACEUTICALS, INC.

What is the focus of Eloxx Pharmaceuticals?
Eloxx Pharmaceuticals is a clinical-stage biopharmaceutical company developing novel ribonucleic acid (RNA)-modulating drug candidates, each designed to be a eukaryotic ribosomal selective glycoside (ERSG), formulated to treat rare and ultra-rare premature stop codon disorders. Premature stop codons are point mutations that disrupt the stability of the impacted messenger RNA (mRNA) and the protein synthesis from that mRNA. As a consequence, patients with premature stop codon disorders have reduced levels of, or no, protein from a gene whose product performs an essential function.

What can be improved about current Cystic Fibrosis (CF) therapies?
Substantial progress has been made with approved breakthrough genetic therapies which are increasing survival and improving the quality of life for cystic fibrosis patients. However, despite this there remains a high unmet medical need among the 10-15% of patients with nonsense mutations for whom there is no approved therapy. At Eloxx, we are addressing this population and believe we are the only clinical stage company targeting CF patients carrying nonsense mutations on one or both alleles of the CFTR gene. We have initiated Phase 2 proof of concept clinical trials.

What are key milestones for 2020 as well as for the next two to three years?
For 2020, completing enrollment and reaching top line data in our phase 2 proof of concept clinical trial for ELX-02 in CF are our top priorities. We are also focused on advancing our IND enabling research for our ERSG library in kidney diseases and ocular disorders. Following the completion of our phase 2 trials, we will seek to engage with the FDA and other global regulatory bodies to gain alignment on a path toward registration and ultimately go to market with these products to provide much needed treatment options to patients with unmet medical need. ■

Responding to COVID–19

PANDEMIC NIGHTMARE ARRIVES

In April of 2018, Bill Gates delivered the annual address at the Massachusetts Medical Society. For the former world's richest man turned global health aficionado, it was an opportune time to diverge from his usual optimistic tone. It is true that the world is on the verge of eradicating polio, HIV is no longer a death sentence and half the globe is now free of malaria. However, Gates chose to focus on a topic where he saw progress had stalled: Pandemic Preparedness.

His thesis insisted that historical precedent should have taught us that pandemic's will reoccur. He warned: "Watching Hollywood thrillers, you would think the world was pretty good at protecting the public from deadly microorganisms… In the real world, though, the health infrastructure we have for normal times breaks down very rapidly during major infectious disease outbreaks. This is especially true in poor countries. But even in the U.S. our response to a pandemic or widespread bioterror attack would be insufficient."

Two years after this speech, the world is collectively struggling through the COVID-19 pandemic and Bill Gates' vision has proven to be prophetic. Why are we in the position of being so unprepared across the board against infectious disease? It can be broken down into two driving factors; one scientific and the other economic.

On the scientific side, discovery of an anti-infective poses unique hurdles because it needs to be toxic to pathogens without being toxic to humans. It also needs to have a reasonable distribution, absorption and dosing profile that makes for a practical drug people can take. Many patients with serious infections like COVID-19 are best treated outside of a hospital to prevent patients from spreading infection. That means an oral bioavailability should be a top priority, because pills can be taken by patients at home.

The second factor is economic. The economics for some anti-infectives do not work, even if they are needed for public health. Evidence of this at play in the marketplace is exemplified by the IV antibiotic therapies from Tetraphase Pharmaceuticals and Melinta Therapeutics. The former company was acquired for a bargain price and the latter went bankrupt before it could reach commercial launch.

The reason it is so difficult to develop a viable company in the infectious disease space is because of reimbursement issues. Certain medicines require healthcare institutions to pay for them out of a fixed fee, regardless of what is needed for their care. This is known as the diagnosis-related group payment (DRG), and the DRG is a disincentive to use innovative medicines since their cost comes directly out of the institutions bottom line. If a hospital limits its usage of a patented, more expensive medicine, it gets to keep a larger portion of the fixed fee it collects from the health insurance provider. This is concerning because a lack of financial incentives, creates conditions where companies are less willing to pursue discovery and development of innovative therapies. The problem for public health is then amplified, because diseases evolve and this renders current anti-infectives obsolete.

There is also an issue of market size. There just are not enough patients. Some medicines needed for the public health fight are for infections that are not prevalent, yet. There is a general lack of willingness to pay for something that does not pose a clear and present danger as COVID-19 does. Building a sustainable infrastructure to fight future threats requires a multi-strategy approach. It requires big investments, but the multi-trillion dollar cost of COVID-19 to our economy suggests that for a far smaller sum we can be better prepared for the next outbreaks. It is of utmost importance to save lives now, but it is equally important take steps to prevent the next crisis from happening.

In summary, infectious disease has had an ebb and flow relationship with our general awareness; epidemics such as Zika, Ebola, and SARS raise the profile of infectious disease in the public consciousness and then recede from memory. As they capture the headlines, these outbreaks mobilize financial and intellectual resources that are needed to treat these emergent and very important threats.

The sad truth about so many disease outbreaks of the past is that being prepared for the next one means keeping up a sustained, multifaceted effort over many years. This includes everything from testing, data surveillance to the continuous development of treatments and vaccines. Important lessons will be learned given the extent of the pain COVID-19 has inflicted on society. One can only hope new methods and incentives will be implemented to prioritize preparedness moving forward. ■

We are learning in real time that global health is American health. People frequently and mistakenly think of global health as a developing country problem. It is, until it arrives at America's shores and then we are forced to respond reactively rather than proactively. This is a risk the US and other Western countries run by not focusing on tropical diseases. For example, Zika virus or dengue virus are now affecting parts of the US. We are now learning that it is not strategically smart to ignore these kinds of things.

- Mike Pollastri, Interim Dean and Professor, Northeastern University, Academic Lead for the Roux Institute

Dr. Trevor P. Castor

President & CEO
APHIOS

How has Aphios evolved since its founding and how has nature influenced the development of your therapeutics?

Aphios' vision is to develop biotechnology products for improving health and treating chronic diseases in an environmentally sustainable manner. Aphios was established in 1993 with an initial focus on developing enabling technology platforms for improving drug discovery, drug manufacturing, drug delivery and pathogenic drug safety focused on the inactivation of viruses and pathogens in the blood supply and our bodies. Aphios is a combination of two Greek words, which means virus free. We spent approximately a decade developing, validating and patenting these platforms and from there, we started developing therapeutic products based on these platforms. In 2003, we began our first big clinical trial for our patented product Zindol for chemotherapy induced nausea and vomiting. That was influenced by nature, because it was a ginger based product. Currently Zindol is on the marketplace as a dietary supplement, while we focus on attaining FDA approval.

We also developed a technology for manufacturing Taxol, a potent anti-cancer agent. Today, we have several products in development, including APH-0812, for which we were just awarded a US patent. It is a combination therapy of a protein kinase C (PKC) modulator and histone deacetylase (HDAC) inhibitor in a nanoparticle that is targeted for HIV latency.

Can you elaborate on the Aphios' partnership with LSU Health Shreveport?

We have a partnership with LSU Health Shreveport to develop drugs for Alzheimers disease and cognitive disorders, as well as for the transplantation of kidneys and the liver. Together we have developed and patented a technology and product for improving the length of which an organ can be preserved before transplantation.

What is Aphios strategy for pushing its products forward and taking them to market?

Aphios' strategy is to license as early as possible. We collaborate with strategic partners and/or license our enabling technology platform to research and develop novel drugs, and for the reformulation of existing drugs to reduce toxicity and improve efficacy and therapeutic index, while extending product life. We will also collaborate with strategic investors and corporate partners to further the development and commercialization of our therapeutic products.

What are your thoughts on the current developments in the neurodegenerative space and the potential for making important strides forward?

There is an association between amyloid plaques and tau entanglements in Alzheimer's disease (AD). The question remains how to prevent this from happening or to reduce it once it does happen. There are three critical neural enzymes that affect amyloid plaques. They are Beta-secretase, Gamma-secretase, and Alpha-secretase. Pharmaceutical companies have focused on Beta-secretase and Gamma-secretase, but these have been difficult to translate into effective clinical treatments for AD.

Aphios' approach is to upregulate Alpha-secretase, which positively impacts amyloid precursor protein, (APP) processing. Both Beta-secretase and Gamma-secretase cleave APP to form insoluble amyloid plaques that set in motion tau fiber assembly. In contrast, Alpha-secretase cleaves APP into a harmless and more soluble product, that supports new synapse formation and is more readily cleared from the brain. Thus, unlike current strategies, which aim to suppress amyloid plaque formation by minimizing Beta- and Gamma-secretase activities, our strategy is to activate Alpha-secretase, which will effectively eliminate the substrate for Beta-amyloid generation, and at the same time lead to positive amyloid precursor processing, to both prevent and reduce amyloid plaques in AD.

Can you elaborate more on Aphios' platforms?

We are leading the way in developing green, enabling biotechnology and nanotechnology drug delivery platforms and enhanced therapeutic products for health maintenance and the treatment of chronic diseases. We source our biodiversity from nature – medicinal plants, marine organisms, or humans. We use supercritical fluid solvents, as a replacement for organic solvents. When compressed, these fluids exhibit enhanced thermodynamic properties of penetration, selection, solvation, and expansion. We manipulate these fluids on a cellular level to increase process selectivity and speed while reducing processing steps, toxic organic usage and manufacturing costs.

This technology is especially relevant with the ongoing corona virus pandemic. Our pathogen inactivation technology can clear viruses from the blood supply, and our photoluminescence molecular flashlight therapeutic can inactivate viruses within our body.

What trends are you currently seeing?

Cannabis-based drugs are becoming a huge trend in the market. Aphios is developing FDA-approved, cannabis-based drugs for treating unmet central and peripheral nervous system disorders of opioid addiction and pain. Cannabinoids have a lot of potential to affect the body. ■

Commercializing Neuroscience

VC BETS BIG ON THE BRAIN

Often referred to as 'the final frontier' of medicine, neuroscience is unquestionably complex. So much so, that stories of high profile failures and headlines of big pharma deprioritizing programs have seemingly muted enthusiasm for the field. Amgen scrapped its R&D program to focus on cancer in 2019, following in the footsteps of Pfizer's decision to do the same in 2018. Others, like Bristol-Myers Squibb, GlaxoSmithKline and AstraZeneca announced cutbacks on CNS disorders a few years earlier.

Amgen's head of R&D, David Reese, explained that the reason for the companies exit rested on several factors, including the industry's "fairly rudimentary" understanding of neurological diseases, the long development programs some of these drugs require, and the clearer opportunities Amgen saw with oncology, inflammation and cardiovascular medicines. There is no doubt neuroscience presents some unique challenges: uncertain diagnoses, long progressive burdens of disease, multiple etiologies and complicated clinical trials are a few of them. As a consequence, there remain few, if any, novel treatments for diseases like Alzheimer's, Parkinson's and depression, each of which affect millions of patients.

Despite the flurry of headlines of a pullback from big pharma, neuroscience has quietly become a hot space for startups. Across a range of neurologic conditions, investors have been fueling entrepreneurs to discover and develop novel therapeutic strategies. According to Bio's 2019 Industry Analysis report, neurology startups received US$1.5 billion in venture funding in 2018, second only to oncology. This suggests financiers expect payoffs in the not-too-distant future, perhaps through a big pharma buyout. Their bet may be well placed too, as industry watchers foresee big pharma lured by emerging treatments for epilepsy, mood disorders and genetic diseases of the central nervous system.

Because there is so much downside risk, the upside potential of investing in the sector is exponential. Patient unmet needs from neurologic disorders are staggering, and the cost to society is enormous. As most OECD countries experience a 'greying' of their populations, the burdens of many of these later-onset neurologic conditions will skyrocket. This creates an imperative to act, and to invest, in new therapies.

Psychiatric disorders such as schizophrenia have gone long periods without advances in treatment. Given the disease affects 1% of the population according to the Mayo Clinic, there is substantial need for disruption in the area. Terran Biosciences is at the forefront of trying to solve this debilitating disorder. The company is developing therapeutics and neuroimaging software to deliver novel treatment solutions and aid in the diagnosis of patients with psychiatric and neurological diseases. "We have seen renewed interest in the space over the last couple of years, and a few groups are really pushing forward on new mechanisms to address the large unmet need. Terran's lead compound, TR-01, is an alpha-2 (α2) adrenergic receptor antagonist, which can be added onto the current standard of care therapies. This makes it the only drug in development as an adjunctive therapy for schizophrenia, and is designed to give patients a new safe and more effective option for improving their current treatment," said chief business officer Dustin Tetzl.

Massachussetts based Aphios are working to develop therapeutics products for CNS disorders. Its approach, as characterized by President and CEO Dr. Trevor Castor, is to: "Upregulate Alpha-secretase, which positively impacts amyloid precursor protein (APP) processing. Both Beta-secretase and Gamma-secretase cleave APP to form insoluble amyloid plaques that set in motion tau fiber assembly. In contrast, Alpha-secretase cleaves APP into a harmless and more soluble product that supports new synapse formation and is more readily cleared from the brain. Thus, unlike current strategies, which aim to suppress amyloid plaque formation by minimizing Beta- and Gamma-secretase activities, our strategy is to activate Alpha-secretase, which will effectively eliminate the substrate for Beta-amyloid generation and, at the same time, lead to positive amyloid precursor processing to both prevent and reduce amyloid plaques in Alzheimers disease."

"The human body has an endo-cannabinoid system to satisfy the CB1 and CB2 receptors. Cannabis-based drugs can thus supplement the body's endo-cannabinoids. There are approximately 65 different cannabinoids, all of which have different potential impacts on the human body. We believe that cannabinoids are great for treating opioid addiction, as some of the same receptors that interact with methadone, the treatment that is used on opioid addicts, interact with cannabinoids. If the receptors can be satisfied by a non-opioid drug, it will be able to alleviate the craving for opioids."

- Dr.Trevor Castor, President and CEO, Aphios

A huge element of this expansion of basic neuroscience understanding has come from the explosion in NIH funding for neuroscience in the first decade of the 2000s. In the 1990s, the NIH channeled US$954 million into neurology research. In the 2000s, this number spiked to over US$8 billion. This was a larger increase than in any other therapeutic area, and has created a wave of insights a decade later that the industry is currently in the process of translating into new therapies.

Developments in neuroscience are always uncertain, but some experts, such as Roche CEO Bill Anderson, believe we are on the cusp of major breakthroughs: "Neuroscience has the potential to be in the 2020s what oncology has been in the last decade."

If such is the case, it will be an exciting road forward for all involved. ■

Dustin Tetzl & Samuel Clark

DT: Chief Business Officer
SC: CEO
TERRAN BIOSCIENCES

SC

DT

What was the opportunity that encouraged you to establish Terran Biosciences?

DT: Terran Biosciences initially started with work on schizophrenia; identifying new therapies and new biomarkers. We decided to build a company around exciting assets licensed from different institutions: two therapeutics and a neuroimaging software program to deliver new treatment solutions and aid in diagnosis of patients with difficult psychiatric and neurological diseases.

Terran is planning to take our late stage schizophrenia compound, TR-01, forward into phase 2b. We also have a preclinical compound with a new mechanism for schizophrenia, TR-36, which we will be bringing through IND enabling studies. The other area in which we are focused is on developing our companion neuroimaging software platform, which is an exciting breakthrough to measure a biomarker which may aid in the diagnosis of patients with schizophrenia, Parkinson's disease, and Alzheimer's disease. We believe that this could be approved through an accelerated pathway by the end of 2020.

How do TR-01 and TR-36 differ from traditional approaches that have addressed schizophrenia?

DT: Terran's lead compound, TR-01, is an alpha-2 (α2) adrenergic receptor antagonist, which is able to be added onto the current standard of care therapies. This makes it the only drug in development as adjunctive therapy for schizophrenia. This compound has already been through proof of concept phase 2 studies, and has shown to be effective on top of standard care, in addition to its effectiveness in both positive and negative symptoms of schizophrenia.

Our early stage T-36 compound is a selective kappa-opioid receptor antagonist, which is also a new mechanism. A few companies are developing these compounds for depression, but we believe that there is a fantastic rationale to bring it into the schizophrenia space as well.

How can imaging and AI improve diagnosis for Parkinson's?

SC: The current standard of diagnosis for Parkinson's can be complicated and can take a long time. The diagnosis workup begins when patients have symptoms. In many cases, this diagnostic workup is a prolonged process that is quite burdensome for patients and the system.

Terran's imaging software platform is able to measure a biomarker which may aid in simplifying the diagnostic process and may be measured early on in their workup. Our platform is able to analyze a brain MRI, which is often performed during first or second patient visits, and give a measurement of a key biomarker called neuromelanin. This biomarker has been shown to be to aid in determining whether a patient has Parkinson's disease or a related disorder. Thought leaders have already published that neuromelanin imaging may become integrated into the workup of Parkinson's, which may allow patients to avoid expensive and invasive SPECT scans with radiotracer IV infusions, and both improve and simplify the process. Terran's technology is the world's first and only software platform that gives both an automated and quantitative measurement of neuromelanin in different regions of the brain.

What are the capital requirements of the business and what is Terran's funding and partnership strategy moving forward?

DT: We are currently in the middle of an active raise for our Series A round. This capital raise will get us through key milestones over the next 2 years to be able to move our imaging product potentially all the way through FDA approval and early launch, as well as move our clinical compound TR-01 through the phase 2b trial and our pre-clinical compound TR-36 through IND enabling studies.

What milestones is Terran looking to achieve with its current raise?

DT: With the current raise, Terran is looking to bring our lead compound all the way through our CMC work and then through the phase 2b study. We want to bring our TR-36 compound through IND enabling studies, to be able to start a phase 1 study. On the imaging side, we will continue to find more pharmaceutical partners who can use our technology in their own studies, and aim to get the platform through FDA clearance and on the market as a clinical tool in a year. ■

Originating Discovery

ACADEMIA MOVES OUTSIDE ITS BUBBLE

There is a common perception that much of the research produced by academia dies in academia without ever having any practical real world application. This is not so often the case as it pertains to the life sciences. America has immeasurable talent coming from its universities and, in recent years, the life sciences industry has looked to tap academia to help develop scientific breakthroughs that can be leveraged to achieve their commercial goals. Conversely, universities find industry partnerships valuable because they help advance their capacity to conduct high quality research, which can be an influential factor in attracting high level academic talent and top tier students.

In analyzing each of the respective biopharmaceutical clusters throughout the US, universities are their backbone: MIT, Harvard and Northeastern University in the Boston-Cambridge areas, Stanford in Silicon Valley, Princeton and Rutgers in New Jersey, Upenn and Temple in Philadelphia, Columbia and NYU in New York and the Research Triangle has North Carolina State, Duke and University of North Carolina at Chapel Hill. Each of these universities is world class and plays an integral role in geographically anchoring the ecosystem.

Although there has always been a relationship between universities and industry in terms of hiring graduates, industry is now much more involved than ever before when it comes to research. Coleen Burrus, head of corporate engagement and foundation relations at Princeton University, noted: "The shift that occurred was around getting the research done on campus out to the world through industry. In the last five years, the number of collaborations has skyrocketed and the number of dollars coming from business to research has quadrupled."

Beyond collaboration, some universities have now taken the initiative not only to advance research, but also to help researchers create commercially viable companies. Rutgers, for example, has its Rutgers University Biomedical Research and Innovation Cores (RUBRIC) program, which is comprised of experts from pharma and biotech, including medicinal chemists, who are rarely found in university settings. The university also has capabilities in research pathology, molecular imaging, and collaborates with Princeton University in high throughput screening. "Because our staff have extensive experience in the pharma industry, they understand what the basic sciences faculty need, and can help them source the necessary data to contribute to academic drug development," said David Kimball senior VP for research and economic development at Rutgers University.

As a result of a greater focus on providing tools for commercialization, these universities are now seeing an increasing number of spinouts that become successful life science companies. A model of a successful transition can be found in Biohaven, which traces its roots to Yale, where it was founded on intellectual property from CEO Vlad Coric. The company focuses its work on neurological innovation and developing novel products that address everything from migraine headaches to Alzheimer's disease, and had its initial public offering in 2017.

Overall, the amplified importance of academia's role in drug discovery and development is an essential one, because the pursuit of interesting ideas and the freedom to question are far more limited in the commercial world. This is why academia will continue to be leaned on to pursue moonshot scientific breakthroughs that hopefully will provide cures to diseases we consider intractable today. ■

Under the current grant system, an academic researcher can get all the funding needed to conduct drug discovery research within their university lab. However to develop a compound to the clinical phase requires a number of preclinical studies requiring millions of dollars that cannot be supported by the traditional R01 style funding mechanisms. Therefore, if the researcher wants to move a particular compound forward they need to go the route of a biotech startup, where they can find the funding sources to develop these potential drug candidates. I think that Universities need to do a better job of identifying how to get investment philanthropy to support this gap in resources to take lab discoveries to IND.

- Anthony Capobianco, Founder and President, StemSynergy Therapeutics

Anne-Marie Maman, Coleen Burrus & Dean Edelman


AM


CB


DE

AM: Executive Director
CB: Head Corporate Engagement and Foundation Relations
DE: Corporate Engagement and Foundation Relations
PRINCETON ENTREPRENEURSHIP COUNCIL

When did Princeton start making a concerted effort to grow its ties to the business community?

CB: Princeton has always had a culture of innovation and cutting-edge research. Pushing the boundaries of discovery has always been central. The shift that occurred was around getting the research done on campus out to the world through industry. We help bridge faculty and business to work together. In the last five years, the number of collaborations has skyrocketed and the number of dollars coming from business to research has quadrupled.

AM: The university commissioned a study to determine how best to incorporate entrepreneurship programs within our academic offerings. It was decided that the university should approach entrepreneurship from what has always been Princeton's core focus, the humanities. What this means is that the program's primary purpose is to serve society collectively. Additionally, we maintained other aspects of Princeton's ethos, such as strong alumni engagement. Some of the resources created to support entrepreneurship on campus are: a hub for students, a summer accelerator, an innovation center for faculty, a wet lab and dry lab co-working space and the entrepreneurship council. Entrepreneurship is the link between research and the market. The university will help both faculty and students who are interested in turning their innovations into companies.

How do you go about tapping the resources of the business community?

CB: We participate in industry events such as conferences and associations. We also meet with companies at an individual level. We receive a lot of attention from industry because they are interested in pursuing collaborations through various mechanisms such as funding and technology licensing. Their profiles range from large to small sized. Companies will approach our team with a concept or focus and we create the links with faculty.

Can you highlight some of your partnerships?

DE: Many of the major pharmaceutical companies are involved with the Princeton Catalysis Initiative, a program designed to promote collaborations which will result in entirely new fields of research. Industry representatives attend symposiums where faculties present their scientific and administrative initiatives. This provides a space for communication, idea exchange and partnerships. Merck, BMS, Johnson & Johnson are all part of this initiative.

AM: The New Jersey Health Foundation is another partnership that promotes research collaborations. It provides funding for university startups, bridging the gap between research and commercialization. It is a non-profit foundation that seeks to advance translational research through discovery grants and VC funding. For example, they are supporting one of our university spin-outs that specializes in metastatic breast cancer, Kayothera. The company was founded by a faculty member, Yibin Kang, and a grad student, Mark Esposito. They are now housed in the Princeton Innovation Center.

In what ways is government policy in New Jersey supporting synergies between university and industry?

CB: There is a strong commitment to the triple helix; industry, business and academia working together. The New Jersey Economic Development Authority provide incentive packages for university-related start-ups such as tax credits and funding. For example, startups can receive additional funding when they are housed in an incubator supported by the NJEDA. Choose New Jersey launched a database called Research with New Jersey. It houses the research information of six in-state institutions such as faculty, awards and patents. This helps industry to find a faculty to work with.

AM: The NJEDA has a variety of incentives. The Angel Tax Credit has recently shifted from 10% to 20%, thanks to Governor Murphy, with additional allowances for underrepresented minorities and women, so it goes up to 25%. This creates financial motivations for investors to focus on New Jersey startups.

What are your goals over the next two years?

CB: My team is tasked with insuring that faculty that are interested in collaborating with industry have the means of doing so. Our focus is strengthening our capacity to provide faculty with opportunities and strengthening the value of the links, making sure they have the resources they need. We also want to promote the innovative and translational research that is taking place in the university.

DE: You cannot create an innovation ecosystem in a bubble, you have to be connected with a network of players and with larger infrastructures. We are working to grow our outreach. ■

David Kimball

Senior VP for Research and Economic Development
RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY

Rutgers, the State University of New Jersey, was established in 1766

In what ways is Rutgers taking advantage of trends to outsource early drug development and what kind of programs do you have to advance and commercialize university research?
The primary program in the biomedical space is RUBRIC, the Rutgers University Biomedical Research and Innovation Cores. These cores are comprised of experts from pharma and biotech, including medicinal chemists, who are rarely found in university settings. We also offer research pathology, have a molecular imaging center, and collaborate with Princeton University in high throughput screening. Because these staff have extensive experience in the pharma industry, they understand what the basic sciences faculty needs, and can help them get the necessary data to contribute to academic drug development.

Can you mention some Rutgers university spin outs?
One example of a company that was spun out of Rutgers is Actinobac Biomed. Dr. Scott Kachlany at Rutgers School of Dental Medicine discovered a protein in the oral cavity that acts as a suppressor of white blood cells. It turns out this protein can be useful in suppressing activated mutant white blood cells, such as are present in lymphoma and leukemia. They formed a company to license this technology from Rutgers and developed this protein as a therapeutic. We helped them raise their series A venture capital funding and now, they have submitted their IND.

What is your vision for the ROI program and how is the university going to leverage its strengths in biomedical and bioengineering to support it?
The Rutgers Optimizes Innovation (ROI) program is one of twelve Research Evaluation and Commercialization Hubs (REACH) in the country funded by the NIH to speed up the translation of biomedical discoveries into commercially viable technologies. It came on the heels of previous accomplishments including the Clinical and Translational Science Award, a US$29 million award from the NIH, received last year by our medical school. The award mechanism of ROI is called HealthAdvance, and through it we will team up with the NIH to give faculty up to US$200,000 over a two-year period for projects that pass the review of industry experts.

Why is New Jersey a good location for startups commercializing research from the university?
Being situated halfway between New York City and Philadelphia, Rutgers–New Brunswick is the perfect nexus to build a collaborative and integrated hub. An Innovation Hub is being planned and will be built in the heart of New Brunswick. There are two fundamental advantages to being in New Jersey. One is the rent prices are cheaper and the other is the unmatched talent pool. Many of the best minds in drug development are still here from the heyday of big pharma and, as a result, New Jersey has the highest percentage of PhDs per capita of any state. There is huge potential in New Jersey.

In what ways is government policy in New Jersey supporting synergies between industry and academia?
Governor Murphy re-funded the New Jersey Commission on Science, Innovation and Technology (CSIT), a group focused on supporting innovation and in-state science and technology initiatives. That program had gone dormant under the Christie administration, which was unfortunate. Furthermore, he established an Office of Innovation to work collaboratively with government, academic, non-profit and private institutions to drive innovation in the state's economy. The state has also been very active in going overseas to build opportunities for economic development, especially for research. The state organizes delegations in an effort to encourage partnerships abroad. Finally, the Evergreen Fund is an initiative where the state matches 1-1 venture capital investments coming into the state through the selling of tax credits. ■

Michael Pollastri

Senior Vice Provost
PORTLAND
Academic Lead
ROUX INSTITUTE AT NORTHEASTERN UNIVERSITY

What was the impetus for the Roux Institute at Northeastern University?
The Roux Institute at Northeastern University is designed to educate generations of talent for the digital and life sciences sectors, and drive sustained economic growth in Portland, the state of Maine, and northern New England. We intend to attract small companies and also incubate new companies in Maine.
We are focusing primarily on machine learning (ML) and artificial intelligence (AI) as it interfaces with a variety of fields. The availability of talent in ML and AI is very limited and in high demand. This expertise is often built internally within companies. This is not a scalable model, so we will be targeting people who are disciplinary scientists who wish to be trained in machine learning and AI, and thus build the workforce in this space.

How do you foresee the impact of machine learning and AI as it pertains to the life sciences industry?
The big challenge is in taking full advantage of the enormous sets of data that the scientific community generates. We can ask deeper questions and apply machine learning and AI as a tool to get answers to questions we cannot obtain by inspection. These tools are not widely applied yet. For example, this technology powerfully impacts image analysis, such as image-based phenotypic screening, or in reading radiological images. The ability to quickly and accurately interpret images can speed the discovery process by speeding analysis and getting more information out of the data that is obtained.

Northeastern is providing a model of experiential education. How do you plan to bring this from the Boston campus to Portland?
The master's degree programs all have experiential components. Since many students will be company employees, their day-to-day jobs will also introduce an experiential aspect to their education. There will also be opportunities for students to undertake co-op opportunities within these Maine-based companies. We also hope to host students from elsewhere in the Northeastern network to do co-ops here. We are also expanding in Maine our experiential PhD program where company employees can complete their PhDs by doing innovative research within the company. We already have a number of these students across the colleges.

To what extent is there a start-up biotech scene and are there any plans for spin-outs?
There is a large entrepreneurship bend to what we are doing. Our intent is that the people who do their research here will be generating intellectual property, which can be spun out into the new ventures. Our collaboration model is very similar to that on our Burlington "Innovation Campus." We have a growing number of start-up companies residing there. A distinguishing feature of that campus is that we are co-located with companies like Raytheon and Rogers Corporation, whose scientists work side by side with Northeastern faculty and researchers. Companies benefit from the expertise that lives within Northeastern, and we are innovating in terms of the intellectual property arrangements that we employ. This is the sort of environment that we are looking to build in Portland.

What is your long-term vision for the development of the Roux Institute?
We want to have several hundred learners in the next five years. We also have aggressive research goals for an operation consisting of faculty members, research scientists and graduate students who will be cooperating. It is a very exciting opportunity. We have launched an Experiential AI postdoc program to attract terminal degree holders to Northeastern to get two years of training in machine learning and AI as applied to their discipline. They will be able to teach and do research during this period, and we expect that a number of these postdocs will become faculty members at the Roux Institute.

Do you have a final message for the life science community?
We are learning in real time that global health is American health. People frequently and mistakenly think of global health as a developing country problem. It is, until it arrives at America's shores and then we are forced to respond reactively rather than proactively. This is a risk the US and other Western countries run, by not focusing on tropical diseases. For example, Zika virus or dengue virus are now affecting parts of the US. We are now learning that it is not strategically smart to ignore these kinds of things. ■

CONTRACT MANUFACTURING AND GENERICS

» Outsourcing is being fueled by a need to accelerate projects through development, and the clinical pipeline for all drug molecules. This is accompanied by high numbers of product approvals by the FDA and EMA. CDMOs with critical mass and which have made investments to match the evolving needs of the current drug pipeline are well-positioned to serve these growing markets. «

- Steven Klosk,
President and CEO,
Cambrex

Contract Development and Manufacturing

NEW OPPORTUNITIES ABOUND

When investment is flowing into the biopharmaceutical industry at all time highs, FDA is approving record numbers of generic drugs and near record novel drugs, it can be expected that manufacturers find themselves with plenty of business. The outsourcing of manufacturing has evolved drastically over the last 20 years, from providing commoditized immediate release tablets of small molecule drugs, to offering a much broader and complex array of services. Spurred by the high cost of drug development, which the medical journal Jama estimates to be near US$1 billion per drug, pharmaceutical companies acknowledged the need to outsource activities that were not fundamental to their core business.

Today, pharmaceutical companies increasingly outsource research activities to contract research organizations (CROs) as a strategy to stay competitive and flexible in a world of exponentially growing knowledge, increasingly sophisticated technologies and an unpredictable economic environment. The R&D tasks that firms choose to outsource include a wide spectrum of activities from basic research to late-stage development: genetic engineering, target validation, assay development, efficacy tests in animal models, and clinical trials involving humans.

Contract development and manufacturing organizations (CDMOs), on the other hand, offer drug product development and manufacturing services, active pharmaceutical ingredient (API) production, and packaging services. There is an increasing degree of overlap between these two types of service providers: some CDMOs are starting to offer CRO services and vice versa, with the aim of becoming 'one-stop shops', covering the whole value chain from drug discovery to commercialization. The increasing outsourcing trend in the pharmaceutical industry demonstrates the success of this business model, as CDMOs are increasingly becoming integral parts of pharmaceutical companies' value chains.

According to Dr. Ramesh Subramanian, chief commercial officer of GVK Bio: "Partnering with a CRO/CDMO allows firms to run multiple programs by extending their capital runway, resulting in higher probabilities for clinical success. Leading contract organizations provide scale, speed, and cost efficiencies that pharma partners can tap into for optimal results. In summary, the drive towards 'Affordable Medicines' is a significant and positive driver of the growth of CDMOs."

Market Structure

The CDMO market is characterized by great fragmentation. A report from Kurmann partners estimated that the top five CDMOs account for only 15% of the total CDMO market size. However, there have been strong efforts to consolidate the sector in recent years. Most pharmaceutical companies, big and small, are looking to work with a small number of suppliers in order to limit the costs and risks involved in technology transfers and to save time, as time to market is a crucial factor in achieving commercial success and profitability. To strengthen their competitiveness, CDMOs are thus choosing to merge, either to extend their range of services for existing dosage forms, to enter the market for another dosage form, or to integrate geographies.

2019 saw Cambrex go from being a publicly traded entity to private after being acquired by private equity firm Pemira Funds for US$2.4 billion. The move follows two large-scale acquisitions by

ACQUISITIONS WITH DISCLOSED DEAL VALUES >$100M BETWEEN 2016-2019

Source: PWC

Year	Acquirer	Area of business (acquirer)	Acquirer location	Target	Target location	Deal value ($m)
2017	Thermo Fisher Scientific	Life sciences	USA	Patheon	USA	7,200
2016	Lonza	CDMO	Switzerland	Capsugel	USA	5,500
2019	Thermo Fisher Scientific	Life sciences	USA	Brammer Bio	USA	1,700
2017	Carlyle, GTCR	Private equity	USA	AMRI	USA	1,500
2019	Catalent	CDMO	USA	Paragon Bioservices	USA	1,200
2017	Fosun Pharma	Pharmaceuticals	China	Gland Pharma	India	1,090
2017	Catalent	CDMO	USA	Cook Pharmica	USA	950
2016	Mylan	Pharmaceuticals	USA	DPT Laboratories	USA	950
2016	Ardian	Private equity	France	Unither	France	715
2017	AGIC Capital	Private equity	China	Ritedose	USA	600
2016	Humanwell Healthcare, PuraCap	Healthcare solutions, CDMO	China, USA	Epic Pharma	USA	550
2017	AGC Asahi Glass	Glass, electronics, chemicals, ceramics	Japan	CMC Biologics	Denmark	500
2018	Cambrex	CDMO	USA	Halo Pharma	USA	425
2016	AMRI	CDMO	USA	Euticals	Italy	358
2018	Cambrex	CDMO	USA	Avista Pharma	USA	252
2016	Reipharm	CDMO	Sweden	Kemwell Biopharma	India	205
2017	Clinigen	Pharmaceuticals, clinical trials	Great Britan	Quantum Pharma	Great Britain	192
2018	Aurobindo Pharma	Pharmaceuticals	India	Generis Farmaceutica	Portugal	154
2018	Clinigen	Pharmaceuticals, clinical trials	USA	CSM	Great Britain	150

Cambrex over the past two years, when they acquired Halo Pharma, a contract provider of drug-product development and manufacturing services, for US$425 million, and Avista Pharma Solutions for US$252 million, which added early-stage development and analytical testing services to their portfolio. According Steven Klosk, president and CEO of Cambrex:"The pharmaceutical industry is increasing the amount of investment it makes in outsourcing across the board, in both development and manufacturing. There has been a trend over several years to reverse the strategy to seek the lowest-cost provider for outsourcing, and we continue to see decisions being

73>>

Emerging biopharma and larger pharma companies have a general request and desire for simplicity and ease of interaction with partners who will handle multiple steps in the process. Their belief is that, with the right partner and capabilities, those additional steps will be handled by a single partner and give them meaningfully faster time to data readout or inflection point. Ultimately, by having one partner with whom you have a single Master Service Agreement (MSA) you can enable them to expedite the processes of a project, making it easier and more beneficial for the sponsor.

- Peter DeYoung,
CEO,
Piramal Global Pharma

Steven Klosk

CEO
CAMBREX

What progress did Cambrex make in 2019 to cement its status as a leading small molecule company?
The two acquisitions that Cambrex made of Halo Pharma and Avista Pharma Solutions in late 2018 and early 2019 have transformed Cambrex into a leading full service, end-to-end small molecule CDMO. These companies have now been integrated into the existing Cambrex business and we can now provide customers with a full range of drug substance, drug product and analytical and testing services across the entire drug lifecycle.
In December 2019, Cambrex announced the completion of its US$2.4 billion acquisition by an affiliate of the Permira funds, having been previously publicly-traded on the NYSE. The Permira funds' investment does not change the company's focus on offering world-leading small molecule services, but will support the ongoing growth of Cambrex by enhancing the company's ability to service its global customer base.

What is driving growth in valuations of CDMO companies?
The pharmaceutical industry is increasing the amount of investment it makes in outsourcing across the board, in both development and manufacturing. There has been a trend over several years to reverse the strategy to seek the lowest-cost provider for outsourcing, and we continue to see decisions being made by innovator companies to now seek partnerships based on quality rather than cost, leading to a rise in projects being partnered with US and European CDMOs.
Outsourcing is being fueled by a need to accelerate projects through development and the clinical pipeline for all drug molecules. This is accompanied by high numbers of product approvals by the FDA and EMA. CDMOs such as Cambrex with critical mass and which have made investments to match the evolving needs of the current drug pipeline are well positioned to serve these growing markets.
Looking at small molecules specifically, the number of small molecules being developed as drug candidates has increased over the past five years. However, what is noticeable from current industry data is that 65% of the current clinical pipeline projects are now sponsored by small and virtual companies rather than big pharma. For Cambrex, this situation presents the opportunity to approach different potential customers with a choice of outsourcing models; leveraging our individual business units or services, or working with us as an end-to-end partner for the smaller companies that are looking for a collaborative approach and a smaller supply chain to manage.

In recent years, the CDMO space has consolidated as a result of large pharma wanting to work with fewer suppliers. Do you see this trend continuing?
There is no doubt that CDMOs that have critical mass should receive a disproportionate share of the growth in the CDMO space as they have the resources, facilities, technical personnel, capabilities and technologies to be strategic partners to the pharmaceutical industry. Cambrex has invested over US$200 million in its facilities to add further capabilities and capacity, and has undertaken three acquisitions since 2016 to build a global network of 12 development and manufacturing sites. These strategic investments and acquisitions have allowed Cambrex to create a broad portfolio of services and expertise to offer virtually all of the capabilities that customers require to develop and commercialize their small molecules.

At what stage are most of Cambrex's clients and has this changed over time?
The client base of Cambrex includes a wide range of large, mid and small innovator pharma companies, and has evolved over time as a reflection of the industry, and as the service offering has broadened too. Cambrex serves hundreds of customers around the world from the pre-clinical development stage, assisting in the filing of an IND, through clinical manufacturing and supply, and onto commercial supply. Currently, Cambrex produces 120 commercial products, with approximately 40-50 for innovators.

What goals does Cambrex wish to achieve over the next 2 or 3 years?
At present, after the recent acquisitions, Cambrex is focusing on growth, and the expectations are to achieve above market growth rates. There are also ongoing plans to invest both internally and externally to add capabilities and technologies to the company's offering that customers value and require to bring their therapeutics to market. Our goal is to make it simpler for customers to work with us and leverage the expertise we have across our global network of sites and across all aspects of small molecule drug development. ■

Manni Kantipudi & Dr. Ramesh Subramanian

MK

RS

MK: Chief Executive Officer
RS: Chief Commercial Officer
GVK BIO

Can you give insights into the strategy and business model of GVK BIO?
We call ourselves a CRDO (Contract R&D Organization) to differentiate our mission. By singularly focusing on the area of R&D, and by having no competing interests with our customers. We partner with firms interested in externalizing R&D to drive value. We support our customers from concept to commercialization in small molecules, while assisting in their journey from gene to clinic in biologics. Our team is agnostic towards geography; we invest where the science is best. Case in point, to build a differentiated biologics platform, we opted to acquire Aragen BioSciences, a company in the San Francisco area, as opposed to building the capability in India. Aragen were leaders in cloning and expressing challenging proteins, a capability that was of high interest to our customers.

What are GVK BIO's expansion plans both in the US and globally?
For small molecules, we are principally focused on our Indian sites for expansion. We have expanded our discovery chemistry operations significantly in both Bangalore and Hyderabad, and now have a team of 1,400 discovery chemists. In addition to two vivariums (Hyderabad, San Francisco) that support our team of around 125 biologists, we are building a third vivarium in Bangalore. Chemical development and manufacturing now has two independent sites in Hyderabad and Vizag with over 280 kL capacity. The GVK BIO team is proud to support over 10 IND filings every year, and over 60 chemical development programs. In addition to drug substance, we have invested in a state-of-the-art formulation development center that assists customers in pre-formulation and formulation development, including parenterals, solid orals, opthalmics, liquids, semi-solids and suspensions. Finally, we are happy to announce that our analytical solutions facility was recently approved by the FDA and supports method development, stability studies, extractables and leachables, among others. On biologics, we have added suites to our large molecule operation in San Francisco, augmenting our capabilities in both cell line development (CLD) and bio-production. Our CLD business has seen rapid growth this year (over 50%), primarily due to our expertise to clone and express difficult proteins. We have now decided to invest in cell culture manufacturing suites. This will allow seamless scale ups of our CLD programs, reducing both lead time and costs.

How has the acquisition of Aragen Bioscience expanded GVK BIO's capabilities?
GVK BIO, prior to Aragen, was primarily a small molecule company. The acquisition propelled GVK BIO's entry into biologics, the fastest growing segment in the life sciences industry. With over 25 years of history, Aragen has been a standout biologics CRO with a phenomenal track record. Three of Aragen's programs for partners have now advanced into commercialization and are now medicines. This emphasis on science has made Aragen an attractive choice for GVK BIO partners worldwide that are interested in large molecule research. We are now levering Aragen's expertise by building Aragen India: this center is currently supporting bio production and will soon advance into higher value services. ■

Peter DeYoung

CEO
PIRAMAL GLOBAL PHARMA

What are the biggest areas of opportunity you see for expansion in North America?
We are excited to expand our capabilities in North America, where Piramal Pharma Solutions (PPS) currently has three facilities: Aurora in Canada, Riverview in Michigan and Lexington in Kentucky. Earlier this year, we announced an investment of CAD$25 million to expand the Aurora facility. This includes new wings with 3,500 sq. feet of incremental space and multiple levels. This will expand Piramal's ability to manufacture APIs in that facility.
The new wing of Riverview was inaugurated in 2019 with a focus on serving the high potency API market. It received an investment of US$10 million, which was used for new QC labs, better client coverage and high potent compound handling at the facility. This enhanced capability enables us to serve the high potency area of small molecule production of API's, which allows us to meet a rapidly growing sub-segment of overall CDMO support that we are seeing in our customer markets.
At our Lexington facility we have the ability to handle containment related sterile fill finish, which is a niche area within the already difficult area of injectables.

How do you weigh organic growth versus inorganic growth opportunities?
Our overall site network has all been acquired companies, apart from two. The approach is a blend of organic and inorganic growth. We find that by acquiring an existing business, we get an additional running operation that is already producing revenue. However, the site is often far from reaching its full potential. By acquiring a site that is going well, we can apply best practices and investment to accelerate growth.
We intend to raise growth equity from investors for our global pharma solutions and critical care businesses, as well as our OTC drug business in India. This will enable us to accelerate both organic and inorganic growth across all three businesses, including Piramal Pharma Solutions.

What is your view on valuations and the potential for M&A in the CDMO space?
Overall, the CDMO industry is experiencing a robust, sustained, strong customer demand. If there is growth in an area, then industry players will try to take advantage of that growth. Secondly, despite there being several large players, the industry is still highly fragmented and no one player commands a dramatic share of the market. Ultimately there is room for consolidation amongst many of the leading players.
In terms of customers wanting to work with fewer, more relevant partners, whether they be large pharma or emerging biopharma, they are all seeking partners who can do more for them. That is driving some CDMOs to look for scale, while others are looking for capabilities. Still others look for geographic coverage. All of them aim to be more relevant to their customers and that drives the desire and need for consolidation. In the M&A context, valuations are tricky, because when everyone is looking to grow valuations expand.

What is the contribution of Indian businesses to the US Biotech industry?
Our integrated offerings are composed of multiple steps. We often provide one step in North America, while subsequently steps two, three and four are being done in different geographies across the world. By providing an overall integrated package, we offer a combination of North American capabilities with those from India and Europe to our global customers, fully supported with seamless project management and tech transfer expertise.
We have facilities and capabilities in India that provide value for our customers' projects. We have high quality facilities in drug products and drug substances in India that have been inspected by all the major regulators and meet the overall equation for what our customer is seeking.

What milestones does PPS seeks to achieve in the next 2 to 3 years?
We are looking to continue our expansion with customers and capabilities in North America, India and the U.K. We are also excited about how our capabilities can continue to maximise value for our customers. We have a significant number of customers that have phase 3 projects and trust us with their most important pipeline products. We are excited to assist more partners in launching critical and life-saving drugs. Combined with capacity enhancements, we believe we can add to their development pipeline. ■

<<69

made by innovator companies to now seek partnerships based on quality rather than cost, leading to a rise in projects being partnered with US and European CDMOs."

Strategic Partners

One of the trends in the market is that emerging biotech companies are heavily dependent on CDMOs for molecule development, as they simply do not have resources. Lab space and hiring researchers can be beyond their capacity. Peter DeYoung, CEO of Piramal Pharma Solutions, asserted: "Emerging biopharma needs to outsource most of the services offered by a CDMO. Our one-stop-shop capability and an integrated offering better enables us to meet dynamic and growing customer demands. That is why we are seeing a lot of growth in what we do for emerging biopharma."
In contrast, big pharma has the resources to develop a molecule, but there are opportunity costs that factor into how they choose to allocate time and resources. DeYoung continued: "When we look at large pharma, obviously they have internal capabilities, but they need to decide between what they do in house versus with a partner. They often place important projects with us across multiple sites and speak about us being a strategic partner, providing them with expanded capabilities that they may not have in the way they need and in the timeline required. This allows them to have flexibility of resources, which if everything was done internally, they could not meet."

Virtual Companies

Another factor contributing to the growth rate of CROs has been the explosion of 'virtual companies', which contract out all or most of their development. The success of a startup is existentially dependent on efficient use of capital, and the virtual model allows them to keep fixed costs down, such as rent, salaries and other overheads.
This is not without its challenges. One difficult aspect is integrating activities across multiple contractors or collaborators, often on different continents. It is not uncommon for companies to have to ship materials across the world and this can create big expenses, vulnerabilities to mishap and lapses in communication.
Despite these drawbacks, more and more virtual or semi-virtual biotech companies continue to be funded that require less infrastructure. These companies are expected to even further integrate with CROs through equity and success-based collaborations.

Conclusion

The end goal for biotech and pharma companies is to propel forwards developing therapies that improve the quality of human life. The question is how does one innovate, but still make affordable medicines? Partnering with a CRO allows for greater capital efficiency and, given the sizeable investments and influx of talent that has moved into the space in recent years, it is a promising growth story. ■

Himanshu Brahmbhatt

Vice President of Development and Sales
SUNRISE PHARMACEUTICALS

Can you give an overview of Sunrise Pharmaceuticals and the areas of fastest growth within the company?
Sunrise Pharmaceutical is a manufacturer with all operations in-house. Sunrise has its own label and currently has over a dozen products in the market. The company is continuously investing back into R&D and we have been working hard pursuing new prospects during the last year. We are currently awaiting at least four or five approvals from the FDA.
Sunrise's business model is opportunistic in its product selection, which has served the company well. Some products that we selected are volume-based commoditized products, but several players have exited the market and hence we were able to gather a substantial market share.

What are your thoughts on the backlash on drug manufacturers related to the opiod crisis?
The government and regulators have taken serious action against those that may have perpetrated the crisis, but as far as the generic industry is concerned, our client base is wholesalers and distributors. Our clients dictate market demand, and we deploy products according to their demand. Sunrise does not currently market any opioids nor it is planning to in near future. Moreover, Sunrise does not market any of its products directly to consumers, nor do we interact directly with doctors, pharmacist or health professionals.The Drug Enforcement Administration (DEA) has implemented a rigorous quota system on all levels of the supply chain and we have been in compliance with all those requirements.

The large drug companies are talking about the impending "patent cliff". Are you seeing that as a potential opportunity?
There are many common products on the FDA's shortage list due to prices having eroded to a point that nobody could afford it. Sunrise sees that as an opportunity. It is better to look at opportunities where there is a vacuum and, at the same time, pursue some strategic, complex molecules, such as injectables. This dual strategy has worked for Sunrise so far. ■

Dr. Jeffrey Reingold

COO
CONTRACT PHARMACAL CORP

What are some specific technologies that CPC is looking to adopt?
We are a solid dose manufacturer and identifying more efficient processes makes us stronger at our core expertise. In addition, we are looking at new dosage forms. We have added liquid fill capsule technology, novel packaging delivery systems and we are evaluating topicals and liquid-filling.

Last May, CPC acquired Florida Pharmaceutical Products (FPP). Why was this a good deal and how will it impact future growth?
The acquisition of FPP filled a gap at CPC in our expertise regarding distribution and marketing of generic drugs. With this addition, we added a new portfolio of products, customers, and resources. It is also productive that there are long-standing relationships among the leadership teams and we are already seeing the benefits. This is a new silo of revenue for CPC and will substantially accelerate revenue-growth.

What is CPC's typical client base?
We have a very diverse client base. This includes big pharma, virtual brands, wholesalers, distributors, retailers, in addition to a large export business. Our core focus is providing innovative contract development, manufacturing and packaging services to the industry. We must remain nimble and always focus on our customer's needs. We do that by immersing ourselves into understanding the true needs of our partners and becoming an extension of them.

What is the market opportunity in the hemp space and what is the plan to develop Uleva?
The future of hemp-based nutrition has arrived. We provide a comprehensive hemp-based line of products for a healthier lifestyle. CPC's expertise for nearly fifty years in developing, manufacturing, packaging and marketing natural products is not equaled. There are companies entering this space without any background, let alone a pharma/nutra background. CPC has put a lot of energy into making sure that our customers can be confident in the safety of their products and the science behind our marketing. Uleva is just a start.

What are your views on the current regulatory landscape for hemp supplements?
We believe it will remain status quo for some time and it will be monitored by FDA using regulatory discretion as they have with 'unapproved' DESI drugs.

What are the big trends and innovations in packaging?
Serialization is something we just put in place for the Rx market. Outside of the US, we distribute and export products that require it, and domestically we are ready. There's a growing demand for personalized medicine and individualized packaging. Getting someone a product that is on-the-go, convenient and easy to take is key. Sustainability is also gaining much attention.

How are you seeing the margins in packaging today?
Packaging is always an area of focus when reviewing efficiencies. Margins are always a challenge in a business like ours. We are adding palletizers and case packers and CPC has invested a tremendous amount of capital and resources into enhancing our packaging services.

How is COVID-19 affecting your business? How might this affect the timelines for molecule development?
We are all working hard to adapt and cope to this fast-changing situation. CPC continues to operate, with several modifications put in place to ensure the health and safety of our staff. With the precautionary measures and the impact to staffing, we are operating at a reduced capacity. All CPC leadership team members are aligned and committed to working together to mitigate any impact on delivering products. Our goal is to make the workplace a safe place, and we are communicating with as much transparency as possible.

Might this epidemic create a de-globalization of the manufacturing process?

We are part of a thriving, global market. This epidemic shows how much we depend on one another and, although I feel our strong networks will remain intact, I expect to see a push for more domestic manufacturing as companies and governments reassess dependencies. CPC is well positioned with its manufacturing and packaging operations based in New York.

What are CPC's two to three year goals?
We are proactive and opportunistic in our growth strategy while advancing the course we have identified. Efficiency building across all departments will remain paramount because it makes us a better partner for our customers. Building our generics business and growing organically with our existing partners will be a focus. New dosage forms will happen. In addition, we will be adding more than 10 billion capacity in tablets/capsules. ■

Gabriele Brambilla

CEO
ALIRA HEALTH

What steps can companies take to advance their therapeutics and design better clinical trials?
Speed, cost, and success rate are all critical elements. The success rate is very difficult for us to control because it is connected to the scientific part. However, we can help facilitate a higher success rate by selecting the right cohort for the study and powering it in the right way. By understanding how the market operates and not being solely clinical, we can decipher whether or not a study in a particular application is sensible. If you are not going to get market acceptance and reimbursement for a particular indication, then it is not wise to pursue.

How does focusing on data analytics allow you to anticipate issues and execute processes more efficiently for clients?
Two years ago we acquired a company called Clinical Insights, which specialized in advanced analytics. A strong foundation in data is essential to support market access strategies and make them last.

In terms of growth, are you looking to grow organically or through acquisition?
For the last four years, we grew by 50% on average every year. 70% of our growth was organic, and 30% came from acquisitions. Now we plan to focus on acquisitions to fill the gaps from a geographical perspective. Our current target is regulatory and clinical acquisitions in Europe. We also want to continue to build our global market access capabilities in Europe, while continuing to strengthen our team in the US.

Over the next two to three years, what goals would you like to achieve?
We have a particular growth target we want to achieve, and to continue to grow into a leading company in the healthcare and life sciences advisory space. The idea is to have incredible capability and expertise at every level of the organization. Historically we have always reached our targets, so we hope to continue doing the same moving forward. ■

Michael Quirmbach

CEO and President
CORDENPHARMA GROUP

What are some of CordenPharma's main business updates since our interview in 2019?
Looking at the year in review, CordenPharma grew to €386 million in 2019, with organic growth of 24.2% compared to 2018. This growth was driven by a few key projects, particularly from the US, and we are looking forward to a strong 2020, with about 10% - 12% growth.
We also completed a large investment in our CordenPharma Colorado peptide facility in Boulder, CO, by installing a large SPPS reactor that allows us to make close to 100 kg of peptides in one batch. In addition, we further invested into our HPAPI manufacturing infrastructure, which can handle high potent oncology compounds.
In Europe, we completed a sizeable investment of about €25 million at our CordenPharma Caponago (IT) facility, where we focus on the manufacturing of injectable drug products comprised of small molecules, biologics, peptides and oligonucleotides. Most notably, our Caponago facility received FDA approval for our new injectable manufacturing lines.

What have been the main market drivers for CordenPharma's U.S. investments?
Our investments are very much in line with increased market demand for HPAPI and injectable capabilities. Furthermore, we continue to experience a very strong demand for our integrated service model, particularly in the development of peptides into injectables using our integrated network of facilities.
We also recently launched an investment in continuous manufacturing at CordenPharma Chenôve, France, which will be coming online shortly – this site will be our Centre of Excellence for Continuous Manufacturing going forward.

Does CordenPharma plan to supplement its organic growth strategy with acquisitions?
As there continues to be consolidation in the industry, we recognize the importance of our own growth. We have identified certain gaps in our service offering today across our four platforms -small molecules, injectables, highly potent & oncology, and peptides, lipids & carbohydrates – and are specifically looking for acquisitions across these four platforms to make our offering stronger. ■

Michael Johnson

CEO
VISIKOL

Please provide an overview of Visikol?
Visikol is a contract research organization focused on early stage drug discovery and development. The focus of the company is on imaging, image analysis, digital pathology and advanced in vitro assays. We work with companies that range from a few researchers in academia with venture capital funding, all the way to the largest pharma companies in the world such as Pfizer and Merck. 95% of our work is done on investigational and early drug discovery projects.

What makes 3D imaging a disruptive technology within the pharmaceutical space?
A significant amount of questions that we are working on with pharma clients are challenging to answer with traditional imaging and traditional cell culture models. For example, if you are trying to understand how a drug is affecting retinopathy, you are trying to look at vasculature in the retina of an eye. That is really challenging to look at under a microscope or to use traditional imaging methods. To assess the ways in which drugs are actually working in complex systems, 3D imaging is the best approach to take. A lot of companies also work with us for 3D cell culture models – growing complex organoids and microtissues in a dish, as traditional 2D cell culture models cannot replicate the type of biology that they are going after. If you create a 3D tumor model, you can understand how the anti-body penetrates into the model more effectively and you can better replicate what is happening within the body.

Which areas have been driving business growth for Visikol?
Visikol does a lot of work in the area of toxicity safety, for example, figuring out if compounds have adverse toxicology consequences primarily in the liver. The liver is one of the main reasons why drugs fail and a lot of companies working with us want to figure out what is happening to the liver. In terms of efficacy, the oncology space is a huge driver for business, specifically immuno-oncology. ■

Jeffrey Speicher

Senior Vice President
AVÉMA PHARMA SOLUTIONS

What is the core expertise and services Avéma Pharma Solutions offers clients?
Avéma Pharma Solutions is a CDMO that is a wholly owned subsidiary of PL Developments, a leading manufacturer, packager, and distributor of over-the-counter (OTC) pharmaceutical products and consumer healthcare goods. The fully integrated environment at Avéma enables companies to bring products to market more quickly because we offer support at every stage of development. Avéma supports a multitude of delivery systems to our clients including liquid oral drugs, Rx controlled substances, large-volume OTC, pouches and gum. We do development work in house and can support pilot trials, commercial manufacturing and NDAs and ANDAs.

When we look at the trends in CDMOs today, how do you anticipate the supply chain changing because of the COVID 19?
I think deglobalization will take place and a lot of businesses will come back to the U.S. Most APIs come from China, are made in India, and are shipped to the United States. Realistically, the big companies will be bringing product manufacturing back, and the quickest way to do that is by partnering with a CDMO that has the capability to manufacture products immediately.

How do you weigh organic against inorganic growth?
We acquired 48 NDAs and sites from Teva last year. In the CMO world, we thought that being tied in with private label companies could be a negative, because it would be hard to do business with larger players that we compete against. However, being associated with private label companies has brought us significant opportunities, as companies that want to get out of manufacturing these drugs come to us to make them.

What is your 2 to 3 year vision for Avéma?
Our primary goal is to land at least three major base customers. We have two Fortune 100 pharma companies already in-house. We are looking to double the size of our manufacturing sites. We are looking to expand our R&D plant in Miami as well. ■

Kamlesh Oza

Senior Vice President
ACG CAPSULES

How has ACG evolved to meet and capitalize on new market trends?
ACG gets involved very early in the process. The company has a Scientific Business Development team who interact with R&D and project teams early on and partner with them not just to help them develop formulations, but also assist in putting their formulations into a capsule. Our business attention is on solid oral dosage forms, which are in hard gelatin capsules and anything that is related to getting into this space is where we would focus. ACG is involved in the development of solid oral dosage products as well as inhaler products. Hard gelatin capsules are also used in drug product inhaling devices.

What technological trends do you foresee for the industry?
What the industry is chasing after is the ability to take a large molecule, put it into a capsule, and get it absorbed through the gastrointestinal tract. Large molecules are not absorbed or are killed in the acidic medium of the stomach. Biologics, such as insulin, tend to be large molecules. Developing this technology will make life much easier for the consumer.

Does ACG have any expansion plans moving forward?
ACG is one of the few capsule manufacturing companies expanding and building facilities around the world. We built a new facility in Brazil, which came online in February 2019. We also expanded our facility in Croatia to more than double its capacity. We are building another facility in India next to our existing facility, and the new facility will come online in October 2020. Moving forward, we aim to further expand our presence in the Chinese and Japanese markets.

What are ACG's objectives for 2020?
We believe that the market leadership of putting products into capsules has fallen onto our shoulders as other manufacturers are not focusing on the capsule business as much as we are. ■

Generics

FIERCE COMPETITION DRIVES DOWN COSTS

In a country where eye-popping prescription drug prices are commonplace, inexpensive generic drugs have acted as a crucial counterweight. Generics are a major boon to society and to future innovators in the pharma industry because the expiry of patents and the loss of market exclusivity herald a massive commoditization of prices for most pharmaceutical products. That, in turn, frees up resources to pay for newer, innovative treatments, that pharma companies otherwise would not have the incentive to pursue.

The way the system functions is that, once a patent is lifted, generics businesses look to find alternative ways to manufacture a drug that should work identically to the brand-name version. Patent expiration puts about 10-15% of total industry revenues at risk of significant price erosion at any given period, and has done so consistently for several decades. The system has proven so cost effective that today, 90% of the approximately 6 billion monthly prescriptions written each year in the US are filled with generic drugs, according to the UBS figures.

Managing to incentivize innovation while also ensuring drug affordability is always a balancing act, because it takes a long time to bring a new drug to market. Consequently, a period of exclusivity is needed to allow drug companies to recoup the costs associated with introducing a new drug. Generic drugs cost less than their brand-name counterparts because generic drug applicants do not have to repeat animal and clinical studies that were required of the brand-name medicines to demonstrate safety and effectiveness. This is why the application is called an abbreviated new drug application (ANDA). The reduction in upfront research costs means that, although generic medicines have the same therapeutic effect as their branded counterparts, they are typically sold at substantial discounts: an estimated 80 to 85% less, compared with the price of the brand-name medicine. This translates into huge cost savings for taxpayers, who fund government sponsored Medicare and Medicaid programs. According to IQVIA, generic drugs saved the U.S. healthcare system in excess of US$1.6 trillion over the last decade.

While generics play an essential role in the healthcare system, the past five years have been a difficult period for their producers. Margins have slimmed considerably and multiples have steeply fallen. The reason for this trend is that buyers in the market have consolidated in a big way. Rather than buying and negotiating prices separately, Walgreens and AmerisourceBegren now buy as one group; Rite Aid, Walmart and McKesson do the same, and CVS and Cardinal Health have also joined forces. According to Jay Shukla, president and CEO of Nivagen: "This puts pressures on suppliers and lowers prices. It decreases the market size for suppliers to sell to. It also exposes business to risks when issues arise in areas, such as regulation, patenting and logistics. In the pharmaceuticals space this is a particularly delicate scenario, because when production halts, it is time and resource consuming to restart it. Nivagen stresses the value of its supply track record and our role in helping buyers diversify risk."

In addition to consolidation amongst the buyers, the deflationary pressure on

The global specialty drugs market has expanded and will present opportunities for generic growth in the oncology, infectious diseases, multiple sclerosis and hepatitis segments. Development and commercialization of specialty generics drug are more complex when compared with conventional generics drugs, and greater opportunities are available for generic companies with capabilities in this area.

- Marc Kikuchi,
CEO and Head of North American Generics,
Dr. Reddy's Laboratories

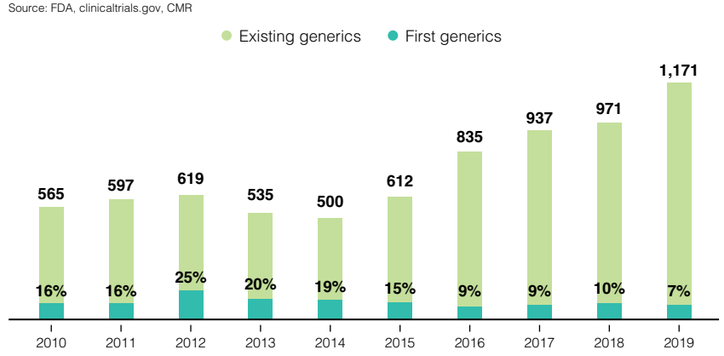
pricing is forcing companies to consider new strategies to survive and remain profitable. "The essence of a successful generics strategy is to lower cost of goods as much as possible, because you can't dictate price and the market price of drugs gravitates toward the lowest cost producer… There are two trends that I believe will occur as a result of decreasing costs. One will be consolidation within the industry. That means taking companies that are marginally profitable and combining them to leverage the overhead across a bigger portfolio of products and sales. Secondly, finding and implementing technologies that reduce the cost of goods. This could be done be through continuous manufacturing or new ways of developing API's. To be competitive, people are going to look to cut costs throughout the continuum of the manufacturing process," said James Gale, founding partner and managing director of Signet Healthcare Partners.

Following this trend, Pfizer has now spun off its Upjohn business that sells off-patent drugs and is expected to merge with Mylan to create a new company called Viatris later in 2020. From Pfizer's end, Mylan comes cheap, as the company was worth US$25 billion just last year, but had a market cap below US$10 billion at the time the acquisition was announced. This merger illustrates efforts to scale up in order to help the new business push back on pricing pressure.

Because margins have tightened and companies can only cut costs up to a certain point, some generics producers are trying to target less crowded areas, such as those on the FDA's drug shortage list. "There are many common products on the FDA's shortage list, due to prices having eroded to a point that nobody could afford to produce them.... Sunrise sees that as an opportunity. Instead of focusing on those blockbuster molecules, which three or four companies are working on, it is better to look at opportunities where there is a vacuum and, at the same time, pursue some strategic, complex molecules, such as injectables," pointed out Himanshu Brahmbhatt, vice president of development and sales, Sunrise Pharmaceuticals.

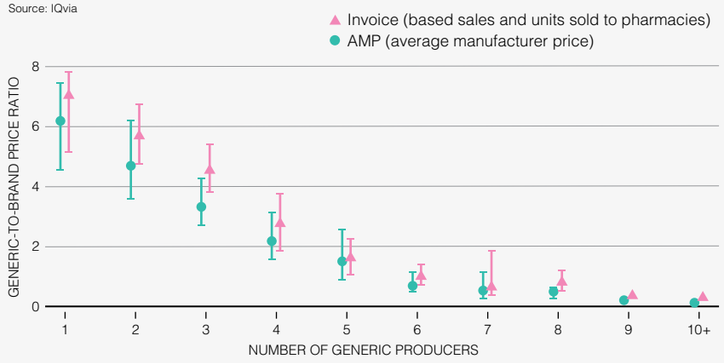
NUMBER OF US FDA ANDA APPROVALS PER FISCAL YEAR

Source: FDA, clinicaltrials.gov, CMR



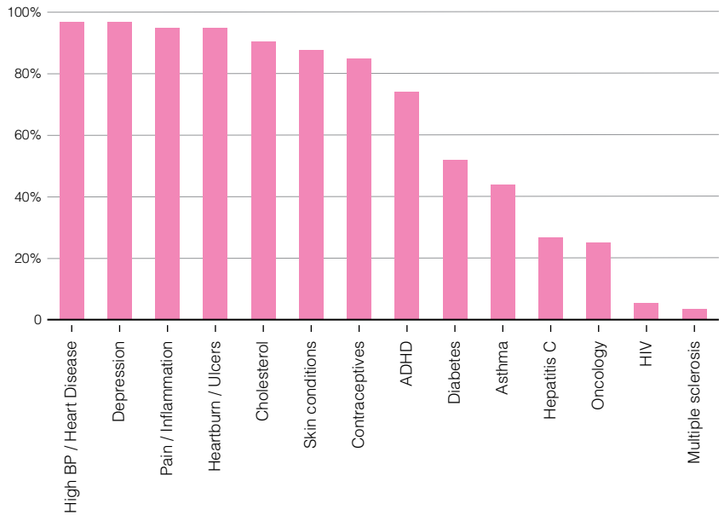
GENERIC COMPETITION AND DRUG PRICES

Source: IQvia



US GENERIC FILL RATES BY DISEASE AREA, % OF PRESCRIPTIONS

Source: IQvia



We are seeing much of the healthcare investment being channeled towards the newer, innovative areas of treatment like gene therapy and certain expensive cancer immunotherapies, like Car-T. Because of their growing cost to the payors, there is a rationing of dollars for other therapeutics. At the low end of the spectrum, there are the lower-technology products, like OTC consumer health products, generics or 505(b)(2) products, which are being pressured as to reimbursement and pricing. Consumer products, while at the lower end of the technology spectrum, have brand name recognition, and are relied on by consumers for everyday treatment. There is generally a steady demand for these products and investor interest has followed.

- James Gale,
Founding Partner and
Managing Director,
Signet Healthcare Partners

OTC

Another essential part of managing healthcare costs in the US are over-the-counter (OTC) medications. Millions of Americans rely on OTC products as an accessible and effective solution for commonly occurring conditions. These medicines are a critical component in advancing consumer health because they allow people to treat or manage many health conditions conveniently and successfully. Because they enable people to self-treat, OTC medicines save the health systems valuable resources and can save consumers time and money.

One of the trends in OTC healthcare is patients are becoming more proactive in solving their health problems and are looking online as well as to brick and mortar pharmacies to take preventative measures. According to Paul Hennessey, senior vice president of operations, quality and technical services at Advantice Health, a newly formed company that acquires and builds health and wellness brands: "Consumers are trying to take more charge of their health care decisions. Consumers have information at their fingertips. They are looking for solutions to common problems they understand. That is one reason why one of our fastest growing segments is online through Amazon. Companies must have a strong online presence to succeed in today's marketplace. The consumer continues to trend towards self-care, and OTC brands are well positioned in this environment"

Although not nearly as prevalent in the news, as novel therapies or generics, one should not underestimate the value these brands can generate. According to James Gale: "We are seeing much of the healthcare investment being channeled towards the newer, innovative areas of treatment like gene therapy and certain expensive cancer immunotherapies, like Car-T. Because of their growing cost to the payors, there is a rationing of dollars for other therapeutics. At the low end of the spectrum, there are the lower-technology products, like OTC consumer health products, generics or 505(b)(2) products, which are being pressured as to reimbursement and pricing. Consumer products, while at the lower end of the technology spectrum, have brand name recognition, and are relied on by consumers for everyday treatment. There is generally a steady demand for these products and investor interest has followed."

Without OTC medicines

90%

OF CONSUMERS

would have gone to the doctor instead

every

$1

SPENT ON OTC MEDICINES

saves the U.S. healthcare system

MORE THAN

$7

Source: Source Healthcare Products Association

Conclusion

Generics are not glamorous, but they are a linchpin of healthcare in the US. Going forward, there will continue to be demand both for great brands and new generics and biosimilars that replace some of the existing blockbuster drugs most people are familiar with today. Despite pressure on pricing, there is still an abundance of opportunity to bring drugs that manage and cure health issues at an affordable cost. ■

Paul Hennessey

Senior Vice President – Operations, Quality and Technical Services
ADVANTICE HEALTH

What was the motivation for establishing Advantice?
RoundTable Healthcare Partners has been very active in the healthcare space since its conception. The executives and the operating partners all have backgrounds in healthcare. They understand the nuances of the industry and what it takes to drive growth and profitability. They were active in other parts of life sciences such as contract manufacturing and durable medical equipment. Moberg Pharma AB decided to shed their OTC business and focus on developing a prescription drug, which created the acquisition opportunity for RoundTable. It was a perfect opportunity for RoundTable to make the investment in an OTC platform focused on health and wellness brands. Advantice Health was thus formed and we are focused on building the Kerasal®, New-Skin®, Dermoplast® and Domeboro® brands.

Can you give us a run down of your product line and explain the focus?
Our mission statement is to help consumers look and feel better through superior health care solutions. We have well recognized brands that people are familiar with and we believe that, with some innovation, we can expand these brands into other relevant segments. We are looking at them with fresh eyes and studying the marketing opportunities from an innovation perspective. We want to expand these brands organically through increased investment and improved marketing campaigns as well as new product innovation.

Are you looking to diversify the product offering and how do you balance in-house development with brand acquisitions?
First and foremost, we are focused on building the brands we have today. We want to become a world class acquirer and builder of health and wellness brands. We are constantly looking for good add-on acquisitions that would complement our existing portfolio.

Would growing organically require a lot more resources?
Yes, for that reason we are looking for partners in that area. We are talking with existing and potentially new partners that have research capabilities and can us down that organic path. That is why CPhI is so important to us. It brings us closer to potential partnerships. In some of these conferences we are able to meet with new companies that we were not aware of and brainstorm new ideas.

What have been the biggest challenges in terms of starting Advantice Health and becoming successful?
Building the culture of a company into a high-performance team is our biggest priority. We believe that culture drives business results. We are through the integration process with the prior owner and have built systems and processes that we can scale and add on additional brands.

Which brands are the fastest growing at the moment?
Kerasal has been our biggest growth driver over the past year. It is a reflection of the fact that consumers want to look better and take care of themselves. Foot care is an area where there is large potential if consumers are made aware of the offerings. It is a small percentage of household penetration and we know the incidence rates are higher. Also, our incremental investments in New-Skin paid off this past year, growing our share in an establish category.

What is your opinion on why consumers are more involved in choosing OTC products?
It is mainly because consumers are trying to take more charge of their health care decisions. Consumers have information at their fingertips. They are looking for solutions to common problems that they understand. That is one reason why one of our fastest growing segments is online through Amazon. You must have a strong online presence to succeed in today's marketplace. The consumer continues to trend towards self-care and OTC brands are well positioned in this environment.

What are some goals you would like to achieve at Advantice over the next two years?
One is organizational; we want to put together the best team possible and fill the organization with great people that share our vision. Second, making sure we have a strategy to grow our current brands and find ways to continue to grow market share. Third, we want to consistently bring product innovation to help consumers find better ways to take care of themselves. ■

Marc Kikuchi

CEO and Head of North American Generics
DR. REDDY'S LABORATORIES

When we spoke last year, Dr. Reddy's had initiated a strategic realignment in its growth strategy. What progress has been made over the last year in this regard?
Dr. Reddy's has been on a transformational journey for the last two years. We re-aligned our strategic priorities to focus on seven chosen growth spaces. These include: US, India, China, Russia, EU, API and Global Hospitals. All these businesses are now operating under the guiding principle of achieving self-sustainability with the aspiration to meet two key financial metrics of 25% EBIDTA and 25% ROCE. We have made significant progress in last few quarters, with strong growth witnessed across the key performance parameters. While we continue to progress well on the organic growth for each of our focused businesses, we are also evaluating multiple inorganic opportunities which can accelerate our growth journey further to reach more patients, and create value for all stakeholders.

One of Dr. Reddy's areas of focus is on optimizing the business risk quotient through the partnership model on high-risk projects. Can you give an example of how this strategy is being manifested in the US?
At JPM earlier this year, we talked about our strategic approach to create maximum value for the organization while limiting the risk or exposure through partnership model. While this approach is applicable to all the high-risk/investments projects across the organization, we have initiated executing on this strategy with the divestiture of the dermatology and neurology brands in US market. Going forward, we are focusing on our core capabilities in R&D to develop differentiated products that provide meaningful health-economic outcomes to patients and payers and collaborate with the right partners to commercialize these assets in the marketplace.

In what ways is Dr. Reddy's working to bring down the cost of treatments for opioid addiction?
As a result of our hard-fought battle to launch the generic version of Suboxone®, physicians can medically treat opioid addiction with a more affordable generic version of buprenorphine and naloxone. Most recently, we announced the launch of Naloxone Hydrochloride Injection USP, 2 mg/2 mL (1 mg/mL) Single-dose Prefilled Syringe, a therapeutic equivalent generic version of Narcan® (naloxone hydrochloride) Injection USP, approved by the U.S. Food and Drug Administration. Naloxone is our second product to market that has been designated as a Competitive Generic Therapy (CGT) by the USFDA. With a CGT designation, we have 180-day CGT exclusivity to market this affordable product.

To what extent has Dr. Reddy's built out its Biologics business over the past few years?
Dr Reddy's is focused on developing biosimilars for global geographies, and we are currently selling six products, while developing a pipeline of products for treatments in oncology and immunology. We have approvals in more than 20 countries around the world. Also we have begun enrolling patients in clinical trials in our Rituximab biosimilar product that will support approvals in the US and EU. We have recently completed commissioning of a brand new single-use disposable manufacturing facility and have plans for future expansion to support production of our growing portfolio of products.

Dr. Reddy's has zero debt on its books, how would you characterize your strategy to invest excess cash moving forward?
We continue to evaluate a number of inorganic opportunities both for the U.S. and other strategic geographies. For example, Dr. Reddy's recently acquired part of Wockhardt's India business for US$270 million and, in the past 18 months, we have placed bids of over US$2.5 billion for acquisition opportunities in the US. The focus remains on investing in the right opportunities that would be synergistic and complement Dr. Reddy's existing capabilities and/or product portfolio.

What are the most significant patent cliffs on the horizon that present an opportunity for Dr. Reddy's to offer generics?
In addition to opportunities for NCE-1 filings for small molecules, other types of drugs will present important opportunities for Dr. Reddy's. For example, the global specialty drugs market has expanded and will present opportunities for generic growth in the oncology, infectious diseases, multiple sclerosis and hepatitis segments, particularly the growing demand for generic drugs in the oncology area. Since development and commercialization of specialty generics drug are more complex when compared with conventional generics drugs, greater opportunities are available for generic companies with capabilities in this area.■

Eric Falcand

Vice President, Head of Business Development and Licensing
SERVIER GROUP

Servier Group opened its first US office in Cambridge, MA in 2018. What is the primary objective of this office?
Building a notable presence in the highly competitive U.S. market has been an aspiration of Servier's for years. When we opened our BioInnovation office in Cambridge in 2018, we were just kicking off our strategic plan for securing a foothold in the United States, and later that same year we opened our first official U.S. Servier outpost, Servier Pharmaceuticals. Headquartered in the Seaport district of Boston, Servier Pharmaceuticals has grown to more than 100 employees, and that figure is projected to double within five years. Servier now has two oncology products on the market. Oncology treatment and care will be the immediate focus in the United States, although plans for expansion to other therapeutic areas and patient communities are underway.
Both Servier Pharmaceuticals and Servier BioInnovation represent a major step forward in Servier Group's global ambitions, and they embody our two-fold objective: to develop a portfolio of innovative drugs, and to expand Servier's presence worldwide to bring life-saving treatments to greater numbers of patients around the world.

What are the biggest areas of opportunity for Servier Group to expand?
Globally, we're continuing to channel our focus in the five therapeutic areas where we see incredible opportunity: cardiology, immuno-inflammatory, neuroscience, metabolism and oncology. Of note, we're placing an increased emphasis on oncology. We founded our presence in the United States when we acquired Shire's oncology branch in 2018, and we are continuing to cement our status as a recognized oncology key player both in the United States and around the world by investigating new combinations of molecules, including BH3 mimetics, CAR-T cell therapy, and next-generation immune checkpoint inhibitors. Over the next two years, we're aiming for oncology to account for 50% of our global R&D budget.

From a revenue standpoint which areas of your business were strongest in 2019 and what are the most important trends driving your strategy?
Our global revenue in 2018/2019 totalled at 4.6 billion euros. Cardiology continues to be one of our strongest areas and has excellent prospects in the pipeline, including new fixed drug combinations, which will likely help drive ongoing strength. Our increased focus in oncology has led to promising growth, with our global oncology revenue growing by 120%. Simultaneously, we've been expanding our generic activities to now include 1500 medicines.

What is the current state of Servier's R&D pipeline?
We have more than 30 projects in clinical development, including 17 new molecular entities, as well as 32 research projects. Two of the molecules we are investigating are in phase 3 of clinical study.
Currently, we have six oncology treatments available to patients, with an additional 12 drug candidates in clinical development and 17 projects in the research phase. Servier research in oncology is focused on treatments targeting the restoration of programmed cell death of cancerous cells (apoptosis) and mobilizing the immune system against cancerous cells (immuno-oncology).

How has the development of CAR-T cells targeting cancer ushered in a new era of therapies based on the adaptability of living cells? How are Servier and Allogene Therapeutics partnering to bring drugs to market in this area?
With the development of CAR-T cells, we've entered into an era of more personalized, targeted treatments. This means that we're in the early stages of harnessing and developing the body's natural defence systems to fight diseases like cancer. In January 2019, we announced that the FDA had cleared the IND application for ALLO-501 in patients with relapsed/refractory non-Hodgkin lymphoma. Servier partnered with Allogene Therapeutics on the development of this drug, and we're also working with additional partners to develop and manufacture lentiviral vectors to support allogenic CAR-T cell technology development.

What objectives does Servier Group seek to achieve in 2020?
We are reaffirming our commitment to CSR by aiming to reduce our CO2 emissions by 25%, and we will be taking actions in 2020 that will set us on the right path to achieve that goal by 2030. Overall, Servier is well-positioned for long-term success and we're not slowing down. ■

TECHNOLOGY AND REGULATORY SERVICES

» There is a race between health care companies trying to understand technology and technology companies trying to understand health care. There are a lot of tech companies focused on big data, creating health care entities and forming partnerships and alliances. The pace at which data is created is been unprecedented... The industry must figure out how it will grapple with this data to access what is relevant, use it to test hypotheses, prototype, test and validate and build it into a business model, all the while respecting privacy laws. «

- Arda Ural,
Partner and Life Sciences Sector Strategy
and Transactions Leader,
Ernst & Young LLP

Image courtesy of Systech International

Disruptive Technology

AI AND DATA SCIENCE USHER IN A NEW ERA OF CLINICAL TRIALS

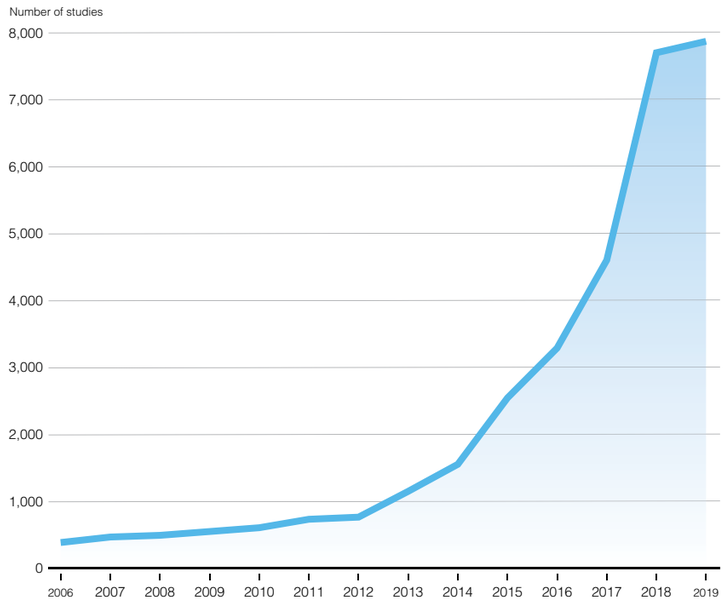
It is said that great drugs are generally made as a result of great patient data. The pace at which data is being created today is unparalleled, and increasingly pharma is paying attention to the opportunity that the effective harnessing of data can bring throughout the lifecycle of a drug. From discovery through to commercialization and use, new technologies are being introduced that are forcing companies, researchers and doctors to reconsider some of their more antiquated practices.

One area with huge potential is in clinical trials. While AI is yet to be widely adopted and applied to clinical trials, it has the potential to transform their development. The applications of AI could lead to faster, safer and significantly less expensive clinical trials. Ed Ikeguchi, president and chief medical officer of AiCure, an AI and advanced data analytics company with intelligent software that captures and understands behavioral data, pointed out: "AI can provide pharma with deeper insights to help inform their decisions. We are working towards objective, numerically quantifiable indicators of how patients are doing over time. Ultimately, we should be able to identify subjects who are at risk of study dropout based upon their pattern of study drug ingestion. If we can predict, identify and prevent study dropouts, we can reduce study time cycles and contribute to statistical integrity. In sum, we can make clinical trials more effective and mitigate risk for pharma companies."

In addition to clinical trials, AI technology has great potential in areas like imaging, where it can assist in digesting medical data used to make diagnoses in a more effective way. In drug discovery, J.P. Morgan's Peter Meath posits: "Using AI can improve the hit rate and target rate, while also making it more efficient and cost effective. It also helps make the value proposition more evident to the market." 88>>

MACHINE AND DEEP LEARNING STUDIES ON PUBMED.COM

Source: The Medical Futurist



Ed Ikeguchi

CEO
AICURE

What challenges in the biopharmaceuticals space are AI and better data collection helping address?

The golden question is how to improve the operational process for pharma so as to shorten the time to market of their new medications and products. Artificial intelligence (AI) is enhancing data analytics and giving us access to a number of different modalities for data collection, such as wearables and mobile applications. It is also resulting in better insights and allowing for more assertive predictability. These two aspects are improving decision making. Historical information can be used to plot trends to inform executives what to expect, so that decisions can be made in advance. That is where the value of AI is contributing most to the drug development lifecycle.

We are working towards objective, numerically quantifiable indicators of how patients are doing over time. Ultimately, we should be able to identify subjects who are at risk of study dropout based upon their pattern of study drug ingestion. If we can predict, identify and prevent study drop-outs, we can reduce study time cycles and contribute to statistical integrity. In sum, AiCure makes clinical trials more effective and mitigates risk for pharma companies.

Can you give us an overview of your technology platform and explain how the data capture works?

We have a suite of adherence products, e-pro and digital biomarkers. AiCure provides software for mobile devices that we put into the hands of patients and subjects in clinical trials. We are able to support the patient through the process by ensuring they stick to the clinical trial protocol, by monitoring that they take medications on time and helping them to ingest the medication in the right way. For the pharmaceutical sponsors, we help corroborate that the clinical trial is conducted properly. Confirmation that the patient is ingesting the medication is the gold standard for what the industry is seeking. We can assure sponsors that their medication's pharmacodynamics will have the best chance to manifest in their subjects as expected, and achieve this remotely from the comfort of patient's homes.

It is about improving the richness of the data as much as the accuracy. We have for many years positioned ourselves not only as an adherence product, but also as a contributor to the understanding of human interaction with medical therapy. Why a person decides to take their medication or not is paramount to understanding how a medication will fare in the real world.

How receptive is the U.S. pharmaceutical industry to AI technology adoption?

Pharma has been able to adopt technology in a very robust and welcoming way. With that being said, pharma is a regulated industry and they have to take on new technologies with some caution to make sure that products are of medical grade. It has become clear that there is both an interest and a need to define new clinical endpoints and methods for assessing patient outcomes. Pharma and regulators are eagerly seeking new ways of assessing disease that are more accurate and less subjective.

What are AiCure's growth plans?

Our approach to business growth is to show value and return-on-investment to our partners. Simply put, we provide the foundations of the science and data that are needed to assess a new drug. Instead of a client-vendor relationship, we develop strong scientific collaborations.

In 2019, we launched a program called AiPEX™ (AiCure's Partnerships for Excellence), in which Syneos Health™, the only fully integrated biopharmaceutical solutions organization which includes a contract research organization (CRO) and contract commercial organization (CCO), has been an exemplary partner. Together, we have made outstanding progress to create a unique offering for the market where we aim to deliver on a site network that is pre-qualified and trained to deliver unprecedented patient engagement, improved adherence, digital biomarkers and quantifiably better data.

What are the company's main objectives and how do you plan to pursue them?

We want to make an impact on clinical outcomes and materially improve the way pharma handles new drug development. Our unique value chain begins with the fact that our technology interacts directly with the study subject every time they dose. ■

Image courtesy of Systech International

Why a person decides to take their medication or not is paramount to understanding how a medication will fare in the real world. Reasons such as side effects may lead to someone's decision to discontinue treatment, and it is critical that sponsors be made aware.

- Ed Ikeguchi, CEO, AiCure

<<86

With a capacity to perform complex analysis much faster than a human can, AI helps researchers comb through complex data to find different uses for existing drugs, help define new drug combinations, or identify opportunities for personalized, targeted treatments.

This capacity is being applied to solve the COVID-19 pandemic. A number of research projects are using AI to identify drugs that were developed to fight other diseases, but could now be repurposed to take on coronavirus. By studying the molecular setup of existing drugs with AI, companies want to identify which ones might disrupt the way COVID-19 works.

BenevolentAI, for example, began turning its attention towards the COVID-19 problem, and the company's AI-powered knowledge graph can digest large volumes of scientific literature and biomedical research to find links between the genetic and biological properties of diseases and the composition and action of drugs.

Data Insights

Alongside the build out in AI capabilities, the explosion of data has provided big opportunities for companies harnessing data to provide market insights. In March of 2020, Clarivate Analytics purchased Decesion Resource Group from Piramal for US$950 million. The deal signals the great potential and value biopharma companies are finding in platforms that are able to sift through large swaths of data and provide market research, real world data, and disease-area expertise. "Having the need to know much more about the marketplace at an earlier stage plays very strongly into what we do. There is a great need for information, knowledge and intelligence," said Thomas Halliday, CEO of Decision Resources Group.

Another area of promise in data analytics is assimilation: the idea that siloed data has enormous latent potential when harnessed and shared properly. Pharmafusion is taking on this issue with their platform that allows for holistic decision making. According to the company's founder and CEO Jonathan Retano: "Companies have data everywhere, but do not have answers nor insight, as the data has not been unified and synthesized. The traditional approach in pharma is that everything has been stratified. The data is owned by a department or controlled by an IT resource. When you think of data as an asset, it has to be fluid and easily assimilated into the whole so that it can be shared."

Conclusion

When it comes to advancing drug development to the key inflection points, data is the ultimate currency of progress and value. For that reason, companies will continue to invest in AI and insight platforms that enhance their ability to execute on R&D and realize commercial opportunities for their products. ■

Thomas Halliday

Global Business Head
DECISION RESOURCES GROUP

Can you describe the growth of Decision Resources Group (DRG) over the last year?

2019 was our best year for the past seven years; we grew our top line by 9% and our bottom line also saw significant growth, driven by our commercial team's focused approach penetrating broader markets.

From a products point of view, our data analytics vertical grew very fast, reflecting a growing need among life science companies for real world evidence to demonstrate value, along with a shift towards incorporating real world data-driven insights, in addition to those derived from traditional methodologies like primary market research.

Over the last year there has been a big shift in our company from being a product-led business to being more customer centric.

What led to Piramal's decision to sell the company to Clarivate?

Piramal acquired DRG approximately seven years ago. From the start, their strategy was very clear in that they were going to exit the investment at some point. Given the growth and business turnaround of DRG in 2019, Piramal felt that it was the right time.

Entering an agreement with Clarivate was a good opportunity for our customers to benefit, as Clarivate has complimentary offerings to ours. They have an excellent, diverse customer base and truly global footprint.

How does the acquisition expand Clarivate's capabilities in the life sciences space?

We wanted to get to a point where we can offer true outcome-driven solutions, from bench to bedside. The combination of DRG's offerings with Cortellis, the Clarivate suite of life sciences intelligence solutions, empowers us to do that.

Clarivate's life sciences business is strong in R&D, helping companies discover, develop and bring new treatments or devices to market, whereas DRG helps companies commercialize their products, supporting them with patient, provider, payer and market insights. We help our clients assess the scale of an opportunity, ensure that patients can access medicines, fine-tune launch strategies, better engage patients and healthcare professionals through traditional and digital channels, and optimize brand performance. We have brought together two companies to create an end-to-end offering that spans the entire lifecycle of a device or molecule. This combination is extremely powerful – and a disruptive play in the marketplace.

What are the most important ways in which AI is enhancing data and analysis, and how is this helping customers to make better decisions?

Just by way of example, recently, we worked with a biopharma on the launch of a product for a severely underdiagnosed condition. A look at our claims data repository, which covers 300 million lives, showed only 150,000 diagnosed patients in the U.S., but the company's clinical team estimated more like 2-3 million sufferers.

So how to identify these undiagnosed patients? Our data scientists and epidemiology analysts, working closely with the company's brand and medical teams, were able to construct a patient profile based on disease marker combinations and symptoms, which show up in claims and EHR data. We were then able to use machine learning to validate and strengthen our model, which allowed us to build an algorithm that would reveal the true size of the patient population and identify a key dynamic driving diagnosis. Based on this information, the company was able to refine its physician targeting and messaging to aid different specialists in correctly diagnosing these patients, potentially saving them months or years of misdiagnoses and improving their health outcomes.

What does the future hold for DRG in the data science space in general?

We are living in a time where our customers have to do much more with less and at a faster rate. The need for quality, real-time business intelligence and the expertise to put it in context is ever more urgent in the complex and fast-changing business environment today's biotechs face. The kinds of information and insights tools we're developing, together with our Clarivate colleagues, will help biotechs get more targeted therapeutics to market faster, better understand and engage their customers, and smooth some of the kinks out of our systems of healthcare payment and delivery to ensure that patients can access life-saving treatments, and that payers know they're getting their money's worth. We're tremendously excited to be in this business at this moment in time. The potential, both in terms of the market and of bettering human health, is really incredible. ■

Jonathan Retano

CEO & Founder
PHARMAFUSION

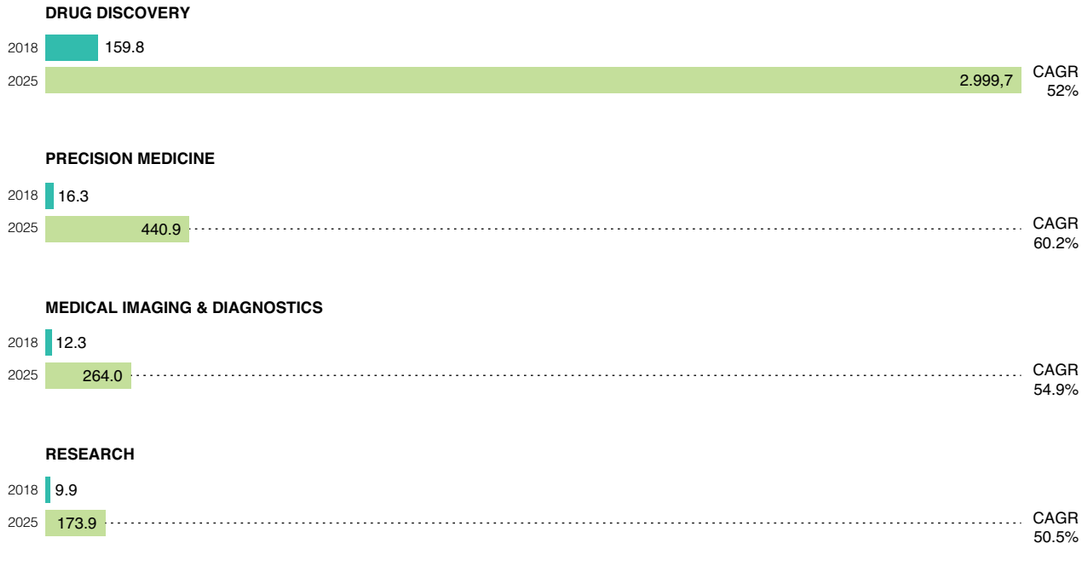
How does Pharmafusion's platform alleviate data problems?
The Pharmafusion platform not only allows for sharing, but also offers a convenience aspect and there is the added benefit of being able to cross-pollenate with other data sets that you might not have thought of doing before. This is why Pharmafusion is called a unified data platform.
The name Pharmafusion 360° was chosen very carefully. Fusion means bringing multiple things into one and we have a 360 degree view of business. What is great about our technology is that it allows for holistic decision making. Once all datasets are unified, a client can see the butterfly effect of how all the data from different departments interact and affect one another Pharmafusion's platform can help companies identify potential issues down the road, much earlier as the data is being unified, synthesized and shared. The platform enables proactive business activities versus reactive business activities. In pharma, too many decisions are made reactively.

Can you give insights into Pharmafusion's client base?
Pharmafusion's client base is mostly pharma manufacturers. The pharma areas we currently operate in include sales and marketing, managed care, clinical, drug monitoring, generics, and factory and trade. I would really like to expand into the space of offering our products to emerging pharma, as they do not have the in-house capabilities of what our platform can offer.

What are Pharmafusion's objectives moving forward?
The goal is to build the brand of Pharmafusion as a best-in-class analytics partner. We are a data, insight and answers analytics company, but at heart, we want to be seen as having a disruptor mentality, stepping outside the bubble.
Concretely, our objective is to continue growing our client base. We aim to hit 20 clients within the next 12 months. We hope to soon have a great marketing engine behind us, whether it is something we fund and build internally or outsource. ■

EXPECTED GROWTH OF THE AI MARKET IN BIOPHARMA BY APPLICATION
MARKET SIZE (USD MILLION)

Source: Deloitte



John Jameson & Debra Webster

JJ

DW

JJ: Senior Scientist, Regulatory Affairs
DW: Director,
Advanced Therapy Medicinal Product Development
CARDINAL HEALTH

How does Cardinal Health Regulatory Sciences fit into the broader strategy of the company and what is the core offering?
DW: Cardinal Health Regulatory Sciences is a business unit in Cardinal Health Specialty Solutions (CHSS), within Cardinal Health, a global integrated healthcare services and products company. CHSS is a significant growth driver of the company. We help develop solutions for our two different consumer groups: biopharmaceutical companies and healthcare providers. The biopharma segment is where Cardinal Health Regulatory Sciences fits in, as drugs become more targeted to treat conditions with smaller populations, biopharma companies need experienced partners, who can help get products to the market faster, ensuring the delivery of products with longer-term viability. We have four business units within the biopharma segment: (1) the Regulatory Sciences group, which helps companies navigate regulatory interactions; (2) the Insights and Engagement group, which helps companies make more informed product strategy decisions using real-world evidence, and delivers precision marketing solutions to support commercialization; (3) the 3PL group, which optimizes the channel across proven distribution options; and (4) the Sonexus™ Access and Patient Support group, which helps to provide comprehensive access and patient support services to allow for patient adherence with some services that are needed for advanced therapies.

What are the most important elements of developing an effective regulatory strategy?
JJ: As part of developing the strategy, it is critical that internal and external stakeholders are strategically aligned in communication. A lot of the issues that we help sponsors deal with in the advanced therapies space occur because of bottlenecks and a lack of strategic alignment internally with how you demonstrate understanding of your product and how you want to communicate that to external stakeholders like investors, health authorities and patient advocacy groups, who can play an important role on the journey to approval.

What are the biggest developments that you are seeing in the advanced therapies area?
DW: The development in gene therapies is rapidly evolving. There are now a plethora of gene modification techniques, so it has become more about selecting the appropriate method based on an understanding of the disease. Additionally, for cellular and engineered cell therapies, there is a shift from the use of autologous to allogeneic cells, which will impact translatability and commercialization. Many advanced therapies will be combinatorial with respect to use of multiple cutting-edge technologies in a single product, such as the use of genetically modified cells grown on a 3D printed scaffold or delivered using specialized devices.
JJ: We are merely scratching the surface of gene editing in terms of capabilities. There is a lot of progress being made in the area of multiplex gene editing and we are seeing new technologies emerge such as CRISPR/Cas platforms using different Cas proteins, as well as base editing techniques that enable precise point mutations while limiting undesired editing byproducts. On the other hand, these advances also create complex nonclinical and manufacturing challenges that need to be considered early on in development.

How has the FDA submission process evolved over time and how can companies best prepare themselves to navigate the approval process?
JJ: Particularly for cell and gene therapies, the technologies can be very novel, and the clinical populations are often rare with poorly understood progression. Rare monogenic disorders can potentially be cured with gene editing, so products targeting these populations require smaller trials and more compressed clinical development. Unlike the typical 3-phase clinical development process, advanced therapies targeting a rare disease often start with a phase 1/2 trial, whereby, if they obtain promising early data, they proceed straight into registrational studies. This means that it is even more critical to be strategically aligned and seek FDA feedback at an early stage.
DW: In the advanced therapies space, there has also been a big shift in FDA's focus for these products on the chemistry, manufacturing, and controls (CMC) side. There is a growing need to get early advice on CMC aspects to avoid roadblocks later in development. Because of the complexities involved in manufacturing these products, it is important to limit manufacturing changes to de-risk your product and keep pace with the other aspects of development. ■

Regulatory Services

A PUSH TO INNOVATE

Regulatory services and compliance departments are not typically known for their technological prowess. However, companies from contract packaging to legal services are now investing heavily in offering state of the art technology that helps clients meet compliance requirements. The pharmaceutical packaging industry has made measurable progress in beefing up its technology capabilities in recent years, due mostly to the passage of the Drug Supply Chain Security Act (DSCSA).

This piece of legislation was implemented to create an electronic system to track and trace prescription drugs in the US. The purpose of DSCSA was threefold: the first priority was verification of the legitimacy of a drug product down to the package level, second was to be able to easily detect illegitimate products in the drug supply chain, and thirdly, the system should aid in a more interoperable supply chain, facilitating more successful drug recall situations and full item traceability.

The solution to complying with these new regulations was a highly technical and specific one and as a result the industry is evolving now that major milestone dates have passed. The pharmaceutical serialization software market has gone from introductory to mature in an incredibly short amount of time.

With a relatively small number of players dominating the industry and the transience of major new opportunity, the industry is now seeing consolidation. According to David DeJean, senior vice president of Systech International, who was acquired by Markem-Imaje in Q1 2020 for their software and integrated solutions capacity: "There are a lot of vendors who were purely focused on regulatory business. The US went live at the end of 2018 and Europe went live at the end of 2019, which resulted in basically 80% of the market share in the world becoming compliant to the regulations. A significant amount of company values were determined based upon a bubble of regulatory compliance. If they did not have something to take them beyond the regulatory business, they were basically lost. Systech has always invested in technologies and innovations, such as fingerprinting, so as not to get lost in this bubble."

One of the factors that distinguish businesses in this highly competitive environment is to offer technology that goes beyond compliance. DSCSA is only focused on the US, therefore, other parts of the world may or may not have similar legislation in place that protects brand integrity. Markets like Sub-Saharan Africa and Southeast Asia have between 20% and

95>>

David DeJean

Senior Vice President
SYSTECH INTERNATIONAL

The World Health Organization (WHO) established that approximately 50% of all drugs on the internet are likely to be counterfeit. Within some of the African markets as much as 20% to 30% of all products are counterfeit.

Can you give an overview of how prevalent counterfeiting and diversion is within the pharmaceutical space?

The current counterfeit estimates for the drug market is over US$200 billion annually. Diverted pharmaceuticals are a significant part of the US$1.7 trillion number that is being thrown around for the gray market on a global commerce level. The World Health Organization (WHO) established that approximately 50% of all drugs on the internet are likely to be counterfeit. Within some of the African markets as much as 20% to 30% of all products are counterfeit. In the pharmaceutical segment the high value, high risk products are the ones that are mostly counterfeited and diverted. We see oncology products that are destined for hospitals in Africa being diverted into high value markets such as the US and Europe.

Can you elaborate on the dangers of counterfeiting and diversion for consumer safety and from a business perspective?

In the US there is the Drug Supply Chain Security Act (DSCSA), where the sole purpose is to keep products within the legitimate supply chain safe. The biggest issue with the DSCSA today is the timeline for implementation. What is implemented today is only serialization of items by manufacturers and sharing data with wholesalers. There is no mandated data integration and visibility throughout the entire pharmaceutical supply chain from manufacturing through to pharmacy. Because of the implementation timelines, it will not be until well after 2023 that we have an 'interoperable' supply chain in the US, with all levels sharing data.

The way the regulation was implemented is that by the end of 2019, all pharmaceutical manufacturers, by law had to be serializing products, as well as providing serialized data into the supply chain. The law then phases in the copackers, then the wholesalers and then the retailers. While we are working on making the supply chain safe, there are still holes where diverted and counterfeit products can slip in.

Taking into consideration the global nature of the supply chain, how do regulations specific to one country solve global issues?

The DSCSA is only focused on the US, as the FDA, who only has responsibility for the US market, controls it. The EU, China, Turkey all have their own regulations which are variants of the same type of policy where you serialize a product, you aggregate it, track it through the supply chain and share data with trading partners, but all have different implementations.

The scary part is that in the worst places in the world, where products are counterfeited 20% to 30%, there are no regulations and there will most likely not be any for a long time to come, as the cost of implementing regulations makes it prohibitive. These parts of the world include South East Asia, sub-Saharan Africa and some South American countries. Here there is a prevalent amount of illicit product and the drug cartels manage it now, because there is so much money in it and so little enforcement. It then becomes the responsibility of the brand to make sure their products are safe. Companies in these regions are starting to implement digital authentication methods, such as our fingerprint technology, which is much cheaper than serialization. This is a way in which brands deliver value and can engage with their customers.

How can Systech's product offerings help big pharmaceutical companies ensure their product quality at a global level?

We focus on three areas of solution offering to our customer base. One is compliance, the second area is the traceability of products, and we also handle expiration information, so if somebody scans a product and it is expired, we can alert them to it. Systech focusses on providing visibility from manufacturing all the way to the consumer's hand. On top of serialization we will provide a unique digital fingerprint to products, which we can authenticate anywhere in the world. In doing this, we provide a layered anti-counterfeiting and diversion technology outside of the regulations. An important feature of the digital fingerprint is that it can be integrated into a product line without the use of additives. ■

Julien Faury

VP Operations
ADENTS

What value proposition does Adents present to its clients?
Our approach is all software based. We provide software, that is not cost prohibitive and that can be instrumental to a company's business. The base subscription incudes all of the regulations and is constantly being updated for new markets and regulations anywhere. That gives clients a huge advantage because it is no longer necessary to spend on new modules every time a new regulation comes in.

How can companies use third party tools for purposes outside of compliance?
Our platforms are valuable in a variety of applications. We just signed a major partnership with a company called JPA, a leading company in warehouse management solutions. Our track and trace technologies have been very important for them, especially for cold chain monitoring. We can detect items that need to be excluded very precisely and have the capacity of making them unavailable to avoid the products from reaching the shelves. We bring value together, because we amass both of our databases and this allows us to better advise our clients.

How has the industry around serialization evolved since 2017?
Traditional actors in packaging are now strengthening their capabilities with serialization companies. In 2013, everyone tried to do their own serialization and they saw that it was more of an IT process than a packaging process, so they did not get very far. Now, the IT companies that succeeded are being bought by the big names in packaging.

What direction is Adents headed in terms of strategy?
We want to be the data management platform for track and trace by enriching our network of partners to interconnect them. With the strengthening of our data and distribution platform, we are confident we have the strongest offering. We work to insure supply chains are accurate and punctual and we want to help pharmaceutical companies deliver their product the best way possible. ■

Shabbir Dahod

President and CEO
TRACELINK

What was the big idea that drove you to found Tracelink a decade ago?
Early on, it was evident that counterfeit drugs posed a huge risk to the security of the supply chain and the safety of patients. TraceLink was founded to help companies in the pharmaceutical supply chain meet critical global compliance requirements and protect patients. We developed the Life Sciences Cloud; a cloud-based, track and trace software that has grown to be the world's largest integrated digital supply network for the life sciences supply chain. Today, TraceLink connects the end-to-end pharmaceutical supply chain, with over 1,280 customers and more than 280,000 trading partners. Now, the journey has continued and TraceLink has been innovating on its decade long vision of enabling an end-to-end pharmaceutical supply chain that allows the whole industry to share information to improve product availability, security and safety.

In terms of product security, how has the industry transformed over the past decade?
A lot of improvement has happened. Information sharing 10 or 11 years ago between players in the pharma supply chain was nil, but now many players across the entire supply chain have expressed an interest in working together to share information about specific products.

What do you see as the next iteration in the development of the industry and solutions Tracelink will provide?
The pharmaceutical supply chain is extremely complex and highly regulated. Digital transformation has been slowly taking place, and supply chain leaders are being forced to rethink the way they operate and adapt to on-going business challenges and unpredictable supply chain disruptions. Manual processes and siloed solutions are simply inadequate and unable to ensure a safe, secure, global drug supply chain, much less one that addresses industry issues such as drug shortages, drug recalls, ingredient availability, and inventory management. Now more than ever, supply chain leaders are looking for more agile, digital supply chain processes to implement. This can all be done at speed and scale using a shared collaborative platform, which TraceLink has. ■

The pharmaceutical supply chain is extremely complex and highly regulated. Digital transformation has been slowly taking place, and supply chain leaders are being forced to rethink the way they operate and adapt to ongoing business challenges and unpredictable supply chain disruptions. Manual processes and siloed solutions are simply inadequate, and unable to ensure a safe, secure, global drug supply chain, much less one that addresses industry issues such as drug shortages, drug recalls, ingredient availability, and inventory management. Now more than ever, supply chain leaders are looking for more agile, digital supply chain processes to implement. This can all be done at speed and scale using a shared collaborative platform.

- Shabbir Dahod, President and CEO, Tracelink

Image courtesy of © 2020 Contract Pharmacal Corp

<<92

30% of their drugs counterfeited according to World Health Organization figures. As a result, global brands shipping products to jurisdictions with few regulations risk brand integrity issues.To ensure this does not become a problem, Systech offers a unique digital fingerprint for products which can be authenticated anywhere in the world. DeJean explained: "We provide a layered anti-counterfeiting and diversion technology outside of the regulations. An important feature of the digital fingerprint is that it can be integrated into a product line without the use of additives."

Legal Compliance

Outside of track and trace and the world of packaging, the legal world is also finding opportunities in technological innovation. Porzio Life Sciences offers a suite of compliance tools and services that help clients comply with HCP laws, regulations, industry codes, and industry standards around the world. "Many companies lack the internal resources to handle reporting, so we have created an easily outsourced service. Even large organizations are looking to us for reporting and to have access to our systems so they can see the data for auditing, monitoring, analytics, and business intelligence. We have been able to become much more involved in dealing directly with our clients' business units, sales forces, and third party vendors to ensure information is accurate and complete. In the past, internal life sciences personnel handled this. Now, Porzio has become an outsourced transparency and aggregate spend office for many companies," said John Patrick Oroho, executive vice president and chief strategy officer of Porzio Life Sciences.

Conclusion

Serialization and legal compliance technologies are the first step towards a move in which compliance solutions are enhanced by new innovations. Those companies looking ahead to the next technologies and offering unique and differentiated platforms that help ease the burden of doing business will be best placed for success in the long term. ■

INDUSTRY OUTLOOK

» The last six to eight years have been great for healthcare and biotech. Underlying that are real secular changes in drug discovery and development. We are reaping the benefits of the genomics boom in the early 2000s, which yielded new drug targets, coupled with many new tools at our disposal to make drugs and to evaluate biology. Overall, the tools and information at our disposal are at a dramatically different place than they were 20 years ago, which has contributed to many transformative new drug approvals and strong capital market performance for the companies delivering those drugs. «

- Michael Gladstone,
Principal,
Atlas Ventures

Image courtesy of Alira Heath

Conclusion

NAVIGATING 2020

Most years never play out exactly the way annual reports predict. There are far too many variables to account for, and inevitably, unforeseen shocks arise. Many had foreseen 2020 as being a strong, yet uncertain year given the presidential election in November and the vilification of pharma on display across political party lines. Even prior to the arrival of COVID-19 on US shores, Gallup polls listed healthcare as the single most important issue for American voters.

The negative rhetoric has now been notched down due to the instrumental role pharma is playing in the fight against COVID-19, however, there are still many significant unknowns lurking around that could impact the state of the US biopharmaceutical industry.

Questions around funding availability for companies developing non-Covid related therapeutics abound. Companies that are pushing drugs through clinical trials must find ways to continue to reach critical inflection points. Yet it will be difficult to amass the data and patient enrollment needed in an environment of social distancing and fear of exposing immunocompromised patients to disease.

Fortunately the industry entered into the COVID pandemic from a position of great strength. Funding has been near all time highs across many therapeutic areas, and FDA approvals remain high. This has created a robust ecosystem of financiers, drug developers, CRO/CDMO's, consultants and technology firms devoting themselves to bringing innovative new therapies to patients.

Working in the industry's favor is the fact that drug development is a long investment cycle business, therefore, most VC's and investors are not willing to pull their money because of short term volatility. There is also an estimated US$1.4 trillion of liquidity on biopharma balance sheets, according to EY. These dynamics should position the industry well in the event of a downturn.

All flaws aside, the industry at its core is about improving patient outcomes and quality of life. In times like this, it is abundantly clear that innovation, speed, and technology will drive breakthroughs that save lives. ■

Francesco Nigris

President and CEO
NICOS GROUP

What insights can you give into Nicos Group's product and service portfolio?

Nicos Group supplies and installs Nicomac modular clean rooms suitable for non-certified and certified (ISO 5 through ISO 8) pharmaceutical areas. We provide complete design and build, project management, construction and installation out of our New Jersey facility. Our hard wall modular clean room system combines the need for a flexible solution with the request for durability and flush surfaces.

In our portfolio of products, we also have LST and LT machines, which are stopper processors that are fully automated, designed to meet the latest cGMP standards. These machines were the first equipment we started to import from Europe to North America. The equipment is used for washing, rinsing, siliconizing, sterilizing, drying, and cooling.

Nicos Group aims to continue its success in a quality driven industry through always adding innovation to our products. Consistency is a key factor for our success. Our strategy is to keep doing things in the right way and continue educating the industry that there are possibilities to do things differently and better than what they are used to. We will continue to be quality driven moving forward. ■

Dr. Thomas Dobmeyer

CEO
PHARMALEX

PharmaLex recently joined ventures with Arbour Group. What inspired this new development, and how will your organization benefit?

We have a strategy combining organic and inorganic growth. Arbour Group is very well-known in computerized systems validation and connected health. We see a trend in pharma going toward automated services, and Arbour Group supports biotech companies in these areas. We want to expand our service offering into this domain and strengthen our foothold in the U.S. Arbour Group has offices in Dubai, as well as in Manila in the Philippines, which is an offshoring location that strengthens our presence in the Asia Pacific region.

In December 2019, we merged with a UK company offering promotional compliance, which is a very highly regulated area, because you need to make sure that the promotional claims are in line with what has been approved and is scientifically sound and compelling. This expands our service offering to the United Kingdom and amplifies our service offering to more downstream commercial areas. In December 2019, we embarked on a joint venture with a strategy consulting group based in the Netherlands. We now have offices close to the European Medicines Agency, which is an advantage. ■

Joe Luke

VP Sales and Marketing
REED-LANE

Can you give an overview of Reed-Lane's expansion into cold storage?

Reed-Lane expanded and added cold storage space, which was validated in 2019. Immediately after, we added a packaging room dedicated for secondary packaging, such as labeling of vials and ampoules next to the cold storage area.

How have the serialization regulations passed a few years ago effected Reed-Lane's business?

We have picked up some business, especially from CMO's who do not have the ability to serialize products. This opens the door for Reed-Lane to then package the product followed by serialization. In some other cases, contract packagers were not ready to implement the serialization and aggregation, which has led to us acquiring new clients. We have a new carton serialization room coming online in 2020.

Has the streamlined FDA process led to an uptick in business for Reed-Lane?

To some extent streamlining of drug approvals has led to an uptick in business. With respect to generic pharma there were GDUFA fees, which were forced onto the industry and downstream into the contract manufacturing and contract packaging companies. Several years ago, Reed-Lane was paying US$ 250,000 in GDUFA fees just to be able to package. The FDA and generic industry realized that these fees were not a good idea and fees are now more manageable. As a result we have seen more activity and business due to this faster approval process. ■

"For consultancy services, price sensitivity is very different. Margins in the US are much higher compared to Europe. The same implant can cost four times the price in the US as compared to Italy. The US is funding research for the entire world. In Europe, the healthcare system is a single-payer system, and the providers are mainly government-owned, which makes the process harder for companies. However, the prices are lower in Europe, so it depends on the perspective. Regarding quality of care, we recently made an abstract for ISPOR, where we show that single-payer is not necessarily better for prevention. The US, not being a single-payer system, is interestingly better for prevention."

- Gabriele Brambilla,
CEO,
Alira Health

"The biggest evolution has been the increased use of expedited pathways. Sponsors can aim to be more proactive and better prepared earlier in product development. Effective engagement with the FDA to address data gaps is imperative to avoiding late-stage development problems. Navigating the regulatory process from concept to approval is best accomplished by advance preparation and effective communication. There is an emphasis on making sure you understand your product, from how it works to demonstrating that you can manufacture it consistently."

- Debra Webster,
Director, Advanced Therapy Medicinal Product Development,
Cardinal Health

"Today's cancer patients face many challenges, including staying on therapy while pursuing a busy lifestyle and family life and financial toxicity brought about by large co-insurance bills. We have been interested in developing drugs that are soluble and can be given orally in order to ease the treatment burden of patients, especially with regard to extensive treatment. At the same time in leukemia, intravenous agents may be more bioavailable compared with oral drugs as the cancer is in the bloodstream. At this time we want fewer patients coming to the hospital because of the COVID-19 pandemic and having a drug available both intravenously and orally may be a flexible solution. Over the long-term this not only increases the value of the drug but may also save costs for the healthcare system by reducing admissions or care provided in the hospital setting."

- Spiro Rombotis,
CEO,
Cyclacel Pharmaceuticals

"Apart from the current COVID-19, there are four major challenges biopharma companies face today. First, a decrease in innovative drug molecules and increase in generic competition. Second, achieving market access and adequate pricing. Third, the demand for transparency and having better educated patients, and last, patient centricity in three different dimensions; first, from a patient care point of view, second, individualized medicine and third, pricing strategy and value-based pricing."

- Dr.Thomas Dobmeyer,
CEO,
PharmaLex

"Proximity to client is a definite advantage, particularly for smaller companies in the earlier stages of development where close contact is a plus. This is another driver for further expansion in the United States – the biggest pool of clients by numbers are the main biotech hubs, but unfortunately there are very few facilities left in these regions."

- Michael Quirmbach,
CEO and President,
CordenPharma Group

"It is critical that we continue to work together with regulators and legislators to foster a system that continues to reward innovation. While strides have been made in recent years, more needs to be accomplished to make sure that there is a rapid path to market of needed therapies while, at the same time, protecting the inventors of these innovative therapies. Intellectual property and long patent lives are critical to recouping the high cost and substantial risk associated with developing new drugs. It may take 10 years or more to get a drug to market and the cost over that period may well exceed US$1 billion. Too often, the patent life a particular drug candidate drives a lot of what companies decide to do with regard to research and development decisions. This is not necessarily the right system for incentivizing innovation. It is not about how long it takes a drug to get to market, it is the period of exclusivity beyond approval that is critical to the success of a product and also its cost structure. The price of drugs varies enormously depending on whether you have two years left on a patent or 10 years."

- Neil S. Belloff,
Chief Operating Officer, General Counsel and Corporate Secretary,
Eloxx Pharmaceuticals

COMPANY/ INSTITUTION	WEBSITE
ASSOCIATIONS	
BioNJ	bionj.org
Biotechnology Innovation Organization (BIO)	bio.org
CPhI	cphi.com
Massachusetts Life Sciences Center	masslifesciences.com
MassBio	massbio.org
NewYorkBIO	newyorkbio.org
BIOTECHNOLOGY & PHARMA	
Abbott	abbott.com
AbbVie	abbvie.com
Advantice Health	advanticehealth.com
Aphios	aphios.com
AstraZeneca	astrazeneca.com
Bayer	bayer.com
Biogen	biogen.com
Bristol-Myers Squibb	bms.com
Cancer Genetics	cancergenetics.com
Celgene	celgene.com
Curis	curis.com
Cyclacel Pharmaceuticals	cyclacel.com
Daiichi Sankyo	daiichisankyo.com
Eli-Lilly	lilly.com
Eloxx Pharmaceuticals	eloxxpharma.com
Gilead Sciences	gilead.com
GlaxoSmithKline	gsk.com
Goldfinch Bio	goldfinchbio.com
Hepion Pharmaceuticals	hepionpharma.com
Hillstream BioPharma	hillstreambio.com
Interna Technologies	interna-technologies.com
Johnson & Johnson	jnj.com
Lonza	pharma.lonza.com
Merck & Co	merck.com
Nivagen Pharmaceuticals	nivagen.com
Novartis	novartis.com
OncoSec	oncosec.com
Pfizer	pfizer.com
Roche	roche.com
Sanofi	sanofi.com
Servier Group	servier.com
Stem Synergy Therapeutics Inc (SSTI)	stemsynergy.com
Takeda Pharmaceuticals	takeda.com
Terran Biosciences	terranbiosciences.com
Tosk	tosk.com
Thermo Fisher	thermofisher.com
Vertex Pharmaceuticals	vrtx.com
XOMA	xoma.com

COMPANY/ INSTITUTION	WEBSITE
ACADEMIC INSTITUTIONS	
Harvard University	harvard.edu
Massachusetts Institute of Technology	mit.edu
Northeastern University	northeastern.edu
Princeton University	princeton.edu
Rutgers University	rutgers.edu
FINANCE	
Atlas Venture	atlasventure.com
Burrage Capital	burragecapital.com
J.W. Childs Associates, L.P.	prospecthillgrowth.com
J.P. Morgan	jpmorgan.com
Signet Healthcare Partners	signethealthcarepartners.com
Third Rock Ventures	thirdrockventures.com
LEGAL & CONSULTING	
Alira Health	alirahealth.com
Decision Resources Group (DRG)	decisionresourcesgroup.com
EY	ey.com
Hart & Chin	hartandchin.com
PharmaLex	pharmalex.com
Porzio Life Sciences	porziolifesciences.com
CONTRACT SERVICES, MANUFACTURING, APIS AND INGREDIENTS	
Avema Contract Services	avemacontractservices.com
Cambrex	cambrex.com
Contract Pharmacal Corporation	cpc.com
CordenPharma	cordenpharma.com
GVK Bio	gvkbio.com
PCI Pharma Services	pciservices.com
Piramal	piramal.com
Sunrise Pharmaceutical	sunrisepharma.com
Reed-Lane	reedlane.com
Visikol	visikol.com
Dr. Reddy's	drreddys.com
SERVICE PROVIDERS	
Adents	adents.com
AiCure	aicure.com
Cardinal Health	cardinalhealth.com
DHL	dhl.com
Systech International	systechone.com
Tracelink	tracelink.com
UPS	ups.com

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

EDITORIAL AND MANAGEMENT TEAM

Project Director: Lucrezia Falcidia (lfalcidia@gbreports.com)
Project Journalist: Jason Spizer (jspizer@gbreports.com)
Project Trainees: Diego Brando (dbrando@gbreports.com),
Maria Filippova Barnachisnkaya (mfilippova@gbreports.com)

Editor: Mungo Smith (mungo@gbreports.com)
Operations Director: Miguel Pérez-Solero (mperezsolero@gbreports.com)
Graphic Design: Gonzalo Da Cunha (gonidc@gmail.com)
Graphic Design (ads): Özgür & Deniz (ozgur@gbreports.com)
General Manager: Alice Pascoletti (apascoletti@gbreports.com)

Your opinion is important to us, please be in touch to share your comments on this report!
For updated industry news from our on-the-ground teams around the world,
please visit our website at gbreports.com, subscribe to our newsletter through our website,
or follow us on Linkedn and Twitter (@GBReports)

THANK YOU

We would like to thank all the executives and authorities that took the time to meet with us.
Also, special thanks to:

CPhI
www.cphi.com

BioNJ
www.bionj.org

MassBio
www.massbio.org

GLOBAL BUSINESS REPORTS